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# Squamous cell carcinoma of the maxilla: Analysis of clinicopathological predictors for disease recurrence and metastatic behavior $\stackrel{\star}{\sim}$

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#### ABSTRACT

*Introduction:* Squamous cell carcinoma of the maxilla only constitutes a small fraction of Head and Neck Cancers. There is thereby a lack of information about frequent tumor staging and localization and their effect on patients' outcome. The main factors that influence longterm survival in HNSCC are the extent of the primary disease and recurrence rate, including local neck metastases.

*Patients and methods:* In this study, clinical outcome and rates of disease recurrence in 68 surgically treated patients with maxillary SCC were evaluated in terms of primary tumor staging and localization. *Results:* It could be demonstrated that maxillary cancer is mostly located in the posterior region of the upper jaw (70%). The rate of neck node metastasis was 35.3%, which is equivalent to the rest of the oral cavity and supports the role of elective neck dissection for patients with clinically negative neck node status. Staging, tumor differentiation, and infiltration of lymphatic structures correlated significantly with the development of local neck node metastases (r = 0.321, p = 0.01; r = 0.348, p < 0.01; r = 0.64; p < 0.01).

*Conclusion:* Maxillary carcinomas exhibit similar rates of locoregional disease recurrence as the rest of the oral cavity. The existence of cervical metastases even in patients with T1 tumors supports the concept of elective neck dissection in early tumors with clinically negative neck status.

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#### 1. Introduction

Squamous cell carcinoma of the head and neck (HNSCC) is the sixth most common cancer in the world, accounting for approximately 5% of all malignant tumors (with regional differences) (Torre et al., 2012). Cancer of the maxilla, however, is relatively rare and accounts for only 0.5–5% of oral cancers in general, depending on anatomical classification (Brown et al., 2000, Pathak et al., 2007, Binahmed et al., 2008, Sagheb et al., 2014). While the available literature can point to a large number of epidemiological studies

that investigate cancers of the head and neck or the oral cavity in general, few authors have examined maxillary carcinoma exclusively.

It is widely accepted that the prognosis of HNSCC is mostly influenced by the extent of the disease at the primary site and the stage of local neck node metastasis (Snow et al., 1982, Gold et al., 2009, Jones et al., 2011, Teymoortash and Werner, 2012). A 5-year survival rate of over 80% for small tumors and metastasis-free neck nodes is reduced to around 40% if metastases occur (Rao et al., 1998). In the past, there has been controversy regarding whether carcinomas of the maxilla exhibit a similar risk of regional metastases and local disease recurrence to other subsites of the oral cavity (Montes et al., 2011, Brown et al., 2013, Eskander et al., 2013, Yang et al., 2014).

Lin et al. demonstrated the significant impact of TNM stage on survival in patients with SCC of the hard palate or the maxillary alveolus, while the incidence of occult cervical metastases in oral

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SCC has been shown to be over 20% by several authors (Lin and Bhattacharyya, 2009, Beltramini et al., 2012, Psychogios et al., 2013).

A better understanding of lymphatic drainage and factors promoting regional metastasis as well as the occurrence of relapse tumors is therefore essential to an optimized therapy regime (Mourouzis et al., 2010, Teymoortash et al., 2012). This includes defining exact guidelines for the management of the clinically negative neck (Montes and Schmidt, 2008, 2011, Eskander et al., 2013). While some authors have postulated the minor significance of elective neck dissection (Kim et al., 1999), most authors now agree in recommending elective neck surgery for patients with maxillary tumor stages T2–T4 (Morris et al., 2011, Beltramini et al., 2012, Eskander et al., 2013). The most recent publications even argue that patients with low-stage maxillary SCC may benefit from neck treatment (Berger et al., 2015).

The main objective of this retrospective study was to evaluate the most common localization of primary tumors and the prevalence of cervical and distant metastases in patients with carcinoma of the maxilla in comparison with clinicopathological data. The occurrence of relapses or secondary tumors was investigated to identify the origin of potential metastases. Furthermore, survival rates were analyzed in comparison with clinicopathological tumor data.

#### 2. Material and Methods

#### 2.1. Inclusion criteria and data collection

For this retrospective study, we collected data from 68 patients with SCC of the maxilla who had been treated in the Department of Oral and Maxillofacial Plastic Surgery at the University Hospital Würzburg between January 1999 and February 2016. The existence of a squamous cell carcinoma of the maxilla served as our inclusion criterion. Eligible candidates were identified via patient registry and anonymized using SAP (SAP SE, Walldorf, Germany). The primary type of treatment in all patients was the surgical removal of the tumor, while some patients had additionally received stagerelated pre- and/or postoperative radio-chemotherapy. In patients who had received neck dissection, the side and extent of the intervention was documented. Local recurrence and the appearance of secondary carcinoma were taken into account. Newly developed carcinomas that had developed 5 years or more after the first tumor were regarded as secondary carcinomas. Every case of a new tumor in the same localization was defined as disease recurrence. Patient outcome was assessed until February 2017.

#### 2.2. Tumor classification

The collected tumor data included TNM stage, tumor infiltration parameters, differentiation grade, anatomical localization, and the occurrence of a relapse within 5 years after primary treatment.

Tumor localization was classified in terms of.

- the transverse plane: left side, right side, exceeding the center line
- the sagittal plane: anterior (pre-canine), central (post-canine), posterior (molar and retromolar)

Affected tissue was grouped in terms of.

- hard tissue (hard palate, alveolus, maxillary sinus, nasal cavity, and septum)
- soft tissue (soft palate, palatopharyngeal arch, buccal tissue)
- hard and soft tissue

#### 2.3. Statistical analysis

Statistical analysis was performed using Microsoft Excel 2013 (Microsoft, Redmond, WA, USA) and SPSS Statistics <sup>®</sup> (IBM, Armonk, NY, USA). Demographic and tumor-linked data were summarized using descriptive statistics. Survival rates were calculated using the date of diagnosis until death or the end of data collection (December 31, 2011). To determine correlation, we used Pearson's correlation coefficient. A *p*-value of 0.05 or less was considered to demonstrate statistical significance.

#### 3. Results

#### 3.1. Patient data

The patient group (n = 68) consisted of 39 male (57.4%) and 29 female (42.6%) patients, whose ages ranged from 29 to 89, with a mean age of 66.8  $\pm$  13.4 years. Fig. 1 provides an overview of gender-dependent age distribution. All 68 patients underwent surgical tumor removal, and 56 (82.4%) were treated via neck dissection. Ten patients (14.7%) were treated preoperatively via radiotherapy or radio-chemotherapy, whereas 35 patients (51.5%) received postoperative adjuvant therapy.

#### 3.2. Tumor data

Table 1 and Fig. 2 summarise the staging, localization, and the affected tissue for the 68 primary tumors.

Twenty-one patients (30.9%) exhibited local neck node metastases on pathological examination after surgery, 13 (61.9%) of which were ipsilateral and eight (38.1%) of which were contra- or bilateral. No distant metastases were found in the initial staging procedure. Forty-eight (70.6%) tumors were located in the posterior region of the maxilla (in the molar or retromolar region). Fig. 3 shows the distribution of staging in carcinoma of the posterior maxillary region.

#### 3.3. Recurrence rates

Fourteen out of 68 patients (20.6%) suffered from disease recurrence before the end of data collection. The local tumor recurrence rate was 11.8% (eight patients). Seven patients (10.3%) developed secondary carcinomas in the floor of the mouth (four cases) and the maxilla (three cases). Eight patients (11.8%) developed metastases after primary treatment, five (7.4%) of which were neck node metastases and three (4.4%) of which were distant metastases located in the brain, the skin, or the lungs. Of the five cases of late neck metastases, three (60%) were contralateral and two (40%) were located ipsilateral. In total, 24 of 68 patients (35.3%) developed neck node metastases. Table 2 summarizes the recurrence data in relation to time after primary treatment. Nineteen (82.6%) of 23 cases of disease recurrence occurred within the first 3 years after primary treatment.

#### 3.4. Correlation analysis

#### 3.4.1. Correlation of clinicopathological tumor data

In our analysis, staging, tumor differentiation, and lymphatic tumor infiltration were significantly correlated with the occurrence of cervical lymph node metastases (Table 3). There was also a significant correlation between vascular tumor infiltration and the development of distant metastases, which should be regarded critically due to the small number of occurrences (n = 3).

We could not find any significant correlation between tumor localization (transversal or sagittal) and metastatic behavior or disease recurrence.

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