

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

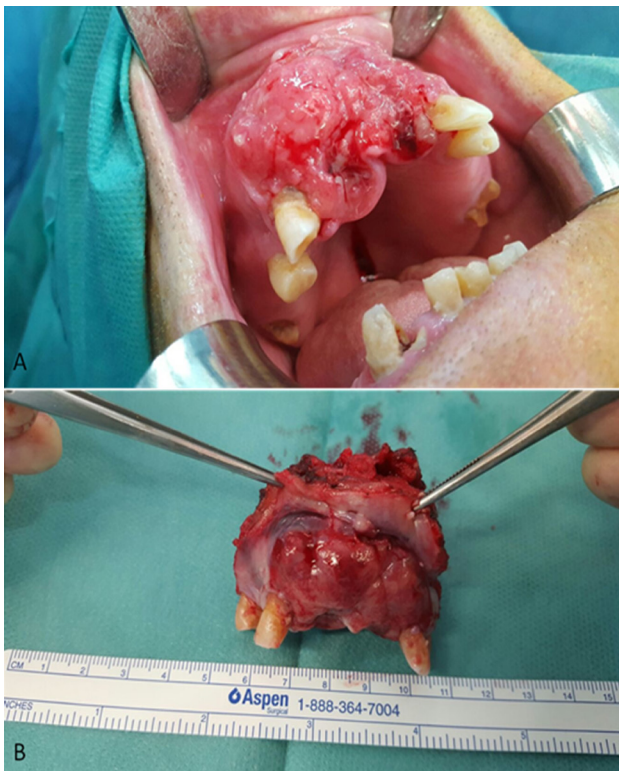


Figure 2: (A) Intraoperative photograph of a patient with T4 squamous cell carcinoma of the maxillary gingiva and bone invasion; (B) maxillary tumour was resected with wide surgical margins

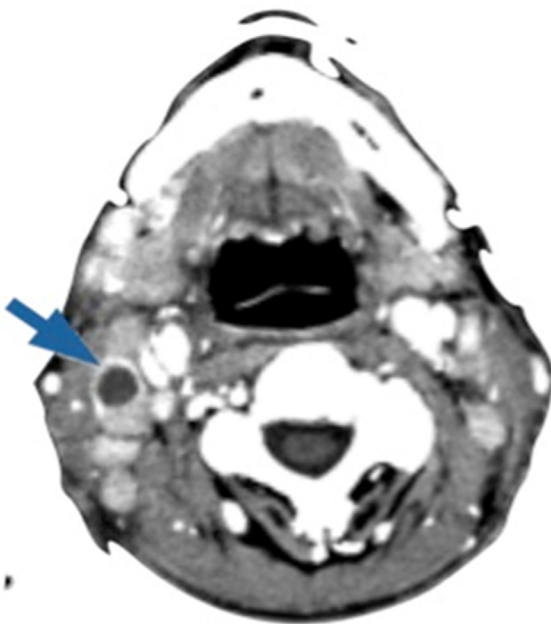


Figure 3: Computed tomography of the neck showing a cervical metastasis (arrow) of maxillary squamous cell carcinoma

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]

