Elective neck dissection in oral squamous cell carcinoma of the upper maxilla: necessary?

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ABSTRACT

Aim: Surgical treatment of clinically negative neck in maxillary squamous cell carcinoma (SCC) of the upper jaw is controversial. The purpose of this systematic review was to define the incidence of cervical metastasis and to assess if elective neck dissection is justified when the neck is not primarily affected. **Methods:** An electronic literature search was conducted in several databases, including MEDLINE, EMBASE, and Cochrane Central databases, for articles written in English. **Results:** Twenty-eight articles were included in the review. The overall cervical metastases rate was 33% and the total initial cervical metastases rate was 16%. Interestingly, the author found that 71% of patients with cervical metastases from maxillary SCC carcinoma were T3/T4 stage. **Conclusion:** This review shows the need for a change in the management of the N0 neck in SCC arising in the maxillary alveolus and hard palate. Elective neck dissection should be performed in patients with T3/T4 tumours with clinic or radiographic negative necks (N0c).

Key words:

Elective neck dissection; maxilla squamous cell carcinoma; surgical treatment; cervical lymph node metastasis

INTRODUCTION

Squamous cell carcinoma (SCC) located in the maxillary gingiva and hard palate is relatively rare and less frequent than SCC from other oral sites such as tongue, floor of mouth or retromolar region. Many studies[1-5]

Table 1: Studies included in the review about patients with squamous cell carcinoma of the upper maxilla

Author	Year	Country	No. of patients	Study	Nodal disease in T3/T4 (%)	Initial nodal disease (%)	Overall nodal disease incidence (%)	Follow-up (months)
Truitt et al.[23]	1999	USA	24	Retrospective	Unknown	17%	33%	60
Ogura et al.[14]	2003	Japan	21	Retrospective	Unknown	29%	67%	Unknown
Simental et al.[11]	2006	USA	26	Retrospective	Unknown	12%	35%	65
Zwetyenga et al.[35]	2006	France	34	Retrospective	91%	18%	32%	Unknown
Montes and Schmid[9]	2008	USA	14	Retrospective	50%	21%	43%	27
Lin and Bhattacharyya[22]	2009	USA	725	Cross-section	64%	14%	14%	Unknown
Kruse and Grätz[12]	2009	Switzerland	30	Retrospective	18%	13%	37%	Unknown
Mourouzis et al.[13]	2010	UK	17	Retrospective	100%	24%	35%	60
Montes et al.[16]	2011	USA	131	Retrospective	55%	24%	31%	1-180
Lubek et al.[18]	2011	USA	37	Retrospective	67%	5%	16%	49
Nicolai et al.[34]	2010	Italy	86	Retrospective	31%	9%	22%	Unknown
Wang et al.[36]	2010	Taiwan	79	Retrospective	100%	9%	22%	Unknown
Valentini et al.[25]	2010	Italy	19	Retrospective	Unknown	5%	11%	Unknown
Beltramini et al.[26]	2012	Italy	65	Retrospective	86%	12%	22%	43.3
Morris et al.[15]	2011	USA	139	Retrospective	71%	8%	31%	57
Brown et al.[10]	2013	UK	43	Retrospective	81%	7%	37%	94
Poeschl et al.[33]	2012	Austria	74	Retrospective	100%	Unknown	22%	6-130
Dalal and McLennan[30]	2013	UK	30	Retrospective	100%	27%	36%	60
Feng et al.[27]	2013	China	129	Retrospective	65%	0%	24%	Unknown
Eskander et al.[32]	2013	Canada	97	Cohort	53%	24%	41%	Unknown
Sagheb et al.[29]	2014	Germany	138	Retrospective	60%	38%	46%	43
Zhang et al.[37]	2015	China	100	Retrospective	79%	9%	34%	46
Philip et al.[24]	2014	UK	39	Retrospective	95%	33%	46%	38
Givi et al.[39]	2016	USA	199	Retrospective	50%	6%	22%	52
Berger et al.[40]	2015	Germany	171	Retrospective	78%	Unknown	44%	Unknown
Yang et al.[28]	2015	China	62	Retrospective	69%	15%	37%	37
Troeltzsch et al.[41]	2016	Germany	92	Retrospective	40%	16%	29%	42
Moreno-Sánchez et al.[42]	2016	Spain	20	Retrospective	100%	30%	45%	53

have evaluated the need for elective neck dissection in these intraoral common sites when there is no clinical or radiographic suspicious of lymphadenopathy.[6-10] Controversies remain regarding the strategy of treatment for patients with maxillary SCC,[11-15] including indications for unilateral or bilateral elective neck dissection and postoperative adjuvant treatment.[16-20] Only a few authors[21-25] have focused on the management of the neck in SCC of the maxillary gingiva, maxillary alveolus and hard palate.[26-30]

Traditionally, when there is no clinical or radiographic suspicious of lymphadenopathy, management has been to watch and wait. However, in recent studies,[31-35] it has been proven that a higher rate of occult cervical metastases in SCC of the maxilla has been found[36-40] and elective neck dissection in these patients has been recommended in order to reduce recurrences.[41-43]

A systematic review was conducted in order to clarify if elective neck dissection is necessary in management of SCC of the maxillary gingiva, maxillary alveolus and hard palate, and to identify the risk of cervical metastases in patients with maxillary SCC.

METHODS

An electronic literature search was conducted in several databases, including MEDLINE, EMBASE, and Cochrane Central databases, for articles written in English from their respective dates of inception to December 2015. The searching keywords were "cervical metastases" OR "cervical metastases" OR "neck metastases" AND "maxillary squamous cell carcinoma" OR "maxilla squamous cell carcinoma" OR "squamous cell carcinoma of upper maxilla" AND (limit to clinical trial OR randomized controlled trial).

The abstracts of yielded results were reviewed and the full text of those with apparent relevance was obtained. The references of identified articles were crosschecked for unidentified articles. These journals were *Journal of Oral and Maxillofacial Surgery*; *International Journal of Oral and Maxillofacial Surgery*; *Journal of Oral Surgery*; *British Journal of Oral and Maxillofacial Surgery*; *Head and Neck Surgery*; *Laryngoscope*; *Oral Oncology*; *Journal of Cranio-Maxillo-Facial Surgery*; *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*; and *Revista Española de Cirugía Oral y Maxilofacial*. The searches were limited to articles
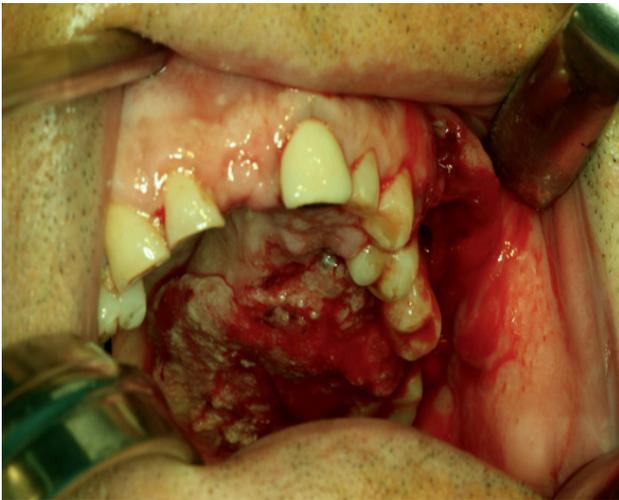
Figure 1: Intraoperative photograph of a patient with T4 squamous cell carcinoma of the hard palate with cervical metastases

published in English. The PICO question was as follows: is elective neck dissection necessary in oral squamous cell carcinoma of the upper maxilla?

The following exclusion criteria were applied: (1) case reports; (2) technical reports; (3) animal or *in vitro* studies; (4) review articles; (5) uncontrolled clinical studies; and (6) publications in which the same data were published by the same group of researchers. The authors carefully assessed the eligibility of all studies retrieved from the databases. From the included studies in the final analysis, the following data were extracted: authors, year of publication, country, study design, number of patients in the groups, initial nodal disease (%), and nodal disease in T3/T4 stage (%), overall nodal disease incidence (%) and follow-up period.

The selected articles were used to assess the rate of cervical metastases in patients with squamous cell carcinoma of the upper maxilla.

RESULTS

The electronic search resulted in 502 entries. Four additional articles were identified by manual searching. Of the 502 articles identified by electronic search, 305 were excluded because they were being retrieved in more than one search. After the initial screening of titles and abstracts, 169 articles were excluded because they were off topic. Thus, 28 articles were included in the review.

Of the 28 articles, 26 were retrospective studies, 1 was a cohort study, and 1 was a cross-sectional study. The studies included 2,641 cases in total [Table 1].

Rates of total cervical metastases

The rates of total cervical metastases were analysed in 28 articles [Table 1] in which metastases was confirmed by pathological examination. The overall metastases rate was defined as the ratio between the number of

pN+ cases and total cases. For the patients without neck dissection initially, those presenting with regional metastases or recurrence during the follow-up period would also be counted as pN+ cases. Several authors reported high rate of total cervical metastases. In a recent study, Berger *et al.*[40] reported 44% of total cervical metastases in a series of 171 patients. Yang *et al.*[31] observed a 37% of patients with cervical metastases during the follow-up in a series of 62 patients. Eskander *et al.*[32] reported a total of 41% of cervical metastases in a well-structured study of a 97 patients. Montes and Schmidt[9] reported a 42.9% rate of regional nodal disease in a series of 14 patients. Brown *et al.*[10] reported a rate of 37.2% in a series of 43 patients.

We can conclude from our meta-analysis about these 28 studies including 2,641 patients that the overall cervical metastases from SCC of the upper maxilla are 33%.

Initial nodal disease

Initial nodal disease was defined as the patients with lymph neck node metastases from the physical and radiologic examination in the first examination and the overall initial metastases rate was defined as the ratio between the number of initial cN+ cases and total cases. This variable was analysed in 26 of the 28 articles [Table 1]. At the time of the primary diagnosis, in a series of 138 patients, Sagheb *et al.*[29] observed 52 (38%) with cervical metastases whereas 53 (38%) patients that had a T3 (*n* = 6) or T4 (*n* = 47) tumour as well. Philip and James[24] reported 33% (13) of patients with neck disease at presentation. Ogura *et al.*[14] observed 28.5% of cervical metastases at presentation in their series of 21 patients with SCC of the upper maxilla. Dalal and McLennan[30] reported a 27% of cervical metastases at initial diagnosis.

From our meta-analysis among 26 studies including 2,396 patients with SCC of the upper maxilla, we can conclude that the overall initial cervical metastases rate is 16%.

T3/T4 nodal rate

We also analysed the incidence of cervical metastases of maxillary SCC in advanced-stage (T3/4) disease, including 24 articles for this purpose. Interestingly, we observed that the probability of lymph node metastases increased with the size of the tumour. Brown *et al.*[10] reported an 81% of cervical metastases in T3/T4 tumours in a series of 43 patients and Berger *et al.*[40] observed a 78% of cervical metastases in patients with T3/T4 stage in a series of 171 patients. Philip and James[24] observed a 95% of cervical metastases in T3/T4 tumours. Even authors such as Poeschl *et al.*[33] or Dalal and McLennan[30] reported that all the patients (100%) with advanced-stage (T3/T4) developed cervical metastases.

From our meta-analysis these 24 studies including 2,551 patients, we observed that 71% of patients with cervical
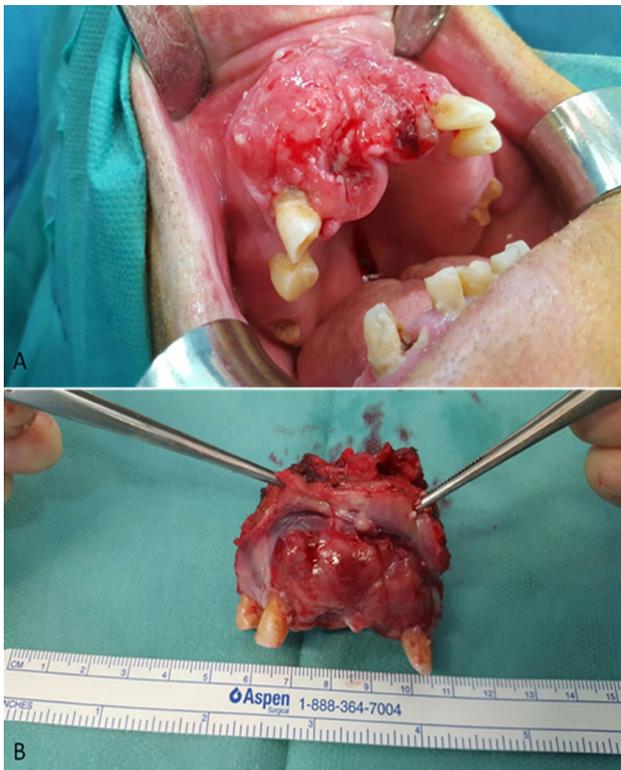
Figure 2: (A) Intraoperative photograph of a patient with T4 squamous cell carcinoma of the maxillary gingiva and bone invasion; (B) maxillary tumour was resected with wide surgical margins
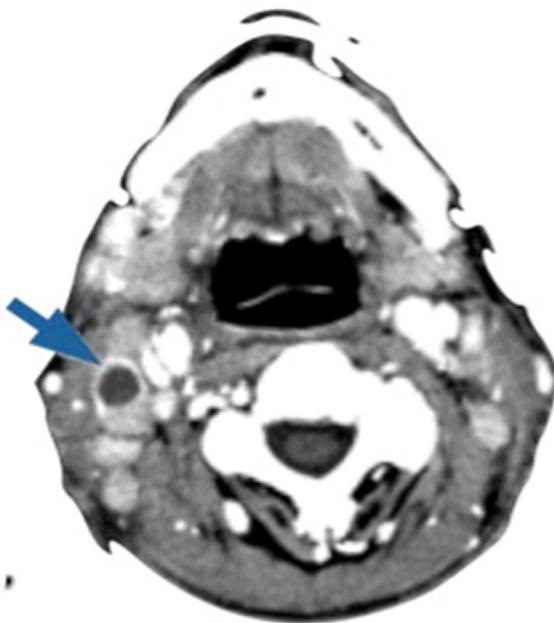

Figure 3: Computed tomography of the neck showing a cervical metastasis (arrow) of maxillary squamous cell carcinoma

metastases from maxillary SCC carcinoma were T3/T4 stage [Table 1].

DISCUSSION

In the last century, few studies have been focused on cervical metastases from SCC of the maxilla. Nevertheless, cervical metastases from SCC of tongue or floor of mouth have been well studied, both sites presenting a high incidence, considering elective neck dissection necessary in patients.

Elective neck dissection is generally performed in patients with SCC of the oral cavity when there is a risk of occult metastases higher than 15%. It is made at the time of surgery of the primary tumour, since most cancers of the oral cavity are treated surgically.[1-5] The risk of cervical metastases of maxillary gingival and hard palate SCC is considered lower than metastases of SCC in other primary sites, and management of clinical NO (cN0) patients is to "watch and wait". The National Comprehensive Cancer Network proposed guidelines for treatment strategies for head and neck cancer, suggesting selective neck dissection for cN0 patients with SCC of the tongue, floor of the mouth, mandibular gingiva, and buccal mucosa.[44] However, there is still no specific strategy for cN0 cases of maxillary SCC.

Recently, several studies reported that cervical metastases of maxillary SCC are much higher than expected and comparable to that of other primary oral sites. Montes and Schmidt[9] reported a 42.9% rate of regional nodal disease in a series of 14 patients with SCC of the maxilla; Brown et al.[10] reported a rate of 37.2% in a series of 43 patients; Simental et al.[11] in a series of 26 patients with SCC of the maxillary alveolus and hard palate found cervical metastases in 34.6%, similar to that observed by Kruse and Grätz[12] (33.6%) in a series of 30 patients. Mourouzis et al.[13] reported a 23.5% incidence of cervical metastases at presentation with maxillary SCC in a series of 17 patients. These reported incidences of cervical metastases are comparable to those observed for SCC of tongue or floor of mouth. Ogura et al.[14] reported a 28.5% incidence of cervical disease at presentation. Recently, Berger et al.[40] reported an overall rate of 44% of cervical metastases in a series of 171 patients. In our series, we founded that 9 of the 20 (45%) patients with SCC involving the palate or the maxillary alveolus [Figures 1 and 2] developed cervical metastases [Figure 3] during disease.[42]

In the 28 articles included in this systematic review, the initial nodal disease was 16% and cervical metastases rate ranged from 11% to 67% with an overall metastases rate of 33% in a total of 2,641 patients, which was similar to the cervical metastases from SCC of other oral sites, such as the tongue or floor of the mouth.

According to the tumour node metastasis classification system, T represents tumour size, depth of invasion, and relation with the surrounding tissue. The association between tumour site, size and grading and the risk of lymphatic metastases is well known for SCC of oral cavity and is not different for SCC of the maxilla.[44]

It is very significant that most of cervical metastases from SCC of the maxilla in the analysed series (71%) corresponded with a tumour size larger than 4 cm (T3 and T4 tumours). This rate of cervical metastases from big-sized tumours may suggest performing elective neck dissection only in patients with advanced disease. This finding has been observed by an American multicenter study by Montes *et al*.[16] about maxillary SCC, which reported a high percentage of cervical metastases in T3 and T4 tumours. Meng *et al*.,[21] in their series of 78 patients with SCC of the maxilla, reported that rates for positive nodal metastases from T1 and T2 tumours were lower than 15%, whereas those for T3 and T4 tumours were higher than 40%. Zhang *et al*.,[37] in a series of 100 patients, observed a 79% of cervical metastases in patients with T3/T4 SCC of the upper maxilla. Brown *et al*.[10] reported an 81% of cervical metastases in T3/T4 tumours in a series of 43 patients, while Berger *et al*.[40] in a series of 171 patients, observed a 78% of cervical metastases in patients with T3/T4 stage. Even others authors have reported that all the patients (100%) with advanced-stage (T3/T4) developed cervical metastases in some point during the study.[13,30,33,42]

Within our meta-analysis, in 24 out of 28 articles, metastases in patients with T3/T4 tumours were analysed, founding a total of 71% of cervical metastases. These data could demonstrate a significant connection between T-stage and metastatic cervical status, and may suggest that patients with advanced-stage (T3/4) disease face a significantly higher risk of metastases.

It is a fact that most clinicians do not routinely perform elective neck dissection when the neck is clinically or radiographically negative. However, the results from our systematic review suggest that elective neck dissection should be performed in patients with locally advanced SCCs of the hard palate and maxillary alveolus, despite the fact that SCC of these sites has traditionally been believe to have a low rate of occult metastases.

In spite of the results observed from this meta-analysis, we believe that it is important to highlight that most of the analysed studies are retrospective, with their intrinsic limitations. Furthermore, several papers are limited by the small number of patients enrolled in the study. Therefore, prospective studies with larger series are necessary.

In conclusion, this systematic review shows the fact that the rate of metastases in patients with SCC of the upper maxilla is high and comparable with metastases from other oral cavity cancers. Thus, the authors believe in the need for a change in the management of the N0 neck in SCC arising in the maxillary alveolus and hard palate. Elective neck dissection should be performed in patients with T3/T4 tumours with clinic or radiographic negative necks (N0c). Prospective studies with a large number of patients are necessary to confirm the results obtained from this study.

Conflicts of interest
There are no conflicts of interest.

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