

Abstract

The Effect of Correlation Between Prognostic Factors and Long-Term Mortality in Tongue Cancers

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Objective: The aim of this study was to review demographic data, prognostic factors, and the effect on mortality of patients who were treated for tongue cancer and followed up at our clinic.

Methods: Data between 2000 and 2013 were retrospectively reviewed. This report includes data from 96 patients. Demographic data, dental prostheses, smoking and drinking habits, CVs, tumor characteristics, treatment methods, recurrence, distant metastasis, second primary tumor presence, postoperative survival, imaging techniques, and follow-up dates were reviewed.

Results: According to the Kaplan—Meier survival analysis, the following results were observed: patients whose tumors were recurring and whose lymph nodes were positive in the neck and according to TNM staging; an increase in clinical and pathological T-N phase; and a decrease in survival time in 3, 5, and 10 years (p<0.05).

Conclusion: Tumor stage, histopathological grade, growth pattern, lymph node and distant metastasis, and second primary tumor are important prognostic factors. The identification of tumors at an earlier stage has increased the survival time.

Keywords: Tongue cancer, prognosis, survival time

Introduction

The incidence of head and neck cancer is increasing in many parts of the world. Oral cavity cancer comprises approximately 3% of all types of cancer, and tongue cancer is the most common type of oral cavity cancer (1). Because a reliable epidemiological study has not yet been conducted, it is not possible to give a clear description of this subject in our country. Although head and neck cancer is usually diagnosed in the sixth decade of the patient's life, the prevalence among young patients (younger than 40 years) is increasing (2). Tongue cancer is more common in men; however, due to an increase in tobacco use, some studies have reported that the incidence of tongue cancer has increased among women as well.

90% of the etiological factors of tongue cancer are associated with cigarettes, cigars, pipes, to-bacco use, passive smoking, and alcohol consumption. Human papilloma virus (HPV) is also an infectious agent whose carcinogenic effects have been well proven (3). Other etiological factors are suppression of the immune system due to human immunodeficiency virus (HIV), long-term trauma secondary to the long-term use of inappropriate dentures, and poor oral hygiene.

Squamous cell carcinoma (SCC) represents over 90% of oral cavity and tongue cancer cases (4). Premalignant lesions are classified as leukoplakia, erythroplakia, oral submucosal fibrosis, and oral lichen planus; studies conducted on this subject state that 6.6%—36.4% of premalignant lesions progress to invasive carcinoma within 1.5—8.5 years. Compared to leukoplakia, erythroplakia has a higher risk of malignancy (5).

The tumor stage, histopathologic stage, growth pattern, lymph nodes in the neck and distant metastasis, and classification of the tumor as secondary or primary are important factors in determining the prognosis and survival in neck cancer cases. In cases of squamous cell carcinoma of the tongue, lymph node metastasis in the neck is quite common, and patients clinically diagnosed with non-metastatic lymph nodes in the neck (N0) have a high rate of occult metastasis.

After histopathological diagnosis, for staging, computed tomography (CT) and/or magnetic resonance imaging (MRI) should be performed. Positron emission tomography (PET) is used in the determination of distant metastases in advanced stage disease (6).

The choice of treatment varies depending on the status of the primary tumor and locoregional lymph node involvement. Surgery and radiotherapy (RT) can be applied as primary treatments

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for tongue cancer. Whereas surgery and RT can be applied at early stages, multimodal therapy should be administered for advanced tumors.

In this study, we aimed to statistically evaluate the demographic information of tongue cancer patients who have been treated and followed up; we also aimed to evaluate the prognostic factors and the effects of these factors on survival.

Methods

In our clinic, the files of 96 patients who were diagnosed with tongue cancer and afterwards treated and followed up between the years 2000 and 2013 were examined retrospectively. According to the information from the files of 96 patients that could be accessed, in their medical history, the patients' demographic information, such as gender, age, dental history, history of smoking and alcohol consumption, and personal background were investigated; also, the tumor location, surgical intervention, relapse zone and incidence time, distant metastasis and presence of secondary malignancy, postoperative survival, and follow-up periods were examined. When the clinical and pathological N stages were compared, 46.1% false positivity and 18.1% false negativity were found. Accordingly, for clinical examination of the neck, the specificity was calculated to be 85.7% and the sensitivity was calculated to be 46.6%. Of the 96 patients who were diagnosed in our clinic, 19 patients completed their treatment in other clinics. The treatment and follow-up processes of these 19 patients were discussed via telephone; thus, they were included in the study.

Statistical analysis

Data analysis was performed using SPSS for Windows 11.5 (Statistical Package for the Social Sciences ver. 10.0, SPSS Inc.; Chicago, Illinois, USA). The statistical significance of the effects of categorical factors on overall survival was evaluated using the log-rank test and Kaplan-Meier survival analysis. For each variable, the 3 to 5-year and 10-year survival rates, the average survival time, and 95% confidence intervals for this period were calculated. The statistical significance of the effect of age on the overall survival rate was assessed using univariate Cox proportional hazard regression analysis. In addition, the age-related relative risk and 95% confidence intervals were calculated.

To examine the effects of the variables that were found to have an impact on overall survival as a result of univariate statistical analysis and the effects of risk factors that were considered to be clinically effective, multivariate forward elimination Cox proportional hazard regression analysis was used. Variables identified as p<0.10 in the univariate analysis were included in the multivariate model as candidate risk factors.

For p<0.05, the results were considered statistically significant. Written patient consent was obtained from patients who participated in this study.

Results

Of the patients, 53 were male (55.2%) and 43 were female (44.8%); the male/female ratio was 1.2/1. The youngest patient was 19 years old and the eldest was 86 years old; the average age was calculated to be 57.1. Eleven patients (11.5%) were under 40 years

of age. Smoking, alcohol, dental prostheses, and poor oral hygiene were identified as predisposing factors.

Preoperative biopsy results of 96 patients were reported as 87 SCCs (90.6%), 3 adenoid cystic carcinomas (3.1%), 3 verrucous carcinomas (3.1%), 1 malignant epithelial tumor (1.1%), 1 mucinous cyst (1.1%), and 1 marginal zone lymphoma (1.1%). We found that 19 patients received treatment and underwent follow-up procedures at other clinics. Of those 19 patients, it was found that 16 patients had SCCs, 1 had verrucous carcinoma, 1 had lymphoma, and 1 had adenoid cystic carcinoma. Seventy-seven patients underwent operations in our clinic; the patients who did not undergo operations were referred to radiation and medical oncology clinics for RT and/or chemotherapy (CT). In our clinic, partial glossectomy and hemiglossectomy surgeries were performed on the patients. Of the postoperative histopathological diagnoses, 67 were SCCs (87.0%), 3 were adenoid cystic carcinomas (3.9%), 1 was low-grade mucoepidermoid carcinoma (1.3%), and 1 was verrucous carcinoma (1.3%). While the preoperative diagnosis of five patients was reported to be SCC, no tumor was observed in the remaining tissue after excision of the mass by excisional biopsy (6.5%). For the closure of postoperative defects, the primary closure method was used in most cases (n=47); however, in some cases, the repairs were conducted with sternocleidomastoid muscle (n=3), pectoralis major muscle flap (n=3), split thickness graft (n=22), or free flap (n=2).

After the tumor was removed perioperatively, cryosection pathology from the surgical margins was studied, and negative surgical margins were obtained. Postoperative histopathologic reports showed that 7 patients (9.1%) had tumor continuity on the surgical margins, 1 (1.3%) had a focus of carcinoma *in situ*, and 3 (3.9%) had dysplasia. Twelve patients (15.5%) were reported to have perineural invasion, and 1 patient (1.2%) was reported to have lymphovascular invasion. These patients were transferred to radiation oncology and medical oncology clinics upon consultation.

64 patients underwent neck dissection, 52 patients underwent ipsilateral supraomohyoid dissection, 11 patients underwent bilateral supraomohyoid dissection, and 1 patient underwent radical neck dissection.

The patients were evaluated with the TNM staging system.

The numerical distribution and survival percentages based on the stages of the patients are shown in Table 1.

The numerical distribution of the patients based on the T stage is shown in Table 2.

The numerical distribution of the patients based on the N stage is shown in Table 3.

Table 1. Numerical distribution and survival percentages of the patients according to stage

| | Number of cases | Total (%) | Number of patients who died | Survival (%) |
|---------|-----------------|--------------|-----------------------------|-----------------|
| Stage 1 | 18 | 21.7 | 3 | 61.1 |
| Stage 2 | 20 | 24.1 | 2 | 60.0 |
| Stage 3 | 6 | 7.2 | 0 | 16.7 |
| Stage 4 | 10 | 12.1 | 6 | 30.0 |

| Table 2. Numerical distribution of the patients according to T staging | | | | | | | | | |
|--|----------|-----------|-----------|----------|----------|---------------|-------------|--|--|
| | Tx n (%) | T1 n (%) | T2 n (%) | T3 n (%) | T4 n (%) | Unknown n (%) | Total n (%) | | |
| Clinical staging | 0 | 42 (43.8) | 37 (38.5) | 6 (6.2) | 1 (1.1) | 10 (10.4) | 96 (100) | | |
| Radiological staging | 3 (3.1) | 35 (36.5) | 39 (40.6) | 6 (6.2) | 2 (2.1) | 11 (11.5) | 96 (100) | | |
| Intraoperative staging | 0 | 29 (35) | 35 (42) | 6 (7.3) | 2 (2.4) | 11 (13.3) | 83 (100) | | |
| Pathological staging | 5 (6) | 28 (33.8) | 38 (45.8) | 4 (4.8) | 1 (1.2) | 7 (8.4) | 83 (100) | | |
| n: number of patients; T: anatomical size | | | | | | | | | |

| Table 3. Distribution of patients according to N staging | | | | | | | | |
|--|-----------|-----------|----------|----------|---------------|-------------|--|--|
| | N0 n (%) | N1 n (%) | N2 n (%) | N3 n (%) | Unknown n (%) | Total n (%) | | |
| Clinical | 67 (69.8) | 14 (14.5) | 4 (4.2) | 1 (1.1) | 10 (10.4) | 96 (100) | | |
| Radiological | 57 (59.3) | 18 (18.8) | 7 (7.3) | 3 (3.2) | 11 (11.4) | 96 (100) | | |
| Intraoperative | 45 (54.2) | 19 (22.9) | 8 (9.7) | 1 (1.2) | 10 (12) | 83 (100) | | |
| Pathological | 44 (68.8) | 7 (11) | 6 (9.3) | 3 (4.7) | 4 (6.2) | 64 (100) | | |
| n: number of patients; N: lymph node involvement | | | | | | | | |

| Table 4. Comparison of clinical N stage with pathological N stage | | | | | | | |
|---|-----------------|-----------------|-------|--|--|--|--|
| | Pathological N0 | Pathological N+ | Total | | | | |
| Clinical N0 | 36 | 8 | 44 | | | | |
| Clinical N+ | 6 | 7 | 13 | | | | |
| N: lymph node involvement | | | | | | | |

| Table 5. Localization of recurrence | | | | | | |
|-------------------------------------|-----------------|---------|--|--|--|--|
| | Number of cases | Total % | | | | |
| Tongue | 10 | 37.0 | | | | |
| Neck | 7 | 26.0 | | | | |
| Tongue and neck | 10 | 37.0 | | | | |
| Total | 27 | 100.0 | | | | |

| Table 6. Assessment of the effects of demographic and clinical characteristics on overall survival using univariate Kaplan-Meier survival analysis | | | | | | | | |
|--|---|--------|---------|----------------------------------|----------|-------|--|--|
| Survival rate % | | | | | | | | |
| Variable | 3-year | 5-year | 10-year | Average life expectancy (%95 GA) | Log-rank | р | | |
| Gender | | | | | 1.11 | 0.293 | | |
| Male (n=49) | 78.0 | 73.1 | 50.9 | 102.5 (82.9–122.0) | | | | |
| Female (n=34) | 96.7 | 85.6 | 64.2 | 105.9 (86.5–125.3) | | | | |
| History of smoking | | | | | 0.79 | 0.675 | | |
| Non-smoker (n=30) | 96.3 | 83.5 | 60.1 | 111.3 (86.0–136.6) | | | | |
| Quit (n=11) | 80.8 | 80.8 | 0.0 | 92.9 (62.1–124.0) | | | | |
| Smoker (n=28) | 73.3 | 73.3 | U | 85.8 (68.4–103.1) | | | | |
| History of alcohol consum | ption | | | | 1.84 | 0.175 | | |
| No (n=35) | 90.6 | 85.5 | 69.5 | 116.4 (95.7–137.2) | | | | |
| Yes (n=13) | 67.3 | 67.3 | U | 79.5 (49.0–109.9) | | | | |
| Recurrence | | | | | 7.55 | 0.006 | | |
| No (n=53) | 91.9 | 83.9 | 78.9 | 123.3 (107.8–138.8) | | | | |
| Yes (n=27) | 70.4 | 62.5 | 29.2 | 76.4 (53.6–99.2) | | | | |
| General | 85.3 | 78.0 | 56.0 | 107.6 (92.5–122.7) | • | - | | |
| n: number of patients; CI: confi | n: number of patients; CI: confidence interval; U: uncalculated | | | | | | | |

The numbers of patients classified with clinical N0, N+ and pathological N0, N+ are shown in Table 4.

With regard to differentiation, 43.3% of patients with N0 were moderately differentiated, 20.9% were well differentiated, and 2.9% were less differentiated.

Among the patients who underwent glossectomy and neck dissection, the relapse rate was found to be 36.3%. The earliest metasta-

sis in the tongue and neck occurred after 2 months, and the latest metastasis occurred 10 years later (Table 5). Tumor excision and neck dissection revision surgeries were performed as relapse treatments. The patients were given RT in consultation with radiation oncology.

When the multiple primary tumors (second primary tumors) of our patients who were diagnosed with tongue cancer were investigated, it was found that one patient had a simultaneous primary

Table 7. Assessment of the effects of demographic and clinical characteristics on overall survival using univariate Kaplan-Meier survival analysis, continued

| | | Survival rate % | | | | | | |
|-----------------------------------|---|-----------------|---------|----------------------------------|----------|--------|--|--|
| Variable | 3-year | 5-year | 10-year | Average life expectancy (95% GA) | Log-rank | р | | |
| Differentiation | | | | | 4.50 | 0.105 | | |
| Less (n=1) | 100.0 | 100.0 | U | U | | | | |
| Moderate (n=11) | 72.7 | 48.5 | 48.5 | 87.0 (49.7–124.3) | | | | |
| Well (n=30) | 92.6 | 86.0 | 86.0 | 111.6 (96.2–127.0) | | | | |
| Neck dissection | | | | | 0.01 | 0.913 | | |
| No (n=23) | 81.0 | 69.4 | 69.4 | 82.8 (65.3–100.4) | | | | |
| Yes (n=59) | 86.9 | 80.8 | 52.0 | 106.1 (88.3–123.9) | | | | |
| LAP | | | | | 13.11 | 0.0003 | | |
| No (n=42) | 95.2 | 87.1 | 55.1 | 115.3 (96.3–134.4) | | | | |
| Yes (n=13) | 45.4 | U | U | 28.2 (15.2–41.2) | | | | |
| Surgery margin | | | | | 3.51 | 0.061 | | |
| No (n=58) | 88.2 | 81.9 | 58.2 | 113.5 (95.5–131.5) | | | | |
| Yes (n=9) | 58.3 | 58.3 | U | 63.2 (29.0–97.4) | | | | |
| n: number of patients; CI: confid | n: number of patients; CI: confidence interval; U: uncalculated; LAP: lymphadenopathy | | | | | | | |

Table 8. Assessment of the effects of clinical T and N stages on overall survival using univariate Kaplan-Meier survival analysis

| analysis | | | | | | |
|----------------------------|---------------------------|-----------------------|----------------------|----------------------------------|----------|---------|
| | | Survival rate % | | | | |
| Variable | 3-year | 5-year | 10-year | Average life expectancy (95% CI) | Log-Rank | р |
| Clinical T stage | | | | | 39.81 | < 0.001 |
| T1 (n=37) | 90.9 | 80.5 | 80.5 | 123.1 (104.6–141.6) | | |
| T2 (n=31) | 89.2 | 89.2 | U | 89.2 (71.5–106.8) | | |
| T3 (n=6) | 62.5 | 62.5 | 0.0 | 73.8 (20.3–127.3) | | |
| T4 (n=1) | 0.0 | - | - | 5.0 (5.0–5.0) | | |
| Clinical N stage | | | | | 39.00 | < 0.001 |
| N0 (n=59) | 88.8 | 85.4 | 77.6 | 122.7 (107.5–137.9) | | |
| N1 (n=12) | 88.9 | 76.2 | 50.8 | 86.2 (51.8–120.6) | | |
| N2 (n=3) | U | U | U | 5.7 (3.7–7.6) | | |
| N3 (n=1) | 100.0 | 100.0 | 0.0 | 113.0 (113.0–113.0) | | |
| n: number of patients; CI: | confidence interval: U: ເ | ıncalculated: T: anat | omical size: N: lvmp | oh node involvement | | |

Table 9. Assessment of the effects of pathological T and N stages on on overall survival using univariate Kaplan-Meier survival analysis

| | | Survival rate % | | | | |
|-----------------------------------|------------------|-------------------------|--------------------|----------------------------------|----------|-------|
| Variable | 3-year | 5-year | 10-year | Average life expectancy (95% CI) | Log-Rank | р |
| Pathological T stage | | | | | 15.65 | 0.003 |
| Tx (n=4) | 100.0 | 100.0 | 100.0 | U | | |
| T1 (n=26) | 95.6 | 80.3 | 68.8 | 116.9 (92.3–141.5) | | |
| T2 (n=32) | 88.7 | 88.7 | U | 96.4 (81.5–111.4) | | |
| T3 (n=4) | 50.0 | 50.0 | 0.0 | 59.5 (0.0–123.7) | | |
| T4 (n=1) | 0.0 | - | - | 11.0 (11.0–11.0) | | |
| Pathological N stage | | | | | 14.32 | 0.002 |
| N0 (n=40) | 97.5 | 88.8 | 74.9 | 123.7 (106.3–141.2) | | |
| N1 (n=6) | 75.0 | U | U | 38.7 (23.0–54.4) | | |
| N2 (n=6) | 50.0 | U | U | 30.5 (11.4–49.6) | | |
| N3 (n=3) | 33.3 | 33.3 | 0.0 | 41.7 (0.0–111.6) | | |
| n: number of patients; CI: confid | ence interval; U | uncalculated; T: anaton | nical size; N: lyr | nph node involvement | | |

Table 10. Assessment of the effects of all possible risk factors that are considered to have an impact on overall survival according to multivariate prospective eliminated Cox proportional hazard regression analysis

| Variable | Relative risk | 95% confide | Wald | р | | | |
|----------------------|---------------|-------------|-------------|-------|-------|--|--|
| | | Lower limit | Upper limit | | | | |
| LAP | 8.876 | 2.083 | 37.819 | 8.716 | 0.003 | | |
| Recurrence | 4.754 | 1.493 | 15.138 | 6.960 | 0.008 | | |
| LAP: lymphadenopathy | | | | | | | |

tumor (simultaneously detected tumor) in the larynx, and one patient had a simultaneously detected primary tumor in the palate region. One patient had metachronous primary tumors (tumors detected later than six months) in the buccal mucosa and in the palate region, one in the lower lip, one in the retromolar region, one in the soft palate, one in the larynx, and one in the lung. In total, multiple primary tumors were seen in 8 patients, and the incidence of multiple primary tumors was calculated to be 8.3%.

During distant metastasis screening, it was detected that three patients underwent treatment for skin permeation metastasis, three patients for lung metastasis, one patient for bone and lung metastasis, one for brain metastasis, and one for liver metastasis.

In accordance with the data gathered from the files that was suitable for statistical analysis, the demographic information of the patients and the effects of their clinical characteristics on both their survival rates and average life expectancies are also summarized in Tables 6-9.

When this data was evaluated by Kaplan-Meier analysis, in cases where cancer relapse occurred, it was determined that the 3, 5, and 10-year survival rates and average life expectancy were significantly lower and were statistically significantly different from those of patients who did not experience relapse (p<0.05).

In neck dissection, it was determined that the 3, 5, and 10-year survival rates and average life expectancy of lymphadenopathy (LAP)-positive patients were statistically significantly lower than those of LAP-negative patients (p<0.05).

When TNM staging was examined, as the clinical and pathological T-N stages increased, the 3, 5, and 10-year survival rates showed statistically significant decreases (p<0.05).

In Table 10, considering the effects of multiple variables of all risk factors, it was shown that the negative effects of relapse and LAP positivity on survival were statistically significant (p<0.05).

Discussion

Tongue cancer is more common among males in the fifth and sixth decades of life. Recent studies conducted on patients under the age of 40 have shown an increased incidence of oral cavity and tongue cancers (4). In line with the literature, male patients in their fifth and sixth decades formed the majority in our study as well. Because a reliable epidemiological study has not been conducted in our country, it is not possible to present clear information in this regard. However, the proportion of patients under the age of 40 (11.5%) which was determined in our study supports the

fact that the risk of tongue cancer among younger patients has significantly increased.

Although smoking and alcohol consumption are frequently cited etiologic factors for tongue cancer, inappropriate dental prostheses are also a significant factor. In our clinic, of the 67 patients diagnosed with SCC, it was found that 16 patients (23.9%) had dental prostheses; 9 of these patients (56.3%) were non-smokers and did not consume alcohol. Although it is not possible to perform a clear evaluation due to a lack of sufficient data, it was found that improper dental prostheses and poor oral hygiene are also factors for tongue cancer.

In the literature, it is reported that more than 90% of oral cavity and tongue malignancy cases are located in the squamous epithelium; 10% occur in minor salivary gland cells, and only a small portion are rarer tumors such as lymphoma and sarcoma (7). The postoperative histopathologic diagnosis of our patients was 87% (n=67) SCC, while 13% (n=10) were identified as other types of cancer; this is consistent with the literature.

The degree of tumor differentiation in tongue cancer has a significant impact on prognosis and survival. Tumor differentiation is expressed by similarity to the tissue of origin. Tumors are grouped as well differentiated (grade 1), moderately differentiated (grade 2), less differentiated (grade 3), and anaplastic or undifferentiated (grade 4). In a study conducted on this subject, it was reported that as differentiation decreases, negative effects are observed on survival rate, lymph node metastasis, and prognosis (8). In a study conducted in our country on 50 patients, 70% well-differentiated, 26% moderately differentiated, and 4% less-differentiated patients were reported; when their average survival rates were compared, the results were not found to be statistically significant (9). In another study conducted in our country, it was reported that as tumor differentiation increases, life expectancy decreases; no significant difference was shown between well-differentiated tumors and moderately and less-differentiated tumors (10). Our study also supports that as differentiation decreases, the average life expectancy of patients decreases.

After tongue SCC resection, the presence of perineural invasion (PNI) and deep locoregional invasion metastasis, tumor positivity at the surgical margins, and close surgical margins are poor prognostic factors (11). Tongue cancers are tumors that frequently show recurrence within the first year. The presence of tumor tissue at the surgical margin after glossectomy increases the chance of relapse (12). In a retrospective study on 192 patients conducted by Wong et al. (13), positive surgical margins were reported to be associated with local recurrence; 12% of patients were reported to have positive surgical margins, and 55.7% were reported to have close surgical margins (1–5 mm). In our postoperative histopathology reports, it was reported that 7 (9.1%) of our patients had surgical margin positivity, 1 patient (1.3%) had carcinoma in situ at the surgical margin, and 1 patient (1.3%) had dysplasia. Of those patients, six received postoperative RT±CT, and one patient had relapse after receiving combination therapy. In a study on recurrence, it was reported that the total recurrence was 27%-40%; recurrence in the primary tumor zone was 9%-24%, recurrence in the neck was 9%-16%, and the average recurrence time was determined to be 11.5 months (14). According to the study conducted in our clinic, locoregional recurrence cases were detected after 2 months at the

earliest and after 10 years at the latest; 37% of recurrence was in the tongue, 26% was in the neck, and 37% was in the in tongue and neck. After recurrence was detected, tumor resection and neck dissection were performed; patients were referred to medical and radiation oncology departments for postoperative RT±CT.

TNM classification is used in planning treatment, determining prognosis, and assessing treatment outcomes. Anatomical size is classified with (T), lymph node involvement with (N), and distant metastasis with (M). Advanced stage is a poor prognostic factor. An increase in the N stage has an even more significant impact on prognosis. In addition to the presence of lymph node metastases, histopathological parameters such as tumor differentiation, depth of invasion, tumor thickness, and presence of perineural invasion should also be evaluated (15, 16). In a study conducted by Yılmaz et al. (10), the 3-year disease-free survival rate for T1-2 tumors was reported as 78.8%, and that for T3-4 tumors was 54.5%. In yet another study in our country, disease-free survival rates were reported as 18% for early stage tumors and 15% for advanced stage tumors (17). Our study comprised mostly stage 2 patients, with a survival rate of 24.1%. The highest survival rate, in stage 1 patients, was 61.1%, however, in stage 4, this rate decreased to 30.0%. These findings are consistent with the literature.

Yılmaz et al. (10) detected 65.2% N0 in T1-T2 stage patients and 27.3% N0 in stage T3-T4 patients. In our study, the N0 rate in T1-T2 stage patients was determined to be 83.5%. In advanced stage T3-T4 patients, the N0 rate was 42.9%. It was reported that T1 stage patients had no neck metastases. As the stage advanced, the rate of metastasis increased; 7.1% of stage 2 patients, 28.7% of stage 3 patients, and 57.2% of stage 4 patients experienced metastases. Consistent with the literature, these results supported that N0 rates in the T1 and T2 stages were higher than in advanced stage tumors.

It is known that positive lymph nodes in the neck significantly reduce survival. In a study conducted by Capote et al. (18), it was reported that both the 5-year local control and survival rates were higher in patients who underwent elective neck dissection compared to those who did not (71.2%). In the study, it was clear that due to neck metastases in approximately 40% of stage 1 and 2 tongue cancer patients, elective neck dissection is considered to be preferable to the wait and see approach (19).

In a study conducted in our country, it was determined that the false negativity rate in intraoperative N staging was 29.3%, and the false positivity rate was 48.8%. The intraoperative N staging sensitivity was determined to be 76.5%, and the specificity was 51.2%; furthermore, it was claimed that all preoperatively performed examinations failed to completely exclude lymph node metastases, and elective neck dissection was recommended even in early stage patients (20, 21). Also, in the study conducted by Yılmaz et al. (10), 65.9% of patients were reported as clinically N0, 55.7% were pathologically N0, and 44.3% were pathologically N+. When these results are analyzed together, it is clear that elective neck dissection is superior to the "wait and see" approach.

In our clinic, out of 67 N0 patients, glossectomy and elective neck dissection were performed simultaneously on 45 patients, and 22 patients only underwent glossectomy. It was reported that due to relapse in the primary zone, lymph nodes in the neck, or distant

metastasis, 9 (20%) of 45 patients who underwent tumor resection and neck dissection simultaneously received a second treatment; of the remaining 22 patients, 8 (36.3%) patients received a second treatment. It was found that in the first year of our clinic, the wait and see approach for N0 neck patients were preferred; however, in literature reports worldwide, when occult metastasis, recurrence rates, and tumor approaches are considered, simultaneously performed tumor resection and elective neck dissection are currently recommended.

The extent of metastatic disease is another prognostic factor (22). It was determined that the disease-free survival period decreased by 27% in the presence of single lymph node metastasis, by 74% in the presence of three or more lymph node metastases, and by 83% in the presence of extracapsular invasion. Furthermore, it is believed that when preparing a treatment plan for tongue cancer patients and determining which patients require more radical treatment, in addition to the TNM stage, a detailed evaluation of histopathological parameters may contribute to the prolongation of the disease-free survival period (23). In our study, the rate of one single lymph node metastasis case was 9.4%, the rate of two metastatic lymph node cases was 7.8% with a bilaterality rate of 3.2%, and the rate of 3 metastatic lymph node cases was 1.6%; consistent with the literature, as the number of metastatic lymph nodes increased, the survival rate was found to decrease.

In their study, Hicks et al. (14) reported the incidence of distant metastases as 4% and the average metastasis period as 3–127 months. The metastases of lung, bone, brain, liver, and skin permeation were diagnosed within approximately one year. In one study, due to the high risk of recurrence, distant metastasis, and second primary tumor, it is emphasized that patients should be followed for at least five years (24).

To study the postoperative follow-up of the patients, the files of 96 patients were screened retrospectively; the patients for whom file searches could not be completed were contacted by telephone. According to data that we obtained in 2013, 43 patients were still alive, and 18 patients had passed away. Thirty-five patients could not be reached.

Of 84 patients who came to the follow-up sessions, the shortest follow-up period was 2 months, and the longest follow-up period was 146 months. The average follow-up period of these patients was found to be 39.4 months.

Conclusion

To determine the prognosis and survival of tongue cancer cases, tumor stage, histological grade, growth pattern, the presence of lymph node metastasis in the neck, the presence of distant metastasis, and the presence of secondary primary tumor are important factors. Because the presence of these factors indicates poor prognosis, early stage diagnosis improves disease-free survival in tongue cancer cases.

Ethics Committee Approval: Ethics committee approval was not received due to the retrospective nature of this study.

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

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References

- Kademani D, editor Oral cancer. Mayo Clinic Proceedings; 2007: Elsevier.
- Gillison ML. Current topics in the epidemiology of oral cavity and oropharyngeal cancers. Head & neck 2007; 29: 779-92. [CrossRef]
- Machado J, Reis PP, Zhang T, Simpson C, Xu W, Perez-Ordonez B, et al. Low prevalence of human papillomavirus in oral cavity carcinomas. Head Neck Oncol 2010; 2: 6. [CrossRef]
- Gorsky M, Epstein JB, Oakley C, Le ND, Hay J, Stevenson-Moore P. Carcinoma of the tongue: a case series analysis of clinical presentation, risk factors, staging, and outcome. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2004; 98: 546-52. [CrossRef]
- Jaber MA. Oral epithelial dysplasia in non-users of tobacco and alcohol: an analysis of clinicopathologic characteristics and treatment outcome. Journal of oral science 2010; 52: 13-21. [CrossRef]
- Werning JW. Oral cancer: diagnosis, management, and rehabilitation: Thieme; 2007.
- Başerer N. Oral Kavite Kanserleri In: Engin K, Erişen L. Baş-Boyun Kanserleri 1: 237-70.
- Jin WL, Ye WM, Zheng JW, Zhou L, Zhu HG, Zhang ZY, et al. Occult cervical lymph node metastases in 100 consecutive patients with cN0 tongue cancer. Chin Med J (Engl) 2008; 121: 1871-4.
- Sanoğlu T, Yilmaz T, Gürsel B, Sungur A. The effect of lymphocytic infiltration on clinical survival in cancer of the tongue. European archives of oto-rhino-laryngology 1994; 251: 366-9. [CrossRef]
- Yılmaz T, Ünal F, Saraç S, Yücel T, Önerci M, Turan E, et al. Dil kanseri:
 88 hastanın deneyimi. KBB ve Baş Boyun Cerrahisi Dergisi 1999; 7:
 213-8.
- Süslü N, Hoşal AŞ, Aslan T, Sözeri B, Dolgun A. Carcinoma of the Oral Tongue: A Case Series Analysis of Prognostic Factors and Surgical Outcomes. Journal of Oral and Maxillofacial Surgery. 2013.

- Girardi FM, Zanella VG, Kroef RG. Correlation between clinical and pathological data and surgical margins in patients with squamous cell carcinoma of the oral cavity. Braz J Otorhinolaryngol 2013; 79: 190-5. [CrossRef]
- 13. Thake M, Kalantzis A. Excision margins in squamous cell carcinoma of the tongue: A retrospective audit and review of the literature. 2013.
- Hicks Jr WL, North Jr JH, Loree TR, Maamoun S, Mullins A, Orner JB, et al. Surgery as a single modality therapy for squamous cell carcinoma of the oral tongue. American journal of otolaryngology 1998; 19: 24-8. [CrossRef]
- Haksever M. Oral Kavite Kanserlerinde Evreleme, Prognostik Faktörler ve Evreleme Sistemi Üzerine Değerlendirmeler. 2013.
- Hoşal A, Ünal Ö, Ayhan A. Possible prognostic value of histopathologic parameters in patients with carcinoma of the oral tongue. European archives of oto-rhino-laryngology 1998; 255: 216-9. [CrossRef]
- Uğurluer G, Ozyurt S, Aksaray F, Aslan N, Habiboğlu R, Tümöz M. Prognostic factors and survival rates in oral cavity cancers]. Kulak burun boğaz ihtisas dergisi: KBB= Journal of ear, nose, and throat 2006; 16: 64.
- Capote A, Escorial V, Muñoz-Guerra MF, Rodríguez-Campo FJ, Gamallo C, Naval L. Elective neck dissection in early-stage oral squamous cell carcinoma-does it influence recurrence and survival? Head Neck 2007; 29: 3-11.
- Yuasa-Nakagawa K, Shibuya H, Yoshimura R, Miura M, Watanabe H, Kishimoto S, et al. Cervical lymph node metastasis from early-stage squamous cell carcinoma of the oral tongue. Acta Oto-laryngol 2013; 133: 544-51. [CrossRef]
- Kaya S, Yilmaz T, Gürsel B, Saraç S, Sennaroğlu L. The value of elective neck dissection in treatment of cancer of the tongue. Am J Otolaryngol 2001; 22: 59-64. [CrossRef]
- Kocatürk S, Han Ü, Arıkök AT, Babila A, Önal B. Erken evre (T1-2 N0)
 oral dil kanserlerinde tümör kalınlığının gizli metastaz oranlarına etkisi ve boyuna yaklaşım Kulak burun boğaz ve baş boyun cerrahisi
 dergisi 2004-3(1).
- Shah J, Patel S. Cervical lymph nodes. Head and neck: surgery and oncology, 3rd edn Edinburgh: Mosby. 2003: 353-94.
- Alataş N, Sungur A, Akyol U, Ünal F, Yılmaz T, Kaya S. Dilde epidermoid kanserde histopatolojik parametrelerin prognozla ilişkileri. KBB ve Baş Boyun Cerrahisi Dergisi 2000; 8: 202-10.
- Kerawala CJ, Newlands C, Coombes D. Follow-up after treatment of squamous cell carcinoma of the oral cavity: Current maxillofacial practice in the United Kingdom. Br J Oral Maxillofac Surg 2007; 45: 361-3. [CrossRef]