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Importance of chewing, saliva, and swallowing function in patients with advanced oral cancer undergoing preoperative chemoradiotherapy: a prospective study of quality of life

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Abstract. The primary objective of this study was to investigate the quality of life (QOL) of patients with oral squamous cell carcinoma (OSCC) undergoing curative neoadjuvant chemoradiotherapy followed by radical tumour resection and simultaneous oral cavity reconstruction, using two validated questionnaires. A secondary objective was to assess clinical variables predicting post-treatment dysfunction in chewing, saliva, and swallowing. Thirty-five patients with locally advanced OSCC who underwent preoperative chemoradiotherapy were recruited prospectively. All patients completed both the University of Washington Quality of Life version 4 questionnaire (UW-QOL) and the Functional Assessment of Cancer Therapy–Head & Neck version 4 questionnaire (FACT-H&N). UW-QOL and FACT-H&N items were associated with clinical variables. Nearly three-quarters of OSCC patients perceived good to excellent levels of overall QOL after preoperative chemoradiotherapy. Chewing difficulties, decreased salivary function, and swallowing dysfunction were the most frequent complaints of OSCC patients. Items related to food intake were significantly worse in OSCC patients older than 60 years and those with T4 tumours, as well as those without alcohol intake. Chewing, saliva, and swallowing are the most significant issues in patients with OSCC undergoing preoperative chemoradiotherapy. The results of this study may help guide treatment decisions for OSCC patients based on more accurate expectations of adverse effects of cancer treatment.

Key words: oral cancer; quality of life; neoadjuvant chemoradiotherapy; mastication; saliva; swallowing.

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With an estimated 90,000 new cases and approximately 40,000 deaths annually in Europe, oral squamous cell carcinoma (OSCC) represents a major health issue[1]. To date, surgery followed by postoperative radiotherapy or chemoradiotherapy has been considered the mainstay of curative treatment for patients with locally advanced OSCC in most institutions[2]. However, accumulating evidence suggests that neoadjuvant chemoradiotherapy followed by surgery represents an effective alternative option in the management of patients with locally advanced OSCC[3–9]. The neoadjuvant therapy protocol may facilitate tumour down-staging, thus leading to higher curative resection rates, as well as the elimination of distant micrometastases[10].

In the last few years, patient-reported outcomes such as quality of life (QOL) have been used increasingly to complement disease-related clinical measures in the assessment of the risk–benefit profiles of cancer treatment regimens[11–15]. QOL is of particular concern for patients with locally advanced OSCC who experience the adverse effects of multimodal treatment including surgery and radiation or chemoradiotherapy and the late negative sequelae, such as problems with nutritional intake, speaking, and breathing, as well as psychological issues related to functional impairments and facial disfigurement[16–18].

Surgery for advanced OSCC results in a loss of structural integrity in the head and neck region, while functional and aesthetic impairments after tumour surgery depend on the extent of the resection, the tumour site, and the type of reconstruction[19,20]. Radiation-induced side effects have a multifaceted pathogenesis involving inflammation, oedema, hyposalivation, and fibrosis, with subsequent neuromuscular disorders[21]. Concomitant chemoradiation has shown synergistic and additive effects and may increase adverse effects due to the enhancement of radiation-induced fibrosis of the musculature[19]. To date, few studies have analyzed QOL outcomes with an emphasis on oral functions in patients with OSCC undergoing neoadjuvant chemoradiotherapy followed by radical tumour resection[22,23].

The primary objective of this study was to investigate the QOL of patients with locally advanced OSCC undergoing preoperative chemoradiotherapy followed by surgery with simultaneous oral cavity reconstruction, using both the University of Washington Quality of Life version 4 questionnaire (UW-QOL) and the Functional Assessment of Cancer Therapy–Head & Neck version 4 questionnaire (FACT-H&N). Based on these questionnaires, a secondary objective was to assess patient- and treatment-related factors predicting difficulties in chewing, decreased salivary function, and swallowing dysfunction.

Materials and methods

Patients and treatment

A prospective study was conducted including 35 patients with primary locally advanced OSCC undergoing curative neoadjuvant chemoradiotherapy followed by radical tumour resection and simultaneous oral cavity reconstruction at the Medical University of Vienna between 2005 and 2009. Patients eligible for participation in the study had to fulfil the following inclusion criteria: (1) biopsy-proven primary OSCC, (2) clinical TNM stage III or IV, (3) no evidence of distant metastatic disease (M0), (4) no history of other cancer in the head and neck region, (5) reconstruction at the time of surgical resection with either a microvascular free flap or pedicled regional flap, (6) clear resection margins, (7) no evidence of tumour recurrence at the time of recruitment, with a minimum of 1 year disease-free survival, and (8) ability to understand the written and spoken German language.

All patients received multimodal treatment consisting of neoadjuvant chemoradiotherapy and surgery as described previously[24]. In brief, chemotherapy consisted of mitomycin C (15 mg/m^2, an intravenous bolus injection on day 1) and 5-fluorouracil (750 mg/m^2/day, continuous infusions on days 1–5). Concurrent radiotherapy was delivered over 5 weeks for a cumulative dose of 50 Gy (25 fractions of 2 Gy per day). Surgical resection with simultaneous oral cavity reconstruction (microvascular free flaps or regional pedicled flaps) was performed 4–8 weeks after the finalization of radiotherapy. Patients were followed up for at least 5 years (at 3-month intervals during the first 2 years and at 6-month intervals for the next 3 years) or until death. The pathological response to neoadjuvant chemoradiotherapy was assessed in surgical specimens as described previously[25], according to the percentage of vital residual tumour cells in relation to the tumour bed: no vital tumour cells, <5% of vital tumour cells, 5–50% of vital tumour cells, and >50% of vital tumour cells (regression grades (RG) 1, 2, 3, and 4, respectively).

Questionnaires

Eligible patients were recruited prospectively and were asked to complete the questionnaires while waiting to be seen in the outpatient clinic during their follow-up visit at 1 year post-treatment. The study was explained in detail by two investigators (A.H. and C. P.) and written informed consent for participation in the study was obtained from all patients. In order to measure patient QOL the following surveys were used: the UW-QOL version 4, the FACT-H&N version 4, and an in-house questionnaire[26,27]. For all patients, clinical information was obtained from their medical history, physical examination, radiology reports, and medical records found in the Vienna General Hospital Patient Information System (AKIM).

The UW-QOL version 4 questionnaire in the German language used in this study was retrieved from http://www.headandneckcancer.co.uk/For+professionals/Quality+of+Life+(QOL)/UW-QOLv4+Translations.aspx (Fig. 1A; the UW-QOL version 4 questionnaire in English is given in Fig. 1B). The UW-QOL questionnaire consists of four different sections. The first section measures QOL over the past 7 days by addressing 12 items related to the patient's physical and social–emotional function. The items chewing, swallowing, speech, taste, saliva, and appearance comprise the physical UW-QOL subscale, while the items pain, activity, recreation, mood, shoulder function, and anxiety comprise the social–emotional UW-QOL subscale[28]. The item-specific questions have three to six possible response options that are scaled evenly from 0 (worst) to 100 (best). Consequently the questions with six possible responses are scored as 0, 20, 40, 60, 80, and 100, those with five responses as 0, 25, 50, 75, and 100, those with four responses as 0, 30, 70, and 100, and those with three responses as 0, 50, and 100. In the second section of the instrument (UW-QOL importance rating), patients are asked to choose up to three items that affected them the most in the past 7 days. The most important item chosen receives 1 point, while the items not chosen receive 0 points. The third section of the questionnaire includes three global questions, ranked from 0 (worst) to 100 (best). The patients are asked about (1) current health-related quality of life (HR-QOL) compared to 1 month before developing cancer (scored as 0, 25, 50, 75, and 100), (2) HR-QOL during the past 7 days (scored as 0, 20, 40, 60, 80, and 100), and (3) overall quality of life (Overall-QOL) during the

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