Biomarkers and histopathological analysis for risk prediction of recurrence in Oral Squamous Cell Carcinoma (OSCC): a retrospective study

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Introduction

Oral Squamous Cell Carcinoma (OSCC) is the sixth most common cancer worldwide, characterized by heterogeneous cellular and histological features observed by different molecular parameters. The main biomarkers (BKs) associated with oral cavity tumorigenesis are p53, EGFR, Cyclin-D1, p16 and E-cadherin and their expression is associated with poor prognosis and multiples relapses, besides other histopathological prognostic factors associated to lower rates of overall (OS) and disease-free survival (DFS). This study aims to confirm through histopathological assessment (HP) based on morphological tumor criteria and immunohistochemistry analysis (IHC) of the BKs the association with increased local recurrence in patients diagnosed with OSCC submitted to multimodal treatment at A.C. Camargo Cancer Center.

Material and Methods

One hundred patients diagnosed with OSCC submitted to multimodal treatment during 2013-2017 were evaluated and distributed in two groups according to the primary local tumor: A) Patients with OSCC in the floor of the mouth and B) tongue OSCC, both groups treated with only surgery, surgery plus radiotherapy (RT) and/or surgery with RT and chemotherapy. IHC and HP analysis were performed of surgical specimen for detection of these five BKs such as EGFR, p53, E-cadherin, p16 and Cyclin D1. Moreover, after HP for morphological tumor featuring prognostic factors such as clinic-pathological staging, free surgical margins, extra-capsular extension of lymph nodes, perineural and angiolymphatic invasion, depth of pattern infiltration were described. Demographic and clinical data were collected, and the non-parameter Chi-square statistical test was performed for determining association between them. OS and DFS rates were calculated using Kaplan Meier test and logRank test for univariate statistical analysis. Cox regression model was done, and the hazard ratio was established for each independent factor to predict clinical failure (p<=0.05).

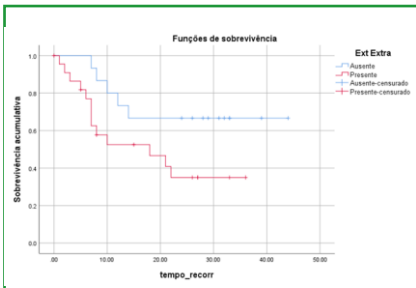
Results

From 100 patients analyzed, 61% were male and 39% female. Regarding local primary tumor, 51% presented OSCC in the floor of the mouth and 49% in the tongue with a mean age of 62 years (R: 29-86). The median of follow-up was 28 months (mean: 26 / SD: +-14,04 / R: 0-71) and the mean of recurrence appearance was 12 months (median: 9/ R: 0-37). Most patients showed an initial stage (I-II) (63.6%), Worst pattern of invasion (WPOI) 3-5 (70.5%), extracapsular extension (EE) (57.5%). Regarding BKs expression, 21.2% p16, 87.9% Cyclin-D1, 63% p53, 53.5% E-cadherin, and 66% EGFR.

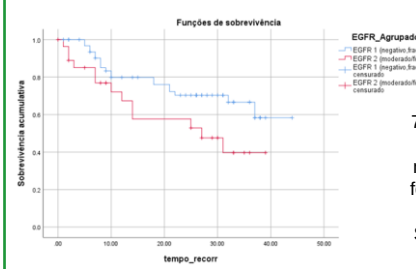
Results

It was observed a statistically significant association between p53 expression and for both sex (p: 0.01), p53 and smoking/alcohol consumption (p:0.04). E-cadherin was associated with lymph node infiltration (p: 0.03). The median OS was 80% vs 60% in 03 years (R: 42-61; I/II vs. III-IV p: 0.06); for DFS was 50% (p: 0.22; I/II vs. III/IV) in 05 years (Range: 27-24 months).

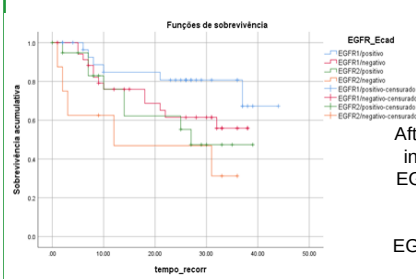
Cox regression showed that EGFR expression HR: 4.9 (p: 0.02/ R: 1.34-18.30) and E-cadherin HR: 0.3 (p: 0.06/R: 0.084-1.03) and EE as morphological tumor criteria (HR: 3.68 / p: 0.056 / R: 1.00-13.48) are independent factors for prediction of clinical failure.



DFS and Extracapsular extension (ECE): After 30 months (2 years and a half), it was 38% for patients who showed EEC and 65% without after the histopathological analysis (**p value: 0.057**).



DFS and EGFR: After 30 months, it was 75% for the EGFR1 group (who included weak and not expression.) and 42% for the EGFR2 group (who included moderate and Strong expression) with a **p value: 0.04**



DFS and EGFR/E-cadherin: After 30 months, it was 80% in patients who expressed EGFR1 and E-cadherin and decreased to 41% in patients who showed EGFR2 and loss E-cadherin, with **p: value: 0.05**

Conclusion

The detection of BKs associated with local recurrence of OSCC is feasible as a potential predictive factor for clinical failure since the initial diagnosis, and through the correlation with demographic data, clinical-pathological and morphological tumor criteria such as tumor size, extracapsular extension, lymphoid infiltrate, infiltration pattern and perineural invasion presented. EGFR expression is a potential biomarker for prediction of OSCC recurrence in patients submitted to multimodal management; however, the loss of E-cadherin expression was considered as a protective factor against oral cancer recurrence for this group. Furthermore, longitudinal studies must be performed to validate these results in the clinical practice.

Acknowledgment and contact

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