Oral squamous cell carcinoma—clinical characteristics, treatment, and outcomes in a single institution retrospective cohort study

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ABSTRACT:

Introduction: Squamous cell carcinoma (SCC) is a common malignancy with high morbidity and mortality.

Aim: The aim of this study was to analyze the data of patients treated for malignant tumours of the oral cavity at the Department of Otolaryngology, Head and Neck Surgery, and Laryngological Oncology Ludwik Rydygier Collegium Medicum in Bydgoszcz between 2003–2011 to assess the influence of risk factors on survival in patients with squamous cell carcinoma of the oral cavity.

Material and methods: Material was collected from 62 patients treated for oral SCC between 2003–2011. Forty-three were men (69.35%) with a mean age of 56.33 years. The medical records were analysed, especially history, operative reports, histopathology reports, survival, adjuvant treatment and recurrence.

Results: All patients underwent surgical treatment (33.87% also had partial removal of the lower jaw, 67.74% adjuvant radiotherapy, 11.29% radiochemotherapy). More than half reported to the doctor within 6 to 15 weeks from the onset of symptoms. The majority smoked and drank alcohol (96.32%). Five-year disease specific survival (DSS) was 68.69%.

Conclusions: The age over 65 did not significantly influence DSS. The location on the anterior two thirds of the tongue gave the best outcome, while the worst outcome was observed in the retromandibular triangle area which was statistically almost significant (p = 0.06843). In the case of higher degrees of local and regional advancement and a higher stadium, a worse outcome was recorded. Positive surgical margins were identified in 11.29% of the cases, but they had no impact on the results of treatment. No worsening of the outcome was proven for the patients who reported to the doctor later than 15 weeks following the occurrence of symptoms.

KEYWORDS: head and neck cancer, oral cancer, staging, survival rate, time-to-treatment

ABBREVIATIONS

DSS – disease specific survival
ECS – extracapsular spread
G – grading
HPV – human papilloma virus
SCC – squamous cell carcinoma
TNM – tumor, node, and metastasis classification

INTRODUCTION

Malignant tumors of the oral cavity are a significant diagnostic and therapeutic problem among head and neck conditions. According to epidemiological data, they are relatively rare (5% of all the malignant tumors) but are characterized by high-grade malignancy and are diagnosed in substantially advanced stages [1].

AIM

The aim of the present study was to investigate the clinical characteristics, treatment methods, and prognoses of oral SCC patients at the Department of Otolaryngology, Head and Neck Surgery, and Laryngological Oncology Ludwik Rydygier Collegium Medicum in Bydgoszcz between 2003–2011 in order to assess the influence of prognostic factors on the survival rate of patients. The analyzed factors were: age, location, locoregional progression, stage, histopathology report, multiple lymph node metastases, surgical margin, the time elapsed between the occurrence of symptoms and reporting to the doctor.

MATERIALS AND METHODS

The retrospective analysis was conducted as a study carried out at the Department of Otolaryngology and Laryngological Oncology
with the Subdepartment of Audiology and Phoniatrics CM UMK of the University Hospital nr 1 in Bydgoszcz. The medical records of all patients who had undergone surgery due to oral squamous cell carcinoma from January 2003 to June 2011 were analyzed, with particular emphasis on history, operative reports, histopathology reports, survival time, adjuvant treatment, and recurrence. The stage of cancer was defined using the TNM staging system of the American Joint Committee on Cancer, 6th edition of 2002.

The statistical analysis of data was carried out using the STATISTICA 12 software: log-rank tests for two groups and chi-squared tests for multiple comparisons. A disease specific survival (DSS) analysis was carried out with the Kaplan-Meier curve. Statistical significance was set at $p \leq 0.05$, two-tailed.

**RESULTS**

Among the 62 patients with oral squamous cell carcinoma, there were 43 men (69.35%) with a mean age of 56.33 years, and 19 women (30.65%) with a mean age of 62.58 years. All the patients underwent surgical treatment, and 21 patients (33.87%) also had partial removal of the lower jaw, while 3 patients (4.84%) had half of the lower jaw removed. Forty-two patients (67.74%) underwent adjuvant radiotherapy, 7 patients (11.29%) – radiochemotherapy, and 13 patients (20.97%) did not need any adjuvant oncology therapy. More than half of the patients (33–53.22%) reported to the doctor within 6 to 15 weeks from the occurrence of any symptoms. The most frequent symptoms reported by the patients were as follows: pain (42 patients, 67.74%), tumors and ulceration in the oral cavity (13 patients – 20.97%), neck tumors (4 patients – 6.45%), trismus and pain radiating to the ear (3 patients – 4.84%). Most of the patients in the analyzed group smoked and drank alcohol (56 patients in both groups – 96.32%). In 20 patients (32.26%), the lesion was located on the anterior two thirds of the tongue, in 23 patients (37.10%) in the floor of the oral cavity, and in 19 patients (30.64%) in the retromandibular triangle area.

The degrees of local and regional advancement are presented in Tab. I., and the stages of advancement are presented in Tab. II. The greatest numbers of cases were diagnosed as T2 (29 patients – 46.78%) and N0 cancers (42 patients – 67.74%), and as stage II cancers (22 patients – 35.48%).

In 3 patients (4.84%), cancer with a G1 grade of differentiation was diagnosed, in 59 patients (95.16%) G2 grade cancer was diagnosed. There was no case of G3 grade cancer. Lymph node metastases were diagnosed in 20 patients. The most frequent location was in field 2 (17 patients – 32.26%).

The patients were operated on through the oral cavity. Due to infiltration of the mandible, mandibulectomy was performed in 21 patients (33.87%), out of which partial mandibulectomy was performed in 18 patients (29.3%) and hemimandibulectomy was performed in 3 patients (4.84%). Positive surgical margins were identified in 7 cases (11.29%), and negative in 55 patients (88.71%). Unilateral lymphadenectomy was performed in 45 patients (72.58%) and bilateral lymphadenectomy was performed in 14 patients (22.58%). The total of 3 patients did not have lymph nodes removed.

Radical surgery of lymph nodes was performed in 2 patients (3.22%) due to multiple lymph node metastases and infiltration of structures other than lymph nodes (muscles, vessels, nerves), and in other cases selective surgery was performed (57 patients – 96.61%). Intraoperative tracheostomy was necessary in 41 cases (66.13%). Forty-two patients (67.74%) were qualified for postoperative radiotherapy, 7 patients (11.29%) for radiochemotherapy, and 13 patients (20.97%) did not receive any adjuvant oncologic treatment.

Local recurrences were diagnosed in 9 patients, lymph node recurrences in 7 patients, local and lymph node recurrences in 7 patients, and no recurrence was diagnosed in 39 patients (62.90%). Complications of surgical treatment were infrequent (8.78%), and they included local hematomas, wound dehiscence, and bleeding.

The highest decrease in the predicted survival time was recorded within the first 24 months following surgery, and 5-year DSS was 68.69%. Subsequently, the predicted survival time of the patients was analyzed, taking into account the selected prognostic factors, i.e., age, location, advancement, histopathology report, survival time, adjuvant treatment, and recurrence. No statistically significant differences were identified ($p = 0.548$) between the groups of patients below the age of 65 and those aged 65 years or more. As far as the analysis of survival times depending on location is concerned, certain differences were identified, but they were not statistically significant ($p = 0.068$). As regards the degree of local advancement, i.e., the T category, patients suffering from higher stage cancer had worse prognoses, but the results were not statistically significant ($p = 0.250$). On the other hand, in the case of the degree of regional advancement (N category), high statistical significance was proved ($p = 0.001$) for the predicted survival times of patients.

Having assessed the stage of advancement, differences were identified, but the results were not statistically significant ($p = 0.096$).
In the group of patients with G1 well-differentiated squamous cell carcinoma, a worse survival rate was confirmed in comparison with G2 moderately differentiated carcinoma, but the G1 group was disproportionately small (3 patients) (p = 0.452).

Having compared the patients with a single metastasis to lymph nodes with the group of patients with multiple metastases, a statistically significant difference and a worse survival rate were revealed in the case of patients with multiple metastases (p = 0.012). The positive surgical margin made the prognoses worse, but with no statistical significance (p = 0.278).

Moreover, patients who reported to the doctor later than 15 weeks following the occurrence of symptoms had worse prognoses, but, similarly, the results were not statistically significant (p = 0.701).

**DISCUSSION**

Oral squamous cell carcinoma is more frequent in men [1], and in this study the percentage of men suffering from this cancer was nearly 70%. The average period of time between the occurrence of symptoms and the date of reporting to the doctor was 6–15 weeks. The most frequent symptom which persuaded the patients to report to a relevant specialist was pain (almost 70% of the patients). The major carcinogens were ethanol and tobacco smoke, the effects of which multiply if they concur. An additional risk factor of carcinogenesis in the oral cavity is a poor condition of the teeth and poor oral hygiene. According to the literature, HPV infection, especially HPV-16, may increase the risk of floor of mouth, gum, tongue, and palate cancers [2–5]. In the analyzed group, more than 96% of the patients drank alcohol and the same number of patients smoked cigarettes. The cancer was most frequently located in the floor of the oral cavity (37.10%), which coincides with the data presented in the literature [6, 7]. The stage of clinical advancement results from the tumor size and lymph node metastases, and it constitutes an important prognostic factor compared among various centers. According to the analyzed materials, the patients most frequently reported to the doctor with stage III and IV oral squamous cell carcinoma (51.60%). For comparison, according to a Dutch study, in 1989–2006, stages III and IV were recorded in 50.1% of patients, in 42.2% of patients according to an American study as of 2004, and in 92.6% of patients according to a study of the Mexican population in 1997–2012 [8–10]. The treatment of oral squamous cell carcinoma is difficult because of its high aggressiveness, the high degree of advancement upon starting treatment, and low patient awareness. There are a few therapeutic options recommended by scientific institutions and associations, but no research has been carried out to compare them in an explicit way. In general, surgical treatment is preferred [11]. This kind of treatment makes it possible to perform histopathological examination of the tumor tissue, assess the presence of lymph node metastases, extracapsular spread (ECS) and nerve or vessel infiltration, and to assess the resection margins. All these information are crucial for making the decision on undertaking adjuvant treatment: radiotherapy or chemoradiotherapy. If the tumor is small and located in the anterior part of the oral cavity and the tongue, access through the oral cavity is sufficient. In the case of tumors located closer to the root of the tongue or in case of trismus, it is necessary to split the mandible to gain access to the tumor or develop upper cheek, lower cheek or visor flaps. If the tumor is located in the immediate vicinity of the mandible, marginal resection is necessary, and in the case of a suspicion of bone infiltration (clinically immovable tumor attached to the mandible or infiltration visible in imaging tests), it is necessary to perform segmental resection or hemiresection [12, 13]. In patients with cancer in the cN0 stage of regional advancement, i.e., clinically with no regional lymph node metastases, elective surgery of fields 1–3 is recommended, and in the event of suspecting lymph node metastases, lymph node surgery of fields 1–5 is recommended [14]. According to the literature, the treatment preferences are different among different treatment centers. According to the research carried out by Goldenberg, the percentage of patients treated with methods other than surgical and patients receiving palliative treatment increases along with age and stage of advancement [15]. Some authors believe that treatment offered by academic centers involves a higher percentage of surgical procedures and higher five-year survival rates [16]. According to the data obtained from French centers, in early stages (I, II) of squamous cell carcinoma located in the root of the tongue, radiotherapy is applied just as often as surgical procedures [17]. According to an American study, patients with stage I and II oral squamous cell carcinoma received, above all, surgical treatment, patients with stage III carcinoma – surgical treatment followed by radiotherapy, and patients with stage IV carcinoma – surgical treatment followed by chemoradiotherapy [12]. According to the long-term observations by White-Gilbertson, the fact of including chemotherapy- and radiotherapy-based treatment into standard surgery in 2004 increased the five-year survival rate in stage IV oral squamous cell carcinoma [13].

Procedures related to unaffected lymph nodes in early stage cancers (T1/T2) are still disputable as there is no factor which would determine the decision on elective surgery or observation of lymph nodes [18].

According to the literature on the subject, selective surgeries should involve the removal of lymph nodes from fields 1–5, which is connected with the anatomy of lymph flow from the oral cavity [18].

The patients from this study were treated in line with the standards presented above. All the patients underwent surgery of cervical lymph nodes. In the case of unfavorable prognostic factors, such as a high stage of advancement, ECS, infiltration of vessels and nerves, and positive surgical margin, surgical treatment was complemented with radiotherapy or radiochemotherapy (79.06%). The most frequent neck procedure was unilateral selective dissection according to the lesion location. Having analyzed the histopathology reports, it was established that regional metastases were most frequently located in field 2 (77.27%), which coincides with the information provided by relevant literature [18, 19].

Oral squamous cell carcinoma is among cancers with moderate prognosis, and chances of five-year survival are similar to the overall average for the head and neck areas. Poorer prognoses are recorded for malignant tumors of laryngopharynx and the parotid glands, and better prognoses are recorded in the case of lips, nasopharynx, and larynx [1].
According to relevant literature, oral squamous cell carcinoma is most frequently diagnosed in high stages of advancement involving metastases to lymph nodes in the neck [7, 21], which makes the prognoses substantially worse. In this analysis, stages III and IV were recorded in 51.6% of the patients.

The five-year survival rate is 56–79.9% [21, 22]. In the analyzed group, the five-year survival rate was 68.69%.

As far as the patients’ age is concerned, the data provided by relevant literature are inconsistent. Some of the studies indicate worse prognoses in elderly patients [23], while others deny the influence of age on the survival rate [24]. Similarly, in this study, no statistically significant differences were observed in the five-year survival rate of patients aged 65 years or more.

In the analyzed group, the influence of cancer location was not statistically significant (p = 0.06843), however, a location on the anterior two thirds of the tongue gave the best prognoses, and the location in the retromandibular triangle area the worst prognoses, which is confirmed by the literature [20].

A major prognostic factor is local and regional advancement, as well as the lesion volume and infiltration of vessels and nerves [20, 25]. In the analyzed group, worse prognoses were identified in higher degrees of local advancement, but these results were not statistically significant. On the other hand, a considerable interrelation was identified in the case of regional advancement, which significantly worsened the five-year survival rate in statistical terms (but it was statistically insignificant p = 0.09629).

Moreover, the prognoses worsened along with the increase in the stage of advancement, which coincides with the data provided in relevant literature [25].

The degree of histopathological differentiation is a commonly recognized prognostic factor in malignant tumors, and this interrelation is particularly strong in oral squamous cell carcinoma [26]. This study does not confirm this thesis, which may be connected with the inappropriate group size (a definite majority of the patients with G2 moderately differentiated cancer with only three patients with G1 well-differentiated cancer and no patients with G3 poorly-differentiated cancer).

According to the literature, the resection margin should be at least 5 mm for oral squamous cell carcinoma, as a smaller margin predisposes patients to local recurrence [20]. However, post-operative adjuvant radiotherapy leads to the destruction of cancer cells that continue to be in the surgical field, and, hence, there are opinions that positive surgical margins do not substantially worsen the prognoses [27]. In the analyzed group, statistically insignificant differences were identified as regards the five-year survival rates of patients with positive and negative surgical margins.

It has been proven that elective surgery in clinically unaffected lymph nodes in patients with low stages of cancer advancement (T1—T2) improves their prognoses [28]. All the patients from the analyzed groups underwent surgery of cervical lymph nodes.

The study demonstrated worse prognoses for patients waiting for treatment for more than 30–60 days [29], as well as a relationship between a delay in treatment and increased morbidity [29, 30]. In the analyzed group, no worsening of prognoses was proven for patients who reported to the doctor later than 15 weeks following the occurrence of symptoms.

**CONCLUSIONS**

1. An age of 65 years or above did not significantly influence the five-year survival rate of patients with oral squamous cell carcinoma;
2. A location on the anterior two thirds of the tongue gave the best outcome, and the location in the retromandibular triangle area gave the worst outcome, but the results were not statistically significant;
3. A worse outcome was recorded in higher degrees of local advancement (T), but these results were not statistically significant;
4. In higher degrees of regional advancement (N) and higher stages of advancement, statistically significant worse outcome was recorded;
5. Positive surgical margins were identified in 11.29% of the cases, but they had no impact on the results of treatment;
6. No worsening of outcome was proven for the patients who reported to the doctor later than 15 weeks following the occurrence of symptoms.

**REFERENCES**


