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Management of the clinically node negative neck in squamous cell carcinoma of the maxilla

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ABSTRACT

Objective: The management of the clinically node negative (N0) neck in patients with squamous cell carcinoma of the maxilla (MSCC) is a matter of debate. In this retrospective cohort study the incidence of occult metastases is determined in clinically N0 MSCCs, as well as histopathological factors associated with occult metastases.

Patients and methods: 95 patients with clinically N0 MSCCs had maxillectomy. 18 patients with elective treatment of the neck were excluded. The remaining 77 patients followed a 'watch and wait' strategy for the neck and were included in this study. The incidence of occult metastases was calculated and Cox regression analysis was used to assess the predictive and prognostic value of clinical and histopathological parameters.

Results: Occult metastases occurred in 14.3% (11/77) in the whole cohort and in 19.0% (11/58) in T2-T4 clinically N0 MSCC. Patients with T4 clinically N0 MSCC, showed the highest rate of occult metastases (24.1%). 45.5% of the occult metastases developed in the contralateral neck. The hazard ratio to develop occult metastasis was 5.39 ($p = 0.017$) for perineural growth and 11.12 ($p = 0.003$) for perivascular invasion. Salvage for cervical recurrence was poor at 40%.

Conclusion: We recommend elective treatment of the neck or improved diagnostics to detect occult metastases in T2-T4 clinically N0 MSCC or when the biopsy specimen shows perineural growth or perivascular invasion. Since the contralateral neck was involved in 45.5% of the regional recurrences, we emphasize the importance of bilateral neck management. Improved diagnostics, like sentinel node biopsy, could possibly further reduce occult metastatic disease.

Introduction

Squamous cell carcinomas of the maxilla (MSCC) may present with or without lymph node metastasis in the neck. Lymph node involvement is the most important prognostic factor for these malignancies [1–4]. A therapeutic neck dissection, radiotherapy or both, is indicated in case of proven lymph node metastasis in the neck. For MSCC with clinically node negative (N0) neck, a 'watch and wait' strategy for the neck is traditionally followed because the metastatic risk is assumed to be low. However, nowadays this 'watch and wait' strategy has become a matter of debate because the impression arises that occult metastases occur more frequently than previously assumed. For squamous cell carcinoma of the oral cavity, elective treatment of the clinically N0 neck is widely applied when the risk of occult metastasis exceeds 15–20% [5–9]. For MSCC, however, few data exists that helps us decide when and how to treat the clinically N0 neck.

In our institution a 'watch and wait' strategy is followed for the neck in patients with clinically N0 MSCC. To evaluate this 'watch and wait' strategy we retrospectively determined the rate of occult metastases in patients with clinically N0 MSCC. Furthermore, we investigated which clinical or histopathological factors correlate with occult metastases.

Patients and methods

The Medical Research Ethics Committee gave approval for this study. MSCC was confirmed by histopathological examination. Staging took place according to the Union for International Cancer Control TNM classification [10] and was performed by physical examination (all), computed tomography (CT) ($n = 53$) and/or magnetic resonance imaging (MRI) ($n = 15$), ultrasound ($n = 56$), ultrasound guided fine needle aspiration cytology ($n = 21$) of

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enlarged or suspicious lymph nodes (e.g. short axis of more than 5 mm or central necrosis) and by chest X-ray (all).

MSCCs were resected with aimed margins of 10 mm and for the clinically N0 neck a 'watch and wait' strategy was followed.

Histopathological examination of the resection specimens included the differentiation grade, resection margins, perineural growth, spindle (spidery) growth and perivascular growth, the diameter of the tumor and the depth of invasion, and invasion into the maxillary sinus. Margins exceeding five millimeters were regarded as 'negative', margins between one to five millimeter as 'close' and margins less than one millimeter as 'positive'.

Based on the guidelines of our National Head and Neck Society [11], postoperative radiotherapy was administered in case of positive resection margins, or in the presence of two or more intermediate risk factors for recurrence (close resection margins, perineural growth, spindle (spidery) growth, pT3/T4 tumors).

Follow-up visits were scheduled every 2 months in the first year, every 3 months in the second year, every 4 months in the third year and every 6 months in the fourth and fifth year, and thereafter only on indication.

Local and regional recurrences were diagnosed through physical examination, histopathological and/or cytological examination.

Data collection

Patients with cT1-4 MSCC, clinically N0 neck and M0 were identified from the departmental database. Excluded were patients previously treated for head and neck cancer, tumors extending to the maxilla from another primary site, history of radiotherapy in the head and neck region for other diseases, incomplete medical records and patients treated off-protocol by either an elective neck dissection or elective radiotherapy to the neck.

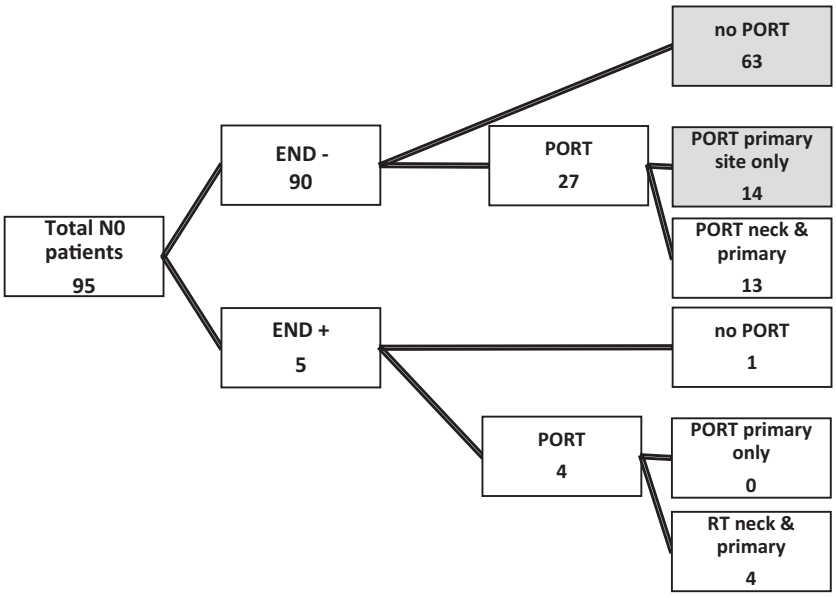
Clinical data were collected from the medical records: age, sex, time of diagnosis, bone invasion, crossing of the midline, cTNM stage, type of operation, pTNM stage, postoperative radiotherapy, date of recurrence, cause of death and follow-up time. Histopathological data were collected from the pathology report: differentiation grade, resection margins, perineural growth, spindle (spidery) growth and perivascular growth, diameter of the tumor and the depth of invasion, and invasion into the maxillary sinus.

Statistical analyses

Overall survival (OS) was defined as the length of the time interval from the histopathological diagnosis to death from any cause. Disease-specific survival (DSS) was defined as the time interval from the histopathological diagnosis to death from disease. In case of no event the patient was censored at the date of the last follow-up. OS and DSS were plotted for T-stage, using Kaplan-Meier survival curves. The significance of differences in survival were assessed with the log rank test. Hazard ratios were estimated by Cox proportional hazard regression. Univariate proportional hazard regression was used to assess the factors that were commonly found to affect the outcome of oral squamous cell carcinoma: age, cT-stage, pT-stage and the histopathological parameters as described previously. Factors found significantly different in the univariate analysis were considered for multivariate Cox proportional hazard regression. Two-sided significance tests were performed. Analysis was aided by the Statistical Package for the Social Sciences (version 21.0 for Windows, SPSS Inc., Chicago, USA). Probabilities of less than 0.05 were accepted as significant.

Results

Between 1990 and 2014, 95 patients had surgery with cT1-4N0M0 MSCC. 18 of these 95 patients were excluded because these patients were treated off-protocol, either with an elective neck dissection (n = 5) or with elective radiotherapy to the neck (n = 13) (Fig. 1). These 18 patients had no clear indication for elective neck dissection or elective radiotherapy to the neck and none of these patients had pN+. In the remaining 77 patients, a partial or total maxillectomy was performed, followed by a 'watch and wait' strategy for the clinically N0 neck. These 77 patients were included in this study. The baseline characteristics of the included patients are listed in Table 1. The histopathological findings of the resection specimen are listed in Table 2. Of these 77 patients, 14 received



Included in the study 77 clinically N0 MSCC (Grey color). END = Elective Neck Dissection, PORT = Postoperative radiotherapy.

Fig. 1. Flow chart with treatment modalities of 95 clinically N0 MSCC.