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Gender differences in prognostic factors for oral cancer

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Abstract. The aim of this study was to assess gender differences in prognostic factors among patients treated surgically for oral squamous cell carcinoma (OSCC). The medical records of 477 eligible patients (345 males, 132 females) obtained from the Brazilian Cancer Institute were reviewed. Survival was calculated by Kaplan–Meier method. Cox regression models were used to obtain adjusted hazard ratios (aHR) for males and females. Multivariate analysis showed that past tobacco use (aHR 0.2, 95% confidence interval (CI) 0.1–0.7) and regional metastasis (aHR 2.3, 95% CI 1.5–3.5) in males, and regional metastasis (aHR 2.2, 95% CI 1.2–4.3), distant metastasis (aHR 6.7, 95% CI 1.3–32.7), and hard palate tumours (aHR 11.8, 95% CI 3.3–47.7) in females, were associated with a higher risk of death. There were no differences in survival between males and females. Regional metastasis was found to be a negative prognostic factor in OSCC for both genders. Past tobacco use was an independent prognostic factor for worse survival among males, while distant metastasis and hard palate tumours were independent prognostic factors for worse survival among females. Further studies are necessary to corroborate the relationships found in this study.

Key words: oral cavity; squamous cell carcinoma; gender distribution; survival analysis; epidemiology.

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Oral cancer accounts for 4% of all neoplastic diseases worldwide, and oral squamous cell carcinoma (OSCC) is the most frequent type, accounting for 90–95% of all cases.[1] In Brazil, oral cancer is the fifth most common malignant neoplasm among males, but it is not among the 10 most frequent neoplasms in females.[2]

Most patients diagnosed with OSCC are males of low socioeconomic status with a history of alcohol and tobacco use.[3] However, special attention should be given to certain groups that do not fit into this well-known profile, as an increasing incidence of oral cancer is being seen among young females that is not related to smoking or alcohol consumption.[4]

A sedentary lifestyle, environmental risks, and alcohol and tobacco use are general predisposing factors to disease.[5] In recent years, some authors have pointed to lifestyle changes as a contributing factor to the change in OSCC profile in females.[6–9] Alcohol and tobacco use is still lower among females than males,[7] and the cancer incidence is six times lower in females than males.[6,8]

Lymph node status appears to be the most important clinical prognostic indicator,[10,11] but studies have shown that tumour differentiation, treatment, and the clinical stage of cancer are also good prognostic indicators.[12,13] There are a multitude of factors involved in the prognosis of oral cancer and probably no single marker can accurately predict the outcome.[11]

Some studies have investigated OSCC in women,[7,14–17] although little is known about survival and prognostic factors, mainly because of the small sizes of the samples studied. Therefore, whether there are gender differences in prognostic factors remains an unanswered question. Identifying the profiles of these OSCC patient populations will allow clinicians to develop gender-specific treatment and care protocols and predict the prognosis. The aim of this study was to assess gender differences in prognostic factors among patients treated surgically for OSCC, based on socio-demographic and clinical prognostic indicators.

Materials and methods

Study population

This was a retrospective study based on data obtained from the Brazilian Cancer Institute Hospital Registry database, performed between 1 February and 28 December 2012. The study sample consisted of 345 males and 132 females diagnosed with primary OSCC. All patients had their histological OSCC diagnosis confirmed between 1 January 1999 and 31 December 2003. They were all living in the city of Rio de Janeiro, had no history of previous tumours, and underwent surgery as primary treatment (operable cases with or without adjuvant radiotherapy) at the Brazilian Cancer Institute. The study patients had tumours involving the following anatomical sites (International Classification of Diseases for Oncology codes): tongue (C02.0, C02.1, C02.3, C02.2, C02.8, C02.9), gingiva (C03.0, C03.1, C03.9), floor of the mouth (C04.0), hard palate (C05.0, C05.8, C05.9), and buccal mucosa (C06.0, C06.1, C06.2, C02.8, C02.9). All patients were followed for at least 1 month after treatment and for 5 years on a regular basis. Data were updated on a yearly basis. The preliminary data were obtained from an electronic database and complemented with a manual review of the medical records.

Data collection

The following socio-demographic and clinical and pathological variables were obtained from the medical records for analysis: age (<40, 40–59, and ≥60 years)[18,19]; tobacco use (none, current, and past) and alcohol use (none, current, and past); body mass index (BMI; <18.5, 18.5–24.9, and ≥25 kg/m^2)[20]; treatment (surgery, or surgery with adjuvant radiation therapy). For alcohol and tobacco use, 'none' meant that the patient did not use these substances or had stopped using them for at least 5 years; 'past use' meant that the patient reported quitting smoking or alcohol use for less than 5 years. Schooling was used as an indicator of socio-economic status (<4, 4–7, and ≥8 years). Anatomical sites were categorized according to the Union for International Cancer Control (UICC) guidelines[21] for oral cancer: tongue, floor of the mouth, gingiva, hard palate, and buccal mucosa. The UICC staging system was used to classify the clinical stage as either early (I/II) or advanced (III/IV). Histopathological grading of the surgery specimens was performed according to the World Health Organization (WHO) grading system[10] and categorized into well-differentiated, moderately differentiated, and poorly differentiated. Metastasis was classified as no metastasis, regional metastasis, and metastasis to distant organs.[17,22]

All data were collected at the time of first record analysis and additional information obtained in the follow-ups was added, up to 28 December 2012. For patients who were lost to follow-up before 5 years, the date of censorship was considered as the last date the patient was contacted by the hospital.

Statistical analysis

The null hypothesis tested was no difference in overall survival between males and females. All analyses were performed separately for males and females. The χ^2 test was used to assess differences between the variables analyzed and by gender. Overall survival was estimated using the Kaplan–Meier method from the date of first histopathological diagnosis to the date of death, or censoring (after 5 years of follow-up). Patients lost to follow-up were censored at the date of the last registered visit to the hospital. Differences in survival rates were assessed using the log-rank test. To assess prognostic factors associated with gender, hazard ratios (HR) were calculated, together with 95% confidence intervals (95% CI). The multivariate analysis of overall survival was performed using Cox proportional hazard regression models. For males and females, model 1 was the univariate analysis (hazard ratio), and variables with a *P*-value of <0.20 were included in the multivariate model to predict independent prognostic factors. The significance level was set at $P \leq 0.05$ for all analyses. Cox regression models were performed separately for males and females, and all selected variables were adjusted for in model 2. The variable 'metastasis' was used as a proxy of staging to adjust for the Cox model, mainly due to a small number of missing values in the medical records. All statistical analyses were run in IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). This study was approved by the Institutional Review Board of the Brazilian Cancer Institute.

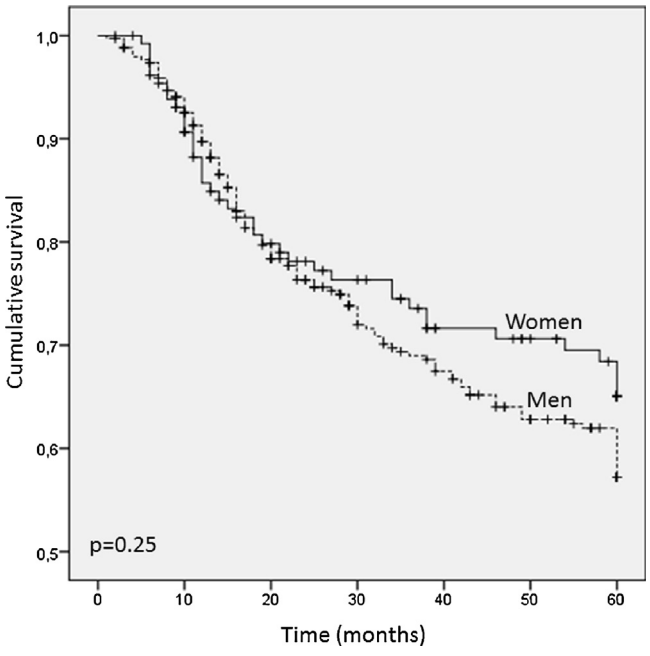

Fig. 1. Kaplan–Meier estimates of survival for patients with oral squamous cell carcinoma, stratified by gender.