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Prediction score for lymph node metastasis from cutaneous squamous cell carcinoma of the external ear

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Abstract

Aims: The frequency of lymph node metastasis (LNM) is higher in cutaneous squamous cell carcinoma (cSCC) of the ear than in other head and neck cSCCs. Nodal dissemination is associated with a significantly worse prognosis and disease-specific survival. The aim of this study was to establish a prediction model for LNM in patients with cSCC of the ear.
Materials and methods: Tumour characteristics of 353 patients with ear cSCC were analysed to assess differences between those with and without LNM and to calculate a prediction score for LNM occurrence.
Results: Regional LNM occurred in 10.5% of patients. Five-year disease-specific survival was significantly lower in the LNM group than in the control group (59% vs. 99%; $p < 0.001$). Recurrence number, invasion of cartilage, tumour depth, and tumour grading were the most important predictors for LNM, with correct prediction of LNM in 94.0% of cases. Our prediction score stratified patients into high and low risk groups ($p < 0.001$) with a sensitivity of 89.2%, a specificity of 94.6%, and an overall accuracy of 94.1%.
Conclusion: Our new prediction model was able to accurately identify patients at high risk of LNM who may benefit from elective lymph node surgery.

Keywords: Ear neoplasms; Squamous cell carcinoma; Lymphatic metastasis; Prognosis; Lymph node excision

Introduction

Cutaneous squamous cell carcinoma (cSCC) is the second most common type of skin cancer, with an incidence of 30 new cases per 100,000 people per year in Europe, and the incidence continues to rise by 4–8% per year.[1–3] The ears are a frequent site of cSCC occurrence in the head and neck area, with cSCC being the most common histological type of cancer of the auricle.[3–7]

cSCC of the ear most often develops in the helix and antihelix, followed by the retroauricular region and cavum conchae.[8,9] This malignancy usually develops slowly, and the currently reported frequency of initial regional lymph node metastasis (LNM) ranges from 4% to 11%[8,10–15]; however, rates of upto 37% have also been previously described.[16,17] The development of secondary LNM ranges from 6% to 13%; therefore, the total mean risk of LNM in cSCC of the external ear is approximately 15.5%, a significantly higher rate than that for overall cSCC.[2,3,18] Five-year overall survival rates for patients with cSCC of the ear without LNM are 87–95%, whereas those in patients with LNM decrease to 25–50%.[4,10,11,15,17,19,20] In general, LNM is the most important prognostic factor in patients with head and neck cSCC.[2,21] Previous studies in 2 Australian cancer centres analysed prognostic factors in patients with metastatic cSCC.[22,23] While characteristics of the primary tumour, with the exception of histologic differentiation (grading), had only limited prognostic relevance,

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immunosuppression and extracapsular spread in nodal metastases were significantly associated with a poor outcome. This research group also developed a revised staging system for head and neck cSCC with nodal metastasis, taking into account the number and size of involved lymph nodes.[24]

Therefore, identifying patients with cSCC of the ear who are at high risk of LNM is crucial for adequate lymph node management and for improving outcomes in these patients. Various prognostic factors for LNM in ear cancer have been reported[4,8,10–16,19,20,25–27]; however, different studies have reported inconsistent and even conflicting results. Moreover, a standardized definition of "high risk" patients who would benefit from elective lymph node surgery has not yet been established.[11,13–15]

Therefore, the objective of this study was to identify clinically useful, assessable preoperative prognostic factors for LNM from cSCC of the ear and to develop a prediction model for LNM to improve outcomes in these patients.

Materials and methods

Patients

Consecutive patients with histologically proven cSCC of the ear who were treated surgically between 2005 and 2011 were retrospectively identified from our institutional database.

This study was approved by the local ethics committee (Ethical Committee of the Westphalian Wilhelms-University Muenster, Approval-No. 2006-088-f-S) and was conducted in accordance with the Guidelines for Good Clinical Practice and in compliance with the Declaration of Helsinki. All participating patients provided written informed consent.

Inclusion criteria for this study were as follows: cSCC of the external ear, absence of other SCCs in the head and neck region, surgical treatment, histologically proven diagnosis of invasive ear cancer, and complete information available in the database. Patients with multiple cSCCs in the head and neck region, those with a history of SCC in the head and neck region (except for previous cSCC of the auricle), and those who previously underwent lymph node surgery were excluded. We assessed only patients with primary or recurrent cSCC of the ear and without history or treatment of any other head and neck SCC. All patients received complete appropriate staging prior to surgery, according to German guidelines.[2] Accordingly, clinical examination of the head and neck region, palpation of head and neck lymph nodes, ultrasonography of head and neck lymph nodes (criteria for pathological nodes: loss of hilar architecture, intranodal necrosis and calcification, hyperechogenicity, round shape (longest-to-shortest ratio <2)), radiography of the chest, and abdominal ultrasonography was performed in all patients. Patients with clinically suspicious or enlarged lymph nodes or those with advanced tumour stages (tumour >4 cm in diameter [>T3], clinical infiltration of surrounding tissues, or tumour affecting more than 1 anatomical region of the auricle) underwent additional computed tomography of the head and neck. Follow-up was conducted every 3 months in the first and second year and every 6 months thereafter; follow-up included clinical examination and head and neck ultrasonography in all patients. In case of suspicious findings, additional diagnostics (computed tomography of the head, neck, and chest or magnetic resonance imaging) were performed. A minimum follow-up time of 6 months was necessary for inclusion in this study. Patients who developed regional LNM during the observation period were classified as the LNM group, and those without LNM were classified as the control group.

Methods

Relevant characteristics and parameters for analysis included age at the time of surgery and first diagnosis, gender, immunosuppression (no/yes), primary tumour site, recurrence number, TNM stage, Union for International Cancer Control (UICC) stage (according to the 2005 classification), histological grading, depth of tumour invasion (tumour depth [TD]), invasion of the perichondrium and cartilage (yes/no), perineural invasion (yes/no), resection margins (R0 = negative margins, R1 = microscopically positive margins, or R2 = macroscopically positive margins), minimal safety margin, lymph node surgery (none, lymph node picking, neck dissection, and/or parotidectomy), time of lymph node surgery (primary [together with tumour resection or within the first 4 weeks of tumour resection] or secondary), adjuvant radiation, local tumour recurrence during the observation period (yes/no), LNM (yes/no), distant metastases (yes/no), and disease-specific survival (DSS).

Statistical analysis

Categorical variables were analysed using the chi-square test and Fisher's exact test. For continuous variables, the Mann–Whitney *U* test was used as a non-parametric test for abnormally distributed data (age and minimal safety margin), and an independent *t*-test was used to analyse normally distributed variables (tumour depth). DSS (time from first diagnosis until tumour-dependent death; data on patients without tumour-dependent death were censored at the last follow-up time) was calculated using the Kaplan–Meier method, and group differences were analysed using the log-rank test.

Binary logistic regression analysis (BLR) was used to model the predictors of LNM, including patient, tumour, and treatment characteristics. Potential predictors identified by the chi-square test, Mann–Whitney *U* test, and independent *t*-test analyses were entered into a stepwise forward fashion using $p < 0.05$ for entry and $p > 0.1$ for removal.