

Long-term results of the combined modality therapy for advanced cervical metastatic head and neck squamous cell carcinoma

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Abstract

Aim: A consensus treatment strategy for advanced cervical metastatic head and neck squamous cell carcinoma has not been established. The aim of this retrospective study was to investigate the outcome of these patients uniformly using a strategy which consists of surgery for the primary tumor and the neck metastases followed by postoperative radio(chemo)therapy.

Methods: We included a selected series of 518 patients with previously untreated head and neck squamous cell carcinoma. The overall survival (OS), the disease specific survival (DSS), the disease free survival (DFS), the local control (LC) and regional control (RC) estimates were calculated. The statistical relationship of various clinical and histopathological variables on the above mentioned estimates were analyzed.

Results: The overall survival probability was 73.2% for pN0 stage, 43% for pN > 1 stages and 31% for pN2c/pN3 stages. The pN stage significantly influenced the survival probabilities in oropharyngeal ($p = 0.0001$) and laryngeal tumors ($p < 0.0001$) in univariate analyses. In multivariate analysis, age, pT stage, pN stage, M stage, and extranodal spreading were independent risk factors for decreased disease-specific survival.

Conclusions: We could show that pN stage is an important independent prognostic factor in head and neck cancer. The presented multimodal treatment protocol provides excellent oncological outcomes and should therefore be standard of care for patients with operable advanced cervical metastatic head and neck squamous cell carcinoma.

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Keywords: Cervical lymph node metastases; Head and neck carcinoma; Multimodal treatment; Survival

Introduction

The prognosis of Head and Neck Squamous Cell Carcinoma (HNSCC) is reported to be significantly related to the presence of cervical lymph node metastases.^{1–4} The lymph node status seems to be the major clinical determinant of patient outcome. The treatment protocols for patients with advanced cervical metastases vary from primary radiotherapeutic approaches for both the primary tumor and the neck metastases to primary surgical therapies and postoperative

radiation therapy. Furthermore, numerous combinations of both forms of therapy in different settings have been reported.^{5–9} Accordingly, various treatment protocols have been proposed to be superior to others.^{10–23} Survival remains the most important factor for this therapeutic decisions but other aspects like treatment related quality of life become an increasingly important determinant. The surgical techniques as well as the radiotherapeutic protocols advanced in the recent years, which improved not only the survival parameters but also the patients' quality of life. In our institution, we uniformly use a well established strategy of surgery for the primary tumor and the neck metastases followed by postoperative radio(chemo)therapy for operable advanced head and neck cancer. The aim of this

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retrospective study was to investigate the outcome of patients with HNSCC uniformly using this treatment strategy. We hereby especially focused on advanced (N2–N3) neck metastases of a primary squamous cell carcinoma. Furthermore, we attempted to identify clinical factors influencing the outcome of this multimodal approach.

Patients and methods

Patients

In this retrospective study, we included a selected series of 518 patients with previously untreated HNSCC treated at our institution between 1992 and 1998. Included in the analysis were patients treated with surgery alone or with a combined surgical and radiotherapeutical approach. Further inclusion criteria were squamous cell carcinoma in histology and a curative treatment intend. Exclusion criteria were carcinomas of unknown primary, sinonasal and salivary gland tumors, patients who did not undergo surgical treatment (radiochemotherapy alone, chemotherapy or no specific oncological treatment) and patients with evidence for distant metastases or second primary tumors at the initial staging examinations. Staging examinations consisted of a panendoscopy, chest-X-Ray/CT-scan of the thorax, ultrasound of the abdomen/CT-scan of the abdomen and, in selected cases, a bone scintigraphy.

All tumors were classified according to the TNM Classification System (UICC, 1997).²⁴ The TNM classification of the tumors and their sites are shown in Tables 1 and 2. The mean age of the patients was 59.6 years (range from 24 to 87 years). The male to female ratio was 6.4:1 (448 vs 70). Follow-up was calculated from the time of surgery until the date of last contact or death. The mean follow-up time was 44.5 months with a minimum of 10 days and a maximum of 104.6 months.

Treatment

All patients in the series were treated according to the following treatment protocol

Surgical treatment was performed if complete resection of the primary tumor was technically achievable according to the clinical and radiological presentation. Surgical treatment was performed using standard operation techniques. In the clinical negative neck (cN0), ipsilateral elective

Table 2
Tumor distribution and associated stages

Site	Disease Stage				Overall
	1	2	3	4	
Larynx	81	87	53	73	294
Oropharynx	6	16	22	60	104
Hypopharynx	3	2	11	49	65
Oral cavity	18	11	8	18	55
Overall	109	118	97	204	518

neck dissection was performed in all patients except for limited laryngeal cancer (T1 and T2). Bilateral elective neck dissection was performed if the primary tumor was located in or crossing the midline. In the clinical positive neck (cN+), a curative radical-modified neck dissection was performed if there was no infiltration of the skull base or the internal carotid artery in the radiological work-up. Postoperative radiotherapy or if feasible radiochemotherapy was performed in any positive neck after pathological work-up (pN+), incomplete resection of the primary tumor, and all pT3/4 tumors independently of the N status. Radiotherapy was performed using linear accelerators with 5 to 6 MeV photon beams in daily fractions of 1.8–2.0 Gy, 5 days a week. A total dose of 50 Gy was delivered to the primary tumor lesions and the bilateral cervical lymphatic drainage. A total dose of 60 Gy was delivered to the primary tumor region and macroscopically involved primary lymph nodes. Incompletely resected tumors or neck metastases with extracapsular spread were treated with up to 66 Gy. Depending on overall performance status, organ function and comorbidities of patients radiotherapy was combined with concurrent carboplatin chemotherapy (AUC 1 on days 1–5 and 29–33). A laryngectomy was performed in 31.1% of all cases, transoral tumor resection in 58.5% of all cases, transcervical tumor resection in 8.5% of all cases, and 68.3% of all patients underwent a neck dissection. Sole surgery was performed in 49.4% of all patients whereas 50.6% of all patients received surgery plus postoperative radio(chemo)therapy. Advanced cervical metastatic disease was defined as pN > 1. Follow-up data was collected at periodic visits in 4 to 6 months intervals at our outpatients department. Follow-up time was defined as the time from the date of the first tumor operation until the date of the last visit or the date of death.

Statistical methods

Statistical analysis of the data was performed using SPSS software for medical statistics. The overall survival (OS), the disease specific survival (DSS), the disease free survival (DFS), the local control (LC) and regional control (RC) estimates were calculated using the Kaplan–Meier method. The statistical relationship of following variables on the above mentioned estimates were analyzed: age, sex, localization of the primary tumor, stage in groups pT, pN, surgery ± RCT,

Table 1
TNM-classification

	pN0	pN1	pN2a	pN2b	pN2c	pN3	Total
pT1	108	3	2	5	1	4	123
pT2	116	20	5	31	14	7	193
pT3	53	18	3	29	15	7	125
pT4	21	7	4	15	21	9	77
Total	298	48	14	80	51	27	518

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