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Prognostic factors in head and neck mucoepidermoid carcinoma: experience at a single institution based on 64 consecutive patients over a 28-year period

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Abstract. Mucoepidermoid carcinoma (MEC) is the most common malignancy of the salivary glands. The clinical behaviour of MEC is largely unpredictable, ranging from indolent tumour growth to highly aggressive metastatic spread. The objective of this study was to determine the clinicopathological predictors of recurrence and survival in patients with head and neck MEC. The medical records of 64 patients who underwent surgical treatment for head and neck MEC between 1982 and 2010 were reviewed. The main outcome measures were disease-free survival (DFS) and overall survival (OS). Clinicopathological parameters evaluated were age, sex, anatomical subsite, histological grade, tumour stage, tumour size, adjuvant therapy, and nodal and margin status. For the entire cohort, the 5-year DFS was 82.8% and the 5-year OS was 67.2%. Histological grade and tumour subsite were statistically significant predictors of OS. Furthermore, tumour stage and nodal status were statistically significant predictors with respect to OS. Advanced tumour stage, high histological grade, submandibular/sublingual localization, and positive nodal status were independent predictors of the prognosis in patients with head and neck MEC. Further studies into the molecular biology of MEC are needed in order to provide new therapeutic strategies for patients with locally aggressive and highly metastatic carcinomas.

Key words: head and neck; salivary gland tumours; mucoepidermoid carcinoma; recurrence; survival.

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Mucoepidermoid carcinoma (MEC) is the most common malignancy of the salivary glands, representing 30–40% of all major salivary gland malignancies and up to half of parotid gland malignancies[1,2]. The clinical behaviour of MEC is highly variable, ranging from indolent tumour growth to highly aggressive metastatic spread. In order to clarify its very variable behaviour, different prognostic factors have been investigated. Conventional clinicopathological parameters such as age, sex, tumour site, stage, TNM status, extracapsular spread (ECS), adjuvant therapy, and margin status have been shown to have predictive value with respect to survival, although inconsistently[3–5]. However, it is generally accepted that the most relevant prognosticators of survival are tumour grade and disease stage[4,6,7].

The aim of this study was to describe head and neck MEC treated at a tertiary care hospital centre (University Hospital Dubrava), as well as to determine the clinicopathological predictors of recurrence and survival in this patient population.

Materials and methods

A retrospective chart review covering the period 1982–2015 was conducted. The following data were collected: age, sex, tumour site, histological grade, stage, type of treatment modality, nodal status, histological status of the surgical margins, disease status, and follow-up.

The study included 64 patients with head and neck MEC treated between 1982 and 2010. Inclusion criteria were histologically proven and surgically treated head and neck MEC. Patients with adverse histopathological features (high-grade tumours, positive margins, perineural invasion, ECS, multiple positive lymph nodes, stage T3 or T4) underwent postoperative irradiation. MEC was staged according to the TNM classification of malignant tumours of the salivary glands.

At the study institution, MEC is categorized as low grade (LG), intermediate grade (IMG), or high grade (HG) carcinoma according to the World Health Organization classification, on the basis of the following data: amount of cystic component, presence of neural invasion, presence of necrosis, number of mitoses per 10 high-power fields (HPF), and presence or absence of anaplasia[8]. Points are given for all of the listed data, which are added together. The point score obtained corresponds to the tumour grade, which in the case of MEC can be low, intermediate, or high grade. None of the patients were lost to follow-up.

Statistical analysis

The χ^2 test or Fisher's exact test was used to assess associations of the clinicopathological parameters. The primary endpoints were disease-free survival (DFS) and overall survival (OS). Follow-up intervals were calculated in months from the date of first surgical treatment to the date of last follow-up or death. A DFS event was defined as a pathologically confirmed recurrence. An OS event was defined as death from any cause. Patients with IMG-MEC were included in LG-MEC due to the small sample size in the IMG group and similar biological behaviour between these two histological subtypes. DFS and OS curves were estimated by Kaplan–Meier method, while the log-rank test was used to test differences between the actuarial curves. Multivariate analysis using the Cox proportional hazards model or logistic regression analysis was not done due to the small sample size of the study group. All statistical analyses were performed using Statistica data analysis software version 10, 2010 (StatSoft, Inc., Tulsa, OK, USA) and *P*-values of <0.05 were considered statistically significant.

Results

Of the 64 patients included, 28 (43.7%) were female and 36 (56.3%) were male. Their mean age at diagnosis was 46.9 years (range 9–80 years). Sixty (93.8%) previously untreated patients presented directly to the study hospital, while four patients (6.2%) were referred to the study hospital due to recurrent tumours. Of those with previously untreated tumours, 44 patients had stage T1/T2 tumours and 15 had stage T3/T4 tumours (advanced disease). The disease stage was unknown for five patients, one with previously untreated disease and the four patients referred from elsewhere. The parotid gland was the most frequent primary tumour site. Clinicopathological characteristics of the study group are summarized in Table 1.

The 5-year OS for the entire cohort were 67.2%. The 5-year DFS was 79.7% with 13 patients (20.3%) developing recurrence. Univariate analysis showed that advanced histological grade and tumour subsite were statistically significant predictors of OS (Figs. 1 and 2). Furthermore, tumour stage and nodal status were statistically significant predictors with respect to OS (Figs. 3 and 4). There was no statistically significant difference in OS based on sex, patient age, adjuvant therapy, or margin status.

Of the 64 patients, 39 (60.9%) had LG-MEC, six (9.4%) had IMG-MEC, and 19 (29.7%) had HG-MEC. The influence of

Table 1. Clinicopathological characteristics of mucoepidermoid carcinoma.

Baseline characteristic	Number of patients (%)
Mean age (years)	46.9
Sex	
Male	36 (56.3)
Female	28 (43.7)
Tumour subsite	
Parotid gland	33 (51.6)
Submandibular/sublingual gland	10 (15.6)
Minor gland	21 (32.8)
Histological grade	
Low	39 (60.9)
Intermediate	6 (9.4)
High	19 (29.7)
Tumour stage	
T1/T2	44 (68.8)
T3/T4	15 (23.4)
Unknown	5 (7.8)
Nodal status	
Negative	50 (78.1)
Positive	14 (21.9)
Margin status	
Negative	56 (87.5)
Positive	7 (10.9)
Unknown	1 (1.6)
Radiation therapy	
No	43 (67.2)
Yes	21 (32.8)
Recurrence	
Local	3 (27.3)
Regional	5 (45.4)
Distant	3 (27.3)

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