Int. J. Oral Maxillofac. Surg. 2016; 45: 141–146
http://dx.doi.org/10.1016/j.ijom.2015.09.005, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Head and Neck Oncology

Evaluation of the level of progression of extracapsular spread for cervical lymph node metastasis in oral squamous cell carcinoma

S. Yamada [1,2], S. Yanamoto[1], S. Otani[1], T. Hasegawa[3], M. Miyakoshi[4], T. Minamikawa[3], N. Ohga[4], T. Kamata[2], T. Komori[3], Y. Kitagawa[4], H. Kurita[2], M. Umeda[1]

[1]Department of Clinical Oral Oncology, Unit of Translational Medicine, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [2]Department of Dentistry and Oral Surgery, Shinshu University School of Medicine, Nagano, Japan; [3]Department of Oral and Maxillofacial Surgery, Kobe University Graduate School of Medicine, Kobe, Japan; [4]Oral Diagnosis and Medicine, Department of Oral Pathobiological Science, Graduate School of Dental Medicine, Hokkaido University, Hokkaido, Japan

S. Yamada S. Yanamoto, S. Otani, T. Hasegawa, M. Miyakoshi, T. Minamikawa, N. Ohga, T. Kamata, T. Komori, Y. Kitagawa, H. Kurita, M. Umeda: Evaluation of the level of progression of extracapsular spread for cervical lymph node metastasis in oral squamous cell carcinoma. Int. J. Oral Maxillofac. Surg. 2016; 45: 141–146.

Abstract. Only a few reports on the level of progression of extracapsular spread (ECS) have been published. The aim of this study was to evaluate the efficacy of the level of progression of ECS in identifying those patients with oral squamous cell carcinoma (OSCC) at a high risk of recurrence who would benefit most from the intensification of adjuvant therapy. The level of progression of ECS for cervical lymph node metastasis in OSCC was divided into three types (A–C), and their relationships with patient prognosis were examined. ECS was observed in 87 of 441 patients with OSCC. The recurrence rate in patients with type C, which was defined as macroscopic tumour invasion into perinodal fat or muscle tissue, was high (69.8%), with 13 cases of death due to distant metastasis. The 3-year disease-specific survival rate for patients with type C was 49.0% and these patients also had a significantly poorer prognosis ($P < 0.01$). The results of the multivariate analysis suggested that the prognosis of ECS in OSCC patients was associated with the level of progression of ECS, especially type C ($P < 0.01$). Overall, the results of this study suggest that the level of progression of ECS is a useful prognostic factor in OSCC patients.

Key words: cervical lymph node metastasis; extracapsular spread; oral squamous cell carcinoma; prognostic factor.

Accepted for publication 7 September 2015
Available online 2 October 2015

Oral squamous cell carcinoma (OSCC) is the most common malignant tumour of the head and neck region and accounts for more than 90% of cancers in the oral cavity.[1] Although recent advances in surgical techniques and anticancer agents have improved tumour regression and survival in patients with OSCC, wide surgical resection of OSCC inevitably results in various oral dysfunctions. Prognostic factors have been examined in OSCC patients, including the level of progression of the tumour (such as the TNM classification and stage classification), differentiation of the primary tumour, the pattern of

invasion, the depth of tumour invasion, vascular invasion, the extent of cervical lymph node metastasis, and extracapsular spread (ECS).[2–4] Regarding treatment strategies for OSCC, cervical lymph node metastasis is important for predicting the prognosis and the application of adjuvant therapy. The extracapsular spread of cervical lymph node metastasis has previously been identified as a strong prognostic factor in OSCC patients at a high risk of recurrence.[5–10]

In 2004, the European Organisation for Research and Treatment of Cancer (EORTC) and the Radiation Therapy Oncology Group (RTOG) reported the findings of two randomized trials (EORTC trial 22931 and RTOG trial 9501) that evaluated the role of concomitant chemotherapy-enhanced radiation therapy (CCRT) in a postoperative setting for head and neck squamous cell carcinoma (HNSCC) patients at high risk of recurrence and metastasis including ECS.[11,12] Concurrent chemoradiotherapy with a high dose of the single agent cisplatin has recently been recognized worldwide as the standard treatment for patients with resectable, advanced HNSCC who are at high risk of recurrence and metastasis. Based on the findings of the long-term follow-up of RTOG trial 9501 and on a pooled analysis of EORTG trial 22931 and RTOG trial 9501, ECS has also been identified as a strong prognostic factor for patients at a high risk of postoperative recurrence.[13,14] However, few studies have examined the level of progression of ECS as an indication for CCRT.[6,7,10]

The aim of the present study was to evaluate the efficacy of the level of progression of ECS in OSCC patients at a high risk of recurrence in identifying those patients who would benefit most from the intensification of adjuvant therapy. The results of this study may improve the postoperative management of patients with advanced OSCC.

Materials and methods

The medical records of all patients treated between January 2008 and December 2012 at Nagasaki University Hospital, Kobe University Hospital, Hokkaido University Hospital, and Shinshu University Hospital for OSCC with neck dissection were reviewed retrospectively. Patients with synchronous or metachronous lesions and those receiving neoadjuvant therapy were excluded. Four hundred and forty-one patients who had undergone surgery for OSCC were identified. Patients with N0 or limited N1 disease generally underwent a supraomohyoid neck dissection. Patients with more advanced nodal disease underwent more comprehensive modified radical neck dissection. Patients with high-risk characteristics (defined as any or all of the following: histological evidence of invasion of two or more regional lymph nodes, ECS, and microscopically involved margins of resection) underwent concurrent chemoradiotherapy with high-dose single agent cisplatin (100 mg/m^2) and radiation therapy ($\geq$60 Gy). If this was not possible due to the poor performance status or general condition of the patient, radiotherapy ($\geq$60 Gy) was performed.

ECS was detected in 87 of the 441 patients. The prepared specimen was obtained for pathological re-examination, and the level of progression of ECS outside of the lymph nodes was scored, with peer-review by two authors at each institution. The level of progression of ECS was divided into three types (Fig. 1): (1) type A: tumour cells are exposed directly to the outside of the capsule due to capsular perforation or disappearance of the capsule, but there are few tumour cells outside the lymph node capsule; (2) type B: there is slight invasion of the tumour cells into perinodal fat tissue, with capsular destruction, seen microscopically; (3) type C: there is macroscopic tumour invasion extending into perinodal fat or muscle tissue.

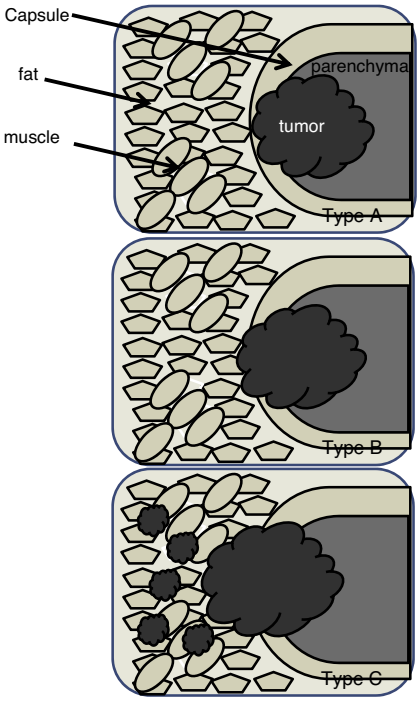

Fig. 1. Level of progression of ECS. Type A: tumour cells are exposed directly to the outside of the capsule due to capsular perforation or disappearance of the capsule; however, few tumour cells are outside the lymph node capsule. Type B: there is slight invasion of tumour cells into perinodal fat tissue, with capsular destruction, seen microscopically. Type C: there is macroscopic tumour invasion extending into perinodal fat or muscle tissue.

The Kaplan–Meier method was used to examine disease-specific survival (DSS) and relapse-free survival (RFS). DSS was defined as the time from the performance of neck dissection to the occurrence of death from OSCC, and RFS as the time from the performance of neck dissection to the occurrence of regional recurrence, distant metastasis, or death from any cause. Differences between survival curves were examined with the log-rank test. Fisher's exact test was used to identify independent risk factors for neck recurrence and distant metastasis in a univariate analysis, and the Cox proportional hazard model was used in a multivariate analysis. Predictors that were not associated with regional recurrence or distant metastasis were not included in the multivariate analysis. Statistical analyses were performed using StatMate IV (ATMS Co., Ltd, Tokyo, Japan). For all analyses, a *P*-value of <0.05 was considered to indicate significance.

Results

Eighty-seven patients with ECS from the population of 441 OSCC patients who underwent the initial surgery without neoadjuvant therapy were included in this study. The characteristics of these OSCC patients with ESC are shown in Table 1. The mean age at diagnosis was 66.7 years (range 32–89 years). The most common primary site was the tongue (50.6%, 44/87 patients); 16.1% of patients had lower gingival cancer, while 12.6% had oral floor cancer and 12.6% had buccal mucosa cancer. The median duration of follow-up was 20 months (range 1–68 months). The recurrence rate, which included regional recurrence and distant metastasis, was 51.7% (45/87 patients). The 13 patients died due to distant metastasis. The mean period that elapsed before recurrence was 4 months (range 1–24 months).

Regarding the level of progression of ECS, type A was identified in 31.0% of patients (27/87), type B in 19.5% (17/87), and type C in 49.4% (43/87). The recurrence rate in patients with type A was 29.6% (8/27 patients), while those in patients with types B and C were 41.2% (7/17 patients) and 69.8% (30/43 patients), respectively. The Kaplan–Meier method