Journal of Cranio-Maxillo-Facial Surgery 43 (2015) 2195–2199

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Occurrence of cervical lymph node metastasis of maxillary squamous cell carcinoma – A monocentric study of 171 patients

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ARTICLE INFO

Article history:
Paper received 19 May 2015
Accepted 25 September 2015
Available online 9 October 2015

Keywords:
SCC
Maxilla
Cervical lymph node metastasis
Neck dissection

ABSTRACT

Introduction: Fewer than 5% of oral squamous cell carcinomas (SCC) are presented in the maxilla. The absence of cervical lymph node metastasis (LNM) is one of the main positive prognostic factors. This single-centre study analysed the cervical lymph node metastasis behaviour in patients with oral SCC of the upper jaw and serves as a basis for a cervical lymph node treatment suggestion.
Material and methods: The retrospective study includes 171 patients with isolated SCC of the maxilla. In addition to tumour resection, 83% of the patients underwent a selective neck dissection (ND). The data of cervical metastasis, TNM-status, tumour grade, tumour location as well as nicotine and alcohol behaviour were statistically analysed.
Results: The average rate of cervical metastasis was 44% in total. Tumour stage significantly affected risk for cervical metastasis (T1 = 6%, T2 = 41%, T3 = 60% and T4 = 60%) ($p < 0.01$). Development of cervical LNM was seemingly influenced by male gender.
Discussion: This study postulates a high rate of cervical metastasis of maxillary SCC. Risk for metastasis is mainly determined by the tumour stage. Alcohol and nicotine abuse have a negative impact on cervical LNM.
Conclusion: Reviewing recent literature underlined by the illustrated data, we put up for discussion the treatment of SCC of the maxilla as similar to therapy protocols for SCC of the oral cavity. This would include an ipsilateral ND even in low tumour stage and in T4 staged tumours on both sides. However, prospective multicentre studies are needed to verify and recommend these therapy assumptions.

1. Introduction

Head and neck cancers are among the ten most common cancers globally (Warnakulasuriya, 2009, Siegel et al., 2014). Thus, SCC, at more than 90%, are the most common type of all malignant tumours in the oral cavity (Johnson et al., 2011; McDowell, 2006; Lambert et al., 2011). Compared to other intraoral locations, SCC of the maxilla are relatively rare (Montes and Schmidt, 2008). Only about 0,5–5% of oral SCC are in the upper jaw (Sagheb et al., 2014), where it is known that oral SCC have unique clinical behaviour relative to those in other head and neck regions (Montes and Schmidt, 2008; Brennan et al., 1991). Nevertheless, it has long been believed that SCC of hard palate and maxillary alveolus have a low nodal metastatic risk (Yang et al., 2014). In contrast to that, recent studies assume a higher risk for lymphatic metastasis of maxillary oral SCC, equal to the rest of the oral cavity (Mourouzis et al., 2010; Morris et al., 2011; Sagheb et al., 2014; Kruse and Gratz, 2009). However, there is uncertainty and controversy involving the management of the neck in patients with maxillary alveolus and hard palate SCC.

It is well-known that the presence of cervical lymph node metastasis (LNM) is crucial for prognostic relevance for patients with SCC (Capote et al., 2007, Kohler and Kowalski, 2011). Furthermore, it is proven that selective neck dissection is beneficial for patients with SCC of the tongue and mouth floor (Yuen et al., 1997; Nouraei et al., 2013). However, clinical N0 necks are monitored closely in many head-neck centres without surgical intervention (Beltramini et al., 2012). Still, it is known that there are over

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http://dx.doi.org/10.1016/j.jcms.2015.09.009
1010-5182/

20% of occult neck LNM in patients with oral SCC reported in the international literature (Psychogios et al., 2013; Sparano et al., 2004). The outcome data of a "watch and wait" strategy for patients with clinical N0 necks are comparable with data of those who underwent a selective ND (Rodrigo et al., 2011).

Either way there are no binding treatment recommendations or guidelines for this kind of tumour entity of the maxilla, especially not in terms of the lymph node treatment justified by the low case numbers. In particular, there is no evidence to support treatment of the clinical N0 neck by SCC of the maxilla (Kim et al., 1999).

Therefore, this retrospective, single-centre study with a large number of patients – compared to other, previously published studies' data – evaluates the incidence of cervical metastasis in SCC of the maxilla and their possible influential factors.

2. Materials and methods

The present study retrospectively included a total 171 patients with an isolated SCC of the upper jaw treated from 1975 to 2009 at the Department of Oral and Maxillofacial Surgery, University of Heidelberg. All patients included underwent a tumour resection, 83% (n = 142) a selective ND. Of all patients evaluated, neck dissection was refused by 17 %. Indication for an ipsilateral neck dissection was given when the staging score was cT $\geq$ 2. For patients with cT1 and cN- Tumours, an ipsilateral neck dissection as well as a watch-and-wait strategy were discussed with the patient in detail. An ND was performed in 108 patients on both sides. Therefore, advanced tumour stage (cT4) and patients with cT $\leq$ 3 cN+ on ipsi- or contralateral neck, indicated a neck dissection on both sides. All patients were staged by clinical and pathological TNM classification of the International Union Against Cancer (UICC). In addition to TNM status, tumour grade, the patients' age and gender, tumour location in the upper jaw (maxillary alveolus, hard palate and soft palate), as well as nicotine and alcohol behaviour were analysed statistically. Exclusion criteria were reoccurrence of an oral SCC as well as the presence of other malignancies, e.g. breast or lung cancer. Primarily SCC of the maxillary sinus or nose with an infiltration of the hard palate were also excluded.

The descriptive statistical analysis is of an exploratory nature. A p-value of less than or equal to 0.05 was considered to denote an exploratory significant difference. Categorical variables were analysed in relative and absolute frequencies. Nicotine and alcohol consumption was specified as categorical parameters (yes/no – selection). To investigate the association between the dependent variable lymph node metastases and possible risk predictors, univariate logistic regression analyses were performed. In addition, to investigate the common influence of potential risk factors for the dependent variable lymph node metastases, a multivariable logistic regression with backward selection was conducted. Further analyses were done concerning the difference of lymph node metastases and nicotine consumption by T-stage and gender, each applying a two-sided chi-square test. The survival data were analysed and presented with Kaplan–Meier graphs.

The proportion of missing values was very low, therefore, missing values were not imputed. Statistical analyses were performed using SPSS version 21.0 (SPSS, Munich, Germany) and Microsoft Excel 2011 (Redmond, Washington, USA). Due to the study's exploratory nature, no adjustment was made for multiple testing. The study was approved by the ethical commission of the medical faculty of the University of Heidelberg.

3. Results

A total 171 patients were retrospectively evaluated. 102 male and 69 female patients with a mean age of 63.6 years (range 28–93 years) underwent total or partial maxillectomy, and 83% of them had a selective neck dissection. Table 1 describes the distribution of cN status stratified for the different T-categories. Therefore combinations of only ultrasound, ultrasound and CT, ultrasound and MRI, CT and MRI, respectively with and without contrast medium could be found. In this period 23 different radiologic devices were in use. As shown in Table 2 the different pathological T-stage contained T1: n = 34, T2: n = 39, T3: n = 10 and T4: n = 88 patients.

Overall, 77 (45%) of the treated patients with a maxillary SCC revealed cervical metastasis. pT-stadium showed a statistically significant dependency for developing cervical LNM ($p < 0.01$): 6% of T1-staged patients had cervical LNM, patients with T2 tumour 41%, T3 60% and T4 60%.

Incidentally, it should be noted that gender had no significant statistical influence for cervical metastatic risk ($p = 0.07$); however, there is a tendency for increased incidence of LNM in male patients. Half the males showed LNM (51 out of 102); 36% of the women with oral SCC had a positive LNM status.

In total, 24 patients showed LNM on both sides of the neck. Categorised in T-stadium, up to 21% of the patients had bilateral positive LN status (pT4). Further, 16% of T1-and T2-staged patients showed occult metastasis. Overall, 4% of the patients showed unexpected cervical LNM after the histopathological examination.

The location of the maxillary SCC was distributed as 60% hard palate, 19% alveolar ridge and 21% soft palate. Therefore, all palatinal SCC were designated as hard-palate origin because of the flowing transition of hard-palate and alveolar ridge.

Furthermore, the location of the SCC showed no statistical significance ($p > 0.6$). The side of maxillary SCC had no influence on cervical LNM ($p > 0.7$) as well. Indeed, we could not demonstrate a correlation of the histological grading and LNM ($p > 0.6$).

The connection of patients' age and the risk for cervical metastasis showed a statistical significance ($p < 0.05$). Accordingly, with increasing age the risk of LNM decreases.

We studied the risk factors that are commonly linked to the aetiology of oral SCC as well; 61% of the patients regularly used tobacco products, and 39% were non-smokers. Overall, 74% of the patients with cervical LNM regularly consumed nicotine products ($p < 0.01$); 46% of the patients indicated regular consumption of alcohol.

Even without statistical significances, the calculated odds ratios shown in Table 3 illustrate the potential risk of each examined variable such as gender, tumour stage, maxillary region, histological grading, and abuse of nicotine and alcohol. The Kaplan Meier graphs show the survival of the study patients. In the absence of LNM in patients with maxillary SCC, the survival on average

Table 1
Clinical LN status in relation to the different clinical T-stages.

c2T-Stage	No.	cN0 (%)	cN1 (%)	cN2a (%)	cN2b (%)	cN2c (%)	cN3 (%)
T1	22	19(86)	3 (14)	–	–	–	–
T2	33	19 (58)	5 (15)	–	3 (9)	6 (18)	–
T3	6	2 (33)	2 (33)	–	2 (33)	–	–
T4	110	36 (33)	11 (10)	–	31 (28)	30(27)	2 (2)

Table 2
Pathological LN status in relation to the different pathological T-stages.

pT-Stage	No.	pN0 (%)	pN1 (%)	pN2a (%)	pN2b (%)	pN2c (%)	pN3 (%)
T1	34	32 (94)	2 (6)	–	–	–	–
T2	39	23 (59)	6 (15)	1(3)	4 (10)	5 (13)	–
T3	10	4 (40)	3 (30)	–	3 (30)	–	–
T4	88	35 (40)	8 (9)	–	26 (30)	17 (19)	2 (2)