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Systemic inflammatory response and survival in patients undergoing curative resection of oral squamous cell carcinoma

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Abstract

Prognostic stratification in squamous cell carcinoma (SCC) of the head and neck has traditionally relied on the pathological staging of a tumour, but it is increasingly being recognised that host-related factors have an important role in the assessment of survival and recurrence. We aimed to evaluate the prognostic value of systemic inflammation scores including the modified Glasgow Prognostic Score (mGPS) in patients undergoing potentially curative resection for oral SCC. We retrospectively identified 178 patients who had curative operations for cancer of the oral cavity and soft palate between January 2006 and April 2011. Among the inclusion criteria were preoperative estimates of C-reactive protein and serum albumin. We analysed established pathological prognostic factors and scores for systemic inflammation as predictors of cancer-specific and overall survival. On univariate analysis, the mGPS was a significant predictor of both cancer-specific ($p < 0.001$) and overall survival ($p < 0.001$), and it remained an independent predictor of cancer-specific (HR: 2.12, 95% CI 1.49 to 3.00; $p < 0.001$) and overall survival (HR: 1.69, 95% CI 1.23 to 2.31; $p = 0.001$) on Cox regression analysis. The mGPS of activated systemic inflammation seems to be a powerful adverse prognostic indicator in resectable oral SCC.

Keywords: Systemic inflammation; Immune cells; Head and neck cancer; Squamous cell carcinoma; Recurrence and survival; Prognosis

Introduction

After curative resection, prognostic stratification has traditionally been guided by the pathological staging of a tumour. Stage, nodal status, lymphovascular and perineural invasion, and status of the margin are considered important in the assessment of survival in patients with squamous cell carcinoma (SCC) of the head and neck.[1–3] However, it is increasingly being recognised that the pathological stage is not the sole determinant of outcome, and host-related factors, particularly the systemic inflammatory response, have an important role.[4,5] A number of measures of systemic inflammatory response have been used, and in previous studies, C-reactive protein, albumin, white cell, neutrophil, lymphocyte, and platelet counts have been reported to have prognostic value.

More recently, these markers have been combined to form systemic inflammation-based prognostic scores of which the modified Glasgow Prognostic Score (mGPS), and neutrophil:lymphocyte and platelet:lymphocyte ratios have been most widely validated.[6–9] Markers of systemic inflammatory response seem to be particularly robust prognostic indicators in operable colorectal (including liver metastases),

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gastro-oesophageal, and renal cancers.[9] They also have value in other common solid tumour cancers,[6] of which one of the least studied in detail is oral cancer. We therefore aimed to evaluate the value of prognostic scores based on systemic inflammation in patients undergoing potentially curative resection of oral SCC.

Methods

Using the records of multidisciplinary meetings and the operating theatres, we retrospectively identified patients who had potentially curative resection of previously untreated SCC of the oral cavity and soft palate between January 2006 and April 2011 at the Southern General Hospital, Glasgow. None had evidence of distant metastatic disease at the time of operation. Those who had had preoperative chemoradiotherapy or clinical evidence of infection or inflammation that would acutely or chronically evoke a systemic inflammatory response were excluded. Those with cancer of the base of the tongue or tonsils were also excluded to minimise the influence of HPV-associated SCC. Patients who died within 30 days of operation and those with missing preoperative data on markers of systemic inflammation were excluded from the survival analysis.

Tumours were staged according to the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) TNM staging systems for head and neck cancer. Data on the presence of lymphovascular and perineural invasion, depth of invasion, and distance to the nearest margin were extracted from pathological reports, and margins were then divided into 3 categories: involved (less than 1 mm from tumour), close (1–5 mm from tumour), and clear (more than 5 mm from tumour). Pathological nodal status was also recorded.[10–13]

The head and neck cancer unit at the Southern General Hospital receives some tertiary referrals. Patients who were discharged postoperatively for local follow-up outside the unit were excluded because follow-up data were not available. Surviving patients were followed up for 5 years (3-monthly intervals for the first 3 years then 6-monthly).

C-reactive protein and albumin concentrations were routinely measured before operations. The limit of detection of the assay was a C-reactive protein concentration lower than 1 mg/L. Concentrations of more than 10 mg/L were considered indicative of a systemic inflammatory response.[14]

The mGPS was calculated using preoperative values for C-reactive protein and albumin. Patients with raised concentrations of C-reactive protein (over 10 mg/L) and hypoalbuminaemia (less than 35 g/L) were given a score of 2. Those with raised concentrations of C-reactive protein without hypoalbuminaemia were given a score of 1. Patients who did not have raised concentrations of C-reactive protein were given a score of 0 regardless of their albumin status (Table 1).

Neutrophil:lymphocyte and platelet:lymphocyte ratios were calculated (Table 1). A neutrophil:lymphocyte ratio of 5 or more was given a score of 1; if it was less than 5 the score was 0. A platelet:lymphocyte ratio of less than 150 was given a score of 0, ratios between 150 and 300 were given a score of 1, and those over 300 were given a score of 2.

Table 1
Inflammation-based prognostic scoring systems.

	Score
The modified Glasgow Prognostic Score	
C-reactive protein ≤10 mg/L and albumin ≥35 g/L	0
C-reactive protein ≤10 mg/L and albumin <35 g/L	0
C-reactive protein >10 mg/L and albumin ≥35 g/L	1
C-reactive protein >10 mg/L and albumin <35 g/L	2
Neutrophil:lymphocyte ratio (neutrophil count:lymphocyte count)	
<5:1	0
≥5:1	1
Platelet:lymphocyte ratio (platelet count:lymphocyte count)	
<150:1	0
150–300:1	1
>300:1	2

Statistical analysis

Variables were grouped using standard thresholds. Deaths up to May 2013 were included in the analysis. We used Kaplan–Meier curves for survival analysis and the log rank test to indicate significance. Probabilities of less than 0.05 were considered significant. Multivariate analysis was done using a Cox proportional hazards model and a stepwise backward procedure was done to derive a final model of the variables that had a significant independent association with survival. Variables were removed from the model only if the corresponding p value was more than 0.1 on univariate analysis. Inter-relations between variables were assessed using contingency tables and the chi square test for trend as appropriate. Analysis was done with the help of SPSS Statistics for Windows (Version 17.0, SPSS Inc., Chicago, USA).

Results

A total 178 patients who had potentially curative resection for SCC of the head and neck between January 2006 and April 2011 were included in the study. Mean (SD) age was 62 (11) years (range 23–89), and 121 (68%) patients were male. Most had N0 disease (61%) and had had no adjuvant treatment (61%). In 131 (74%) the mGPS score was 0. The mean (SD) duration of follow-up among survivors was 38 (10.7) months (median 31, range 28–69). During this period, 42 patients died of head and neck cancer and 14 of other causes.

The associations between clinicopathological factors and cancer-specific and overall survival are shown in Table 2. Kaplan–Meier survival curves showing the association between the mGPS and disease-specific ($p < 0.001$) and overall survival ($p < 0.001$) are shown in Figs. 1 and 2, respectively.