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Prognostic impact of tumor-stroma ratio in oral squamous cell carcinoma - A pilot study

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A B S T R A C T

Background: Several prognostic indicators have been used for many decades in an attempt to predict clinical behaviour of Oral Squamous Cell Carcinoma (OSCC). The prognostic value of TSR is yet to be explored in OSCC. Hence, the aim of the present study was to evaluate the prognostic value of TSR in OSCC patients.
Methodology: A cohort of 60 histologically diagnosed cases of OSCC who underwent Radical Neck Dissection was included in the study. TSR was assessed and patients with > 50% intratumor stroma were quantified as the stroma-poor group and those with < 50% as the stroma-rich group.
Results: The parametric tests were performed for the statistical evaluation of TSR with the clinico-pathological variables and the survival. The 3-year overall survival (OS) and disease-free survival (DFS) rates were 95.23% and 69.04%, respectively, in stroma-poor group and 77% and 44%, respectively in the stroma-rich group.
Conclusion: TSR may serve as a reliable histologic prognostic indicator in OSCC and could be used in routine diagnostic pathology.

1. Introduction

Tumor tissue is composed of epithelial cells and stromal cells recruited from normal tissue. In normal tissue, the stroma may act as a barrier in tumorigenesis by constraining tumor cell proliferation. However in tumor tissue, stromal components could facilitate the process of tumor progression. Although the mechanism underlying is still not clear, tumor-associated stroma and cancer-associated fibroblasts have been found to play an important role in tumor progression phases [1]. Recently, as a consequence of the growing interest in the microenvironment, several studies have been conducted to evaluate the ratio of tumor to stroma (TSR) as a reflection of the microenvironment of cancer and survival outcome in Esophageal Cancer, Breast Cancer, Colon Cancer, and Cervical Cancer [2-5]. TSR has been proven to be an independent prognostic factor for these cancers. Tumor–stroma ratio could be easily implemented in routine haematoxylin-eosin stained slides without any special staining methods, and is simple to determine, reproducible, and performed in quick time. Although to our knowledge, the prognostic value of TSR is yet to be explored in OSCC. Hence, the aim of the present study is to assess the prognostic efficiency of TSR in determining the overall survival and disease free survival of the patients with OSCC.

2. Materials and methods

A retrospective study was planned and an approval from the ethical committee was taken (IRB No- 2015/P/OP/42). A total of 60 surgically resected cases of OSCC treated with Radical Neck Dissection (RND) from the year 2013–2016 were selected from the archives of the Department of Oral Pathology and Microbiology, Shri Dharmasthala Manjunatheshwara College of Dental Sciences and Hospital, Dharwad. The clinical details, 3-year disease-free survival (DFS) and overall survival (OS) were collected from the case file of each patient.

Inclusion criteria:

1) Radical neck dissected cases of OSCC
2) Presence of most Invasive tumor front area

Exclusion criteria:

1) Patients received preoperative chemo- or radiation therapy.
2) Presence of known distant metastasis at surgery.
3) Patients with other malignancies in the past and death or recurrence (distant or loco-regional) within 1 month.
4) The lesional tissue not including the most invasive deep front area.

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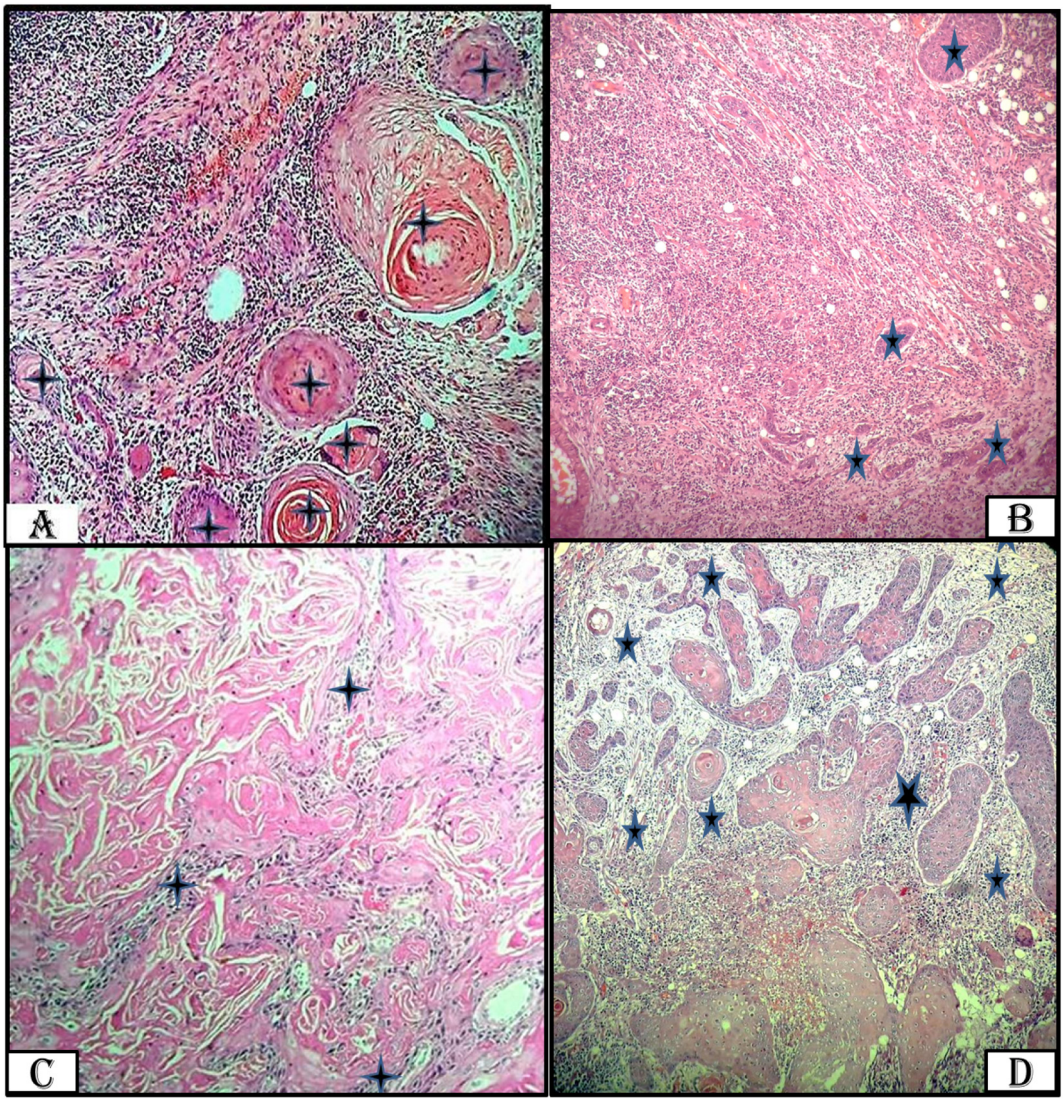

Fig. 1. Haematoxylin and Eosin stained sections of Oral Squamous Cell Carcinoma (OSCC) (original magnification ×10).
A and B: example of stroma-rich (stroma > 50%) (*-tumor)
C and D: example of stroma-poor (stroma < 50%) (*-stroma).

2.1. Histopathological evaluation

Histopathological examination involved routine microscopic analysis of Haematoxylin and Eosin stained sections from the most invasive part of the tumor. Using a 4× objective, the most invasive tumor front of the whole tissue slide was selected. Subsequently using a 10× objective, only those fields were scored where both the stroma and tumor are present and most importantly tumor cells are seen on all sides of the microscopic image field. TSR was visually estimated in a blinded manner by two investigators (KCN and NAS) and scored per tenfold percentage. In case of heterogeneity, the highest stromal percentage was considered decisive.

2.2. Statistical analysis

The cut-off value for the TSR was taken as 50% as previously determined in Colon Cancer [4] and Breast Cancer with the maximum discriminative power [6]. TSR was defined as stroma poor (the proportion of stroma < 50%) or stroma rich (the proportion of stroma > 50%) (Fig. 1). Differences in the clinico-pathological characteristics were assessed using the Chi-square test. The inter-observer variability was analysed using Cohen's Kappa co-efficient. The Cox proportion hazards model was used to determine the hazard ratio of variables on 3 year DFS and OS in univariate and multivariate analysis. Analysis of survival curves was performed using Kaplan-Meier Survival Analysis and survival distributions were evaluated with Log rank statistics. The TSR was then correlated with clinico-pathologic parameters and the disease-free survival (DFS) and overall survival (OS).

3. Results

3.1. Clinicopathological features

60 patients (53 men and 7 women) were included in the present study. The median age of patients was 50 years at the date of surgery. The median follow up time was 36 months (range, 18–48 months). Clinicopathological characteristics of the patients are shown in Table 1.

3.2. Tumor stroma ratio in OSCC

With 4× and 10× objectives, routine Haematoxylin and Eosin stained sections from the primary tumor were analysed for the presence of stromal involvement. TSR was assessed on one section obtained from the most invasive front of the tumor (Fig. 1). TSR was assessed by 2

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