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Treatment Outcomes and Relapses of Squamous Cell Carcinoma of the Maxilla: A Retrospective Study of 25 Years

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Abstract:

Objective: The location of a squamous cell carcinoma at the maxilla is relatively rare. Therefore only little data exists about treatment outcomes and relapses. In a retrospective study, SCCs of the maxilla were analysed regarding local and metastasis relapses and their outcome.

Materials and Methods: All patient records from 1987 to 2011 were searched for the diagnosis of a SCC of the maxilla. The tumors were classified according to the 2003 TNM staging system of the UICC. The therapy was recorded and each case was checked for metastasis and local recurrence.

Results: 121 patients were analysed: 35% of the patients (n=42) were female and 65% (n=79) were male. The average age was 65 years (70y for women, 62y for men). The average follow-up time was 32 months (range 1-131). 27% (n=33) had a relapse with a median disease-free period of 13 months (range 4-140). The intraoral local recurrence with 67% (n=22) made up the largest share, and distant metastases hade the smallest portion with 9% (n=3). Cervical lymph node metastasis are present in 36% (n=12).

The recurrence is associated with the grading and high tumor stage (III-IV). The likelihood of local reoccurrence was higher for patients with an initial R1 resection and of CM if a lymph node was positive at the time of primary operation.

Conclusions: The SCC of the maxilla has aggressive regional and cervical relapse behaviour. Therefore we recommend surgical treatment as the primary management strategy for this patient group and frequent tumor recalls.

Keywords: Oral cancer; Maxilla; Squamous cell carcinoma of the maxilla; Treatment outcome; Relapse behavior.

Introduction

Oral cancer is the sixth most common malignant tumor and is responsible for about 200,000 - 350,000 cancer deaths worldwide each year [1, 2]. Oral SCC is the most frequent of the head and neck malignancies, which account for approximately 3% of all malignancies in the body [3]. The incidence and prevalence vary depending on the geographical region and, consequently, to differences in the distribution of known risk factors such as tobacco or alcohol use [4]. In Central Europe, about 25-30 new cases occur per 100,000 population per year [5].

For oral SCC in particular, the time of diagnosis [6] as well as the tumor size and the presence of lymph node metastasis in the neck are known to be the most important prognostic indicators [7, 8]. Delaying the diagnosis by more than one month worsens the prognosis significantly [6]. Local and cervical recurrent goes along with a poor prognosis [9, 10].

Despite multimodal treatment strategies, about 50% of the patients still die from their oral malignancy. Crucial here is that the majority of patients are diagnosed (~ 60%) in an already advanced stage (III-IV) [11-13].

The maxilla is seldom identified as the site for an oral SCC. Oral SCCs at the maxilla are rare, with a reported incidence of only 0.5% to 2.0% [14]. The relatively rare occurrence of these tumors is most likely the reason why they are often grouped and reported together with oral SCC of other sites or combined with salivary gland tumors of the maxilla [14]. Therefore available specific data regarding treatment outcome and local and cervical metastasis relapses are sparse [15, 16].

The purpose of this retrospective study was to review the outcome of patients with SCC of the maxilla treated at our department in the last 25 years and to analyse factors affecting survival, and local and locoregional control.

Patients and Methods

All patients with primary oral SCC of the maxilla being treated from 1987 to 2011 in the Department of Oral and Maxillofacial Surgery were analysed.

Exclusion Criteria: Non-SCC malignancies of the maxilla, SCC that were not primarily treated at our department, a former SCC in the patient history, and tumors infiltrating from different regions into the maxilla.

Collected Data: Age, gender, alcohol and/ or nicotine consumption, tumor size, metastasis (local and distant), TNMR status, therapy, outcome.

Microsoft ® Office Excel 2010 and SPSS 17.0 for Windows were used for statistical analysis. A t-test was used to show relationships of normally distributed variables. Kaplan-Meier curves with log-rank tests were used to display survival rates. Chi-square and Fisher's exact tests ($n<5$) were used to look for associations between two variables. A p-value of <0.05 was defined as statistical significant.

Results

121 patients with a primary SCC of the maxilla were comprised. The average age was 65 years ± 13 years (standard deviation). 42 patients (36%) were female (age 70 ± 12 years), and 79 patients (64%) were male (age 62 ± 12 years). Men were statistically significant older than women ($p = 0.001$).

The average follow up time was 32 months (range: 0-131). The median tumor-free period was 13 months (range: 4-131), and within the first 2 years after primary therapy about 73% had either a local recurrence or a lymph node metastasis (Figure 1).

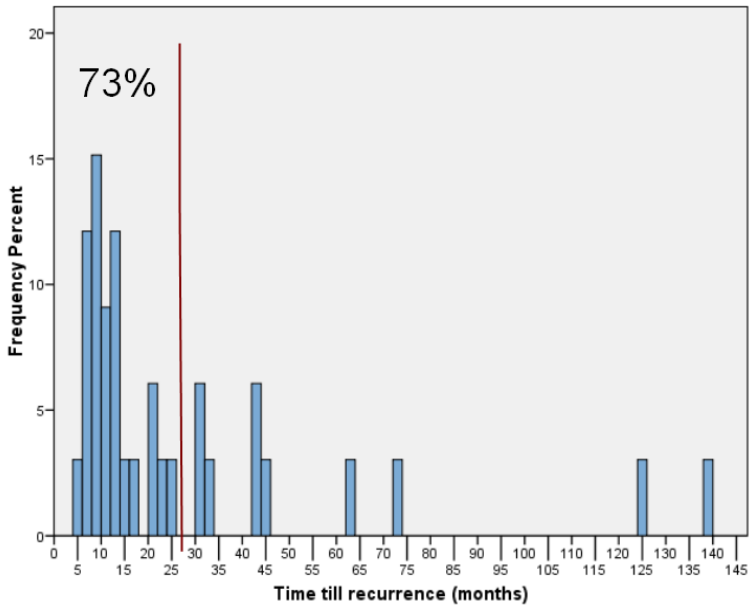


Figure 1: Timeline till recurrence.

Risk Factors

59% of the patients either smoked or consumed alcohol (70% of the men and 40% of the women; $p<0.001$). The subgroup of patients with a recurrence (72%: 83% of the men and 50% of the women; $p = 0.733$) had a slightly higher portion of individuals who smoked and drank alcohol ($p = 0.774$).

Treatment

91% (n=110) of the patients had undergone primary surgical treatment. 8% (n = 10) of the patients had a non-primary operable carcinoma and received neoadjuvant chemo radiotherapy. 1 patient refused any therapy.

In 23% (n=25) out of the patients with primary surgical treatment, no neck dissection was performed. Overall 55% (n=66) of the patients received radiotherapy. 37% (n=45) of the patients were treated with chemotherapy, which was consistently performed in combination with radiotherapy. Table 1 breaks down the therapy the patients received according to their tumor stage.

Table 1: Classification and distribution of the maxillary SCC patients' treatment according to the tumour stage at the point of the initial diagnosis.

Tumore stage	Primary operation	Radiotherapy	Chemoradiotherapy
Stage I (n=34)	97% (n=33)	6% (n=2)	12% (n=4)
Stage II (n=16)	100% (n=16)	0%	19% (n=3)
Stage III (n=15)	93% (n=14)	13% (n=2)	67% (n=10)
Stage IV (n=56)	84% (n=47)	30% (n=17)	50% (n=28)
All patients (n=121)	91% (n=110)	17% (n=21)	37% (n=45)

Among the patient group with relapse, 97% (n=32) underwent primary surgical treatment at the time of initial diagnosis. 63% (n=21) received radiotherapy, and 54% (n=17) were treated with chemotherapy.

27% of the patients (n=33) had either local recurrence or recurrence at a cervical lymph node, distant metastasis, or a second oral malignoma. Five patients had two and two patients had three simultaneous manifestations of tumor recurrence. The intraoral local recurrence with 67% (n=22) made up the largest share, and distant metastases hade the smallest portion with 9% (n=3). Cervical lymph node metastasis are present in 36% (n=12).

The largest share (73%; n=16) of all local recurrences (n=22) had a G2 differentiation. Only one patient (5%) of the group with local recurrence had a G1 tumor. 35% of G3, 20% of G2, and only 4% of G1 tumors from the overall population showed a local recurrence (Table 2). As well, the largest share (75%; n=9) of all CM recurrence (n=12) displayed a G2 differentiation. No patient in the group with CM recurrence had a G1 tumor. 13% of G3 and 12% of G2 tumors from the overall population showed a CM recurrence (Table 3). The differences in the frequency of metastases between the different G statuses are not statistically significant ($p>0.172$).

Table 2: Presence of local recurrence according to the tumour grading at the point of the initial diagnosis.

G stage of all patients with recurrence (n=33)	Portion of local recurrence (n=22) of all patients with recurrence	Portion of local recurrence to the respective G stage of all patients (n=121)
G1 (n=1)	5% (n=1)	4% (n=1 of 25)
G2 (n=24)	73% (n=16)	22% (n=16 of 73)
G3 (n=8)	23% (n=5)	35% (n=8 of 23)

Table 3: Presence of CM recurrence according to the tumour grading at the point of the initial diagnosis.

G stage of all patients with recurrence (n=33)	Portion of CM recurrence (n=12) of all patients with recurrence	Portion of CM recurrence to the respective G stage of all patients (n=121)
G1 (n=1)	0% (n=0)	0% (n=0 of 25)
G2 (n=24)	75% (n=9)	12% (n=9 of 73)
G3 (n=8)	25% (n=3)	13% (n=3 of 23)

Table 4 breaks down the distribution of the local and CM recurrence according to the tumor stage. In a low tumor stage (I-II), only 16% (n=8) developed a local relapse and 6% (n=3) a CM relapse. In comparison to low stage tumors, advanced stage tumors (III-IV) showed a local relapse of 20% (n=14) and a CM relapse of 13% (n=9).

There is no statistically significant difference for the overall occurrence of recurrences between these two subgroups (p=0.376), nor for the local recurrence (p=1.000) or the occurrence of lymph node metastases (p=0.227).

30% of R1 patients developed local recurrence compared to 17% of all patients with an R0 situation after primary surgery (p=0.581; Table 5).

Table 4: Presence of local and CM recurrence according to the tumour stage at the point of the initial diagnosis.

Tumor stage	All patients (n=121)	Relapse (n=33)	Portion of local recurrence of all recurrences (n=22)	Portion of local recurrence to respective tumor stage (n=50; n=71)	Portion of CM recurrence of all recurrences (n=12)	Portion of CM recurrence to respective tumor stage (n=40, n=71)
I-II	50	10	36% (n=8)	16%	25% (n=3)	6%
III-IV	71	23	64% (n=14)	20%	75% (n=9)	13%

Table 5: Presence of local recurrence according to the R stage after primary operative treatment.

R stage of all patients with recurrence (n=33)	Portion of local recurrence (n=22) of all patients with recurrence	Portion of local recurrence to the respective R stage of all patients with primary operative treatment (n=110)
R0 (n=25)	64% (n=14)	17% (n=14 of 83)
R1 (n=8)	36% (n=8)	30% (n=8 of 27)

19% (n=6) of the N2 patients and 11% (n=2) of the N1 patients developed a CM recurrence compared to 6% (n=4) of all patients with an N0 situation after primary therapy (Table 6). There is no statistically significant difference between the different N situations. The p-value between N0 and N2 for CM is 0.056. The four CM in the N0 group were exclusively patients who had no neck dissection as part of their primary therapy. Thus 16% (4 out of 21) of the patients without primary neck dissection at the time of initial diagnosis developed a CM.

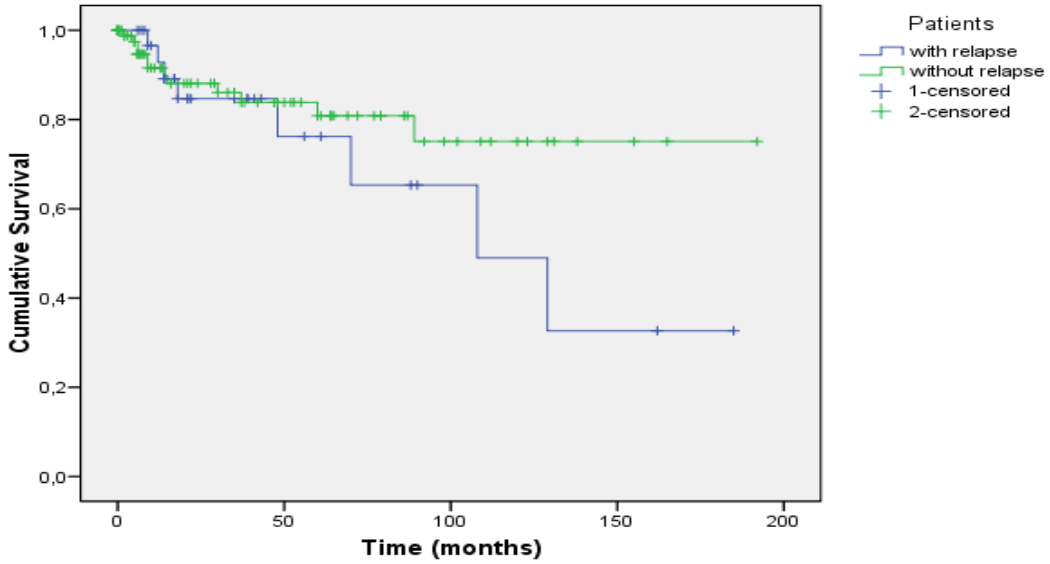
Table 6: Presence of CM recurrence according to the N stage at the point of the initial diagnosis.

N stage of all patients with recurrence (n=33)	Portion of CM recurrence (n=12) of all patients with recurrence	Portion of CM recurrence to the respective N stage of all patients (n=121)
N0 (n=25)	33% (n=4)	6% (n=4 of 71)
N1 (n=8)	17% (n=2)	11% (n=2 of 18)
N2 (n=13)	50% (n=6)	19% (n=6 of 32)

Outcome

The Kaplan-Meier overall survival curves for patients with and without recurrence are shown in Figure 2. The presence of relapses reduces the survival of the patients compared to the group without a relapse (p=0.286). The overall survival time is a mean of 113 months (±18 months) for patients with a relapse in their history of disease compared to 154 months (±10 months) for the control group without relapse.

Figure 2: Overall survival for maxillary SCC based on the presence or absence of relapse during history of disease.



Discussion

This study's demographic data and presence of the risk factors (59%; n=71 out of 121) is supported by the literature [17-22]. In the patient group with relapse, 72% were addicted to tobacco and alcohol, which is far more than the non-relapse group.

Most of the recurrences (80-90%) are seen within the first 2 years after the initial treatment [23, 24]. 73% of the relapses in our collective were detected within the first 2 years after primary therapy, with a median tumor-free period of 13 months.

Recurrence rates of oral SCC have been reported in the range of 25%-48%, which is not surprising considering the aggressive infiltrative nature as well as the high potential for occult CM [25]. 27% of our patients with SCC of the upper jaw developed a local recurrence, recurrence at a cervical lymph node, distant metastasis, or a second oral malignoma.

The histological grading is significantly related to nodal disease at the time of diagnosis [26] and was found to be a significant predictor of locoregional failure and tumour recurrence [27]. We also found a close correlation between low histological differentiation and the occurrence of local and CM relapse.

In addition to the histological grading, an advanced tumor stage (III-IV) seems to be an important factor for relapses [16, 28, 29]. In line with the literature in our collective of patients with SCCs of the maxilla, there is a much higher rate of local recurrence (20%) and CM recurrence (13%) for the advanced stage compared to the stage I-II tumors.

For the CM recurrence, the N status after the primary surgery is an important factor [23]. There seems to be a correlation between CM recurrence and the N stage at the point of primary diagnosis and therapy.

The status of resection margin is not only well known as a significant factor for over-all survival but also for local control [23, 30]. The portion of local relapse is higher for patients with an initial R1 status.

The recurrence of SCC of the oral cavity is associated with a poor prognosis [23, 25, 29]. The presence of relapses decreases the overall survival of our patients compared to the group without a relapse.

Our data expose the aggressive regional and cervical relapse behaviour of SCC of the upper jaw. Therefore we recommend surgical treatment as the primary management strategy for this patient group and frequent tumor recalls.

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