Original Research

Nomograms for predicting survival and recurrence in patients with adenoid cystic carcinoma. An international collaborative study

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Abstract   *Background:* Due to the rarity of adenoid cystic carcinoma (ACC), information on outcome is based upon small retrospective case series. The aim of our study was to create a large multiinstitutional international dataset of patients with ACC in order to design predictive nomograms for outcome.

Methods: ACC patients managed at 10 international centers were identified. Patient, tumor, and treatment characteristics were recorded and an international collaborative dataset created. Multivariable competing risk models were then built to predict the 10 year recurrence free probability (RFP), distant recurrence free probability (DRFP), overall survival (OS) and cancer specific mortality (CSM). All predictors of interest were added in the starting full models before selection, including age, gender, tumor site, clinical T stage, perineural invasion, margin status, pathologic N-status, and M-status. Stepdown method was used in model selection to choose predictive variables. An external dataset of 99 patients from 2 other institutions was used to validate the nomograms.

Findings: Of 438 ACC patients, 27.2% (119/438) died from ACC and 38.8% (170/438) died of other causes. Median follow-up was 56 months (range 1–306). The nomogram for OS had 7 variables (age, gender, clinical T stage, tumor site, margin status, pathologic N-status and M-status) with a concordance index (CI) of 0.71. The nomogram for CSM had the same variables, except margin status, with a concordance index (CI) of 0.70. The nomogram for RFP had 7 variables (age, gender, clinical T stage, tumor site, margin status, pathologic N status and perineural invasion) (CI 0.66). The nomogram for DRFP had 6 variables (gender, clinical T stage, tumor site, pathologic N-status, perineural invasion and margin status) (CI 0.64). Concordance index for the external validation set were 0.76, 0.72, 0.67 and 0.70 respectively.

Interpretation: Using an international collaborative database we have created the first nomograms which estimate outcome in individual patients with ACC. These predictive nomograms will facilitate patient counseling in terms of prognosis and subsequent clinical follow-up. They will also identify high risk patients who may benefit from clinical trials on new targeted therapies for patients with ACC.

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1. Introduction

Adenoid cystic carcinoma (ACC) accounts for less than 1% of all head and neck malignancies and approximately 10% of all salivary neoplasms [1,2]. It is a locally aggressive tumor and surgery remains the mainstay of treatment for these patients since it is relatively resistant to radiation and chemotherapy [3,4]. ACC is characterized by perineural invasion which predisposes patients to local recurrence. In addition these patients have a high prevalence of late distant metastases, usually to lung, which can develop up to 10 years after initial treatment [3,5]. Since ACC is a rare tumor, reports of the clinical and pathological predictors of outcome generally consist of small single-institution retrospective series [6–13]. Most of the reports on ACC are based on cohorts of patients with tumors involving various anatomical locations in the head and neck, and therefore analysis of outcomes on specific tumors or sites have not been possible. Two population based studies on the NCDB and SEER databases have been reported but these studies lack details on many clinicopathological factors as well as details on recurrence [14,15]. This has led to inconsistency in the reported factors which contribute to recurrence and survival. To address this issue we created an international collaborative database with contributions from 10 international institutions recognized as major centers of excellence for the treatment of head and neck cancer.

The current method for predicting outcome for patients with ACC is the American Joint Committee on Cancer (AJCC) TNM staging system. This system stages patients from stage I to stage IV according to the T-status, N-status and M-status of the patient. The TNM system works effectively for a patient population but it is less useful for predicting outcome in an individual patient. In addition, it does not account for other variables which may be important for determining outcomes in individual patients. This includes patient variables such as age, gender, and comorbidities, as well as tumor factors such as the presence of perineural invasion, vascular invasion and margin status. These factors are all important in patients with ACC. Therefore we decided to use this large and unique international dataset to create statistical models (nomograms) and test their capability to predict both recurrence and survival in individual patients with ACC.

Nomograms are statistical tools shown to accurately predict outcome in an individual patient by utilizing multiple variables in addition to the standard TNM