THE ROLE OF HISTOLOGIC RISK ASSESSMENT AS A PROGNOSTIC INDICATOR IN ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Background: Oral squamous cell carcinoma (OSCC) is the most common carcinoma affecting the oral cavity comprising of more than 90% of all oral cancers.The tumor staging of OSCC shows heterogenous prognosis with increased number of patients with loco regional recurrence (LRR) and decreased disease free survival (DFS) related to mortality.

Aims and Objectives: To evaluate the parameters used in Brandwein-Gensler risk model along with lympho-vascular invasion (LVI), depth of invasion (DOI) and lymph node metastases in predicting loco regional recurrence (LRR)in OSCC.

Materials and Methods: This was a retrospective study on T1/2 OSCC patients over a period of 2 years who received treatment by surgical resection. LRR was examined based on recurrence of OSCC at the initial site or in regional lymph nodes.

Results: During our study period a total of 56 cases befitted our inclusion criteria. Univariate analysis identified LVI ($P = 0.627$), DOI ($P = 0.116$), nodal involvement ($P = 0.107$), WPOI ($P = 0.084$), LHR ($P = 0.280$) and only risk category ($P < 0.001$) showed strong statistically significant risk factor for LRR.

Conclusion: Adequate assessment of all the parameters on routine H and E by including Brandwein-Gensler histological risk scoring model at the initial assessment can help in the prognosis and further treatment of the patients with OSCC.

KEY WORDS: Histological risk score, oral squamous cell carcinoma, prognosis, histological parameters.

Introduction :

Oral cancer is the sixth most common cancer worldwide.Oral squamous cell carcinoma belongs to heterogeneous subgroup of head and neck malignant neoplasms affecting lips, anterior two-thirds of tongue, salivary glands, gingiva, floor of the mouth, oral mucosal surface and with the tongue[1]. Tobacco exposure (smoking tobacco), alcohol intake and HPV infection are the common risk factors for OSCC[2] .There are many varied demographic, clinical and histopathological factor which influence the prognosis of OSCC[2,3]. According to latest guidelines for treatment of OSCC include surgical resection followed by adjuvant chemotherapy and radiation depending on the stage of tumor, margin and other prognostic factors[3].The utility of molecular assays in the clinical settings is limited by cost and time issues[4].Therefore histopathology-based scoring system is easy to apply on H&E-stained sections from an adequate sampled tumor–host interface.[4] Based on the study of various histological parameters and assessment of tumor–host junction on routine H&E stains, Brandwein– Gensler developed and validated a predictive model for patients with head and neck squamous cell carcinoma.[4,5]This histologic risk assessment scoring model consists of three major entities WPOI, LHR and PNI in predicting risk of recurrence. A total score of 3 or more is considered as high risk, 1–2 as intermediate risk and 0 as low risk.[6]So this study is been taken up to evaluate the impact of all the parameters used in Brandwein-Gensler risk model along with Pattern of invasion (WPOI),lympho-vascular invasion (LVI), degree of differentiation, depth of invasion (DOI) ,lymph node metastases ,lymphocyte host response (LHR) as prognostic indicator in oral squamous cell carcinoma .

Materials & Methods :

This study was carried out in the department of pathology at Sri Siddhartha Medical college Tumkur. Total 56 cases were included over a period of 2 year from July 2021 to July 2023.
Inclusion criteria - all diagnosed cases of oral squamous cell carcinoma of oral cavity with neck dissection were included.
Exclusion criteria - all the patients who had received chemo/radiotherapy prior to surgery .
The demographic parameters including age and gender were noted from the medical records.
Hematoxylin and eosin-stained slides were retrieved and studied for the histological parameters. Histological parameters including tumor grade, WPOI, DOI, LHR, PNI, LVI and pathological stage and lymph nodal metastases were reviewed and recorded. The cases were analysed by using Brandwein-Gensler risk model given in table1. The cases were divided into three categories according to the total points for each individual case as follows: Low risk = 0, Intermediate risk =1 or 2 and High risk = 3 or greater.
The pathologist performing histopathological assessment was blinded to clinical data variables and patient outcomes. LRR was assessed based on recurrence of OSCC at the initial site or in regional lymph nodes.

Statistical analysis

Descriptive statistics were used to summarize patient histological features and disease classification at diagnosis. All relevant data was entered into the excel sheet of Microsoft Excel. SPSS software, version 21.0 was used. Yates'chi square test was done. A P value of <0.05 was considered to be statistically significant.

Table 1: Brandwein-Gensler risk mode total score - Low risk=0, Intermediate risk=1/2, High risk = ≥3

Variable	Definitions	Point assignment
WPOI		
Type 1	Pushing border	0
Type 2	Finger like growth	0
Type 3	Large separate islands, more than 15 cells per island	0
Type 4	Small tumor islands, 15 cells or fewer, per island	+1
Type 5	Tumor satellites, >1 mm from main tumor or next closest satellite	+3
LHR		
Type1 (Strong)	Dense complete host response rimming tumour lymphoid nodules at advancing edge in each 4x field	0
Type 2 (Intermediate)	Intermediate host response, lymphoid nodules in some but not all 4x fields	+1
Type 3(Weak)	Little or no host response no lymphoid nodule	+3
PNI		
NONE	None	0
SMALL NERVES	Small nerves Tumour wrapping around nerves, <1mm diameter	+1
LARGE NERVES	Large nerves Tumour wrapping around nerves, equal to Or greater than 1mm diameter (20x)	+3

RESULTS

During our study period we had 56 OSCC cases which included surgical resection specimens. Based on 8th edition of AJCC criteria, 10 (17.8%) ,38 (67.8%) ,06 (10.7%) and 02 (3.7%) cases were divided into T1, T2,T3&T4 stages respectively. The median age of presentation was 63.4(+/-13.2) years. The most common site of initial presentation was the buccal mucosa followed by the tongue, alveolus, lip, retromolar trigone, gingiva buccal sulcus and palate in decreasing order of occurrence.There were 32 (57.2%) males and females 24(42.8%) OSCC. The most common histologic subtype in all primary OSCC cases was well differentiated OSCC

Table 2: The age and gender distribution of Patients

Variables	Number of cases/ percentage
Male	32(57.2%)
Female	24(42.8%)
Age range	42-88
Mean age (SD)	63.4(13.2)

Table 3: Histological Risk Assessment with Tumor Size

Tumor staging	Number of cases/ percentage
T1	10(17.8%)
T2	38(67.8%)
T3	06(10.7%)
T4	02(3.7%)

Table 4: The various parameters assessed including univariate analysis (log-rank tests) of the risk factors for LRR

HISTOLOGICAL CHARACTERISTIC	TUMOR STAGE	TUMOR STAGE	TUMOR STAGE	TUMOR STAGE	STATISTICAL SIGNIFICANCE
Pattern of invasion					
WPOI1	01	00	00	00	
WPOI2	04	02	00	00	P=0.084
WPOI3	03	21	03	00	
WPOI4	02	15	03	02	
WPOI5	00	00	00	00	
Degree of differentiation					
Well differentiated	07	35	05	02	
Moderately differentiated	03	03	01	00	P=0.53
Poorly differentiated	00	00	00	00	
LVI					
Present	-	02	-	-	P=0.627
Absent	10	36	06	02	
DOI					
≤5mm	10	28	06	-	P=0.116
6-10mm	-	10	-	02	
Nodal involvement					
Present	-	16	02	02	P=0.107
Absent	10	22	04	-	
LHR					
Strong	02	22	04	-	P=0.280
Intermediate	08	16	02	02-	
Limited	-	-	-		
Risk category					
Low	08	22	06	-	P=<0.001
Intermediate	02	16	-	-	
High	-	-	-	02	

Univariate analysis identified LVI (P =0.627), DOI (P = 0.116), nodal involvement (P =0.107), WPOI (P =0.084), LHR (P = 0.280) and risk category showed (P< 0.001) which was statistically significant.
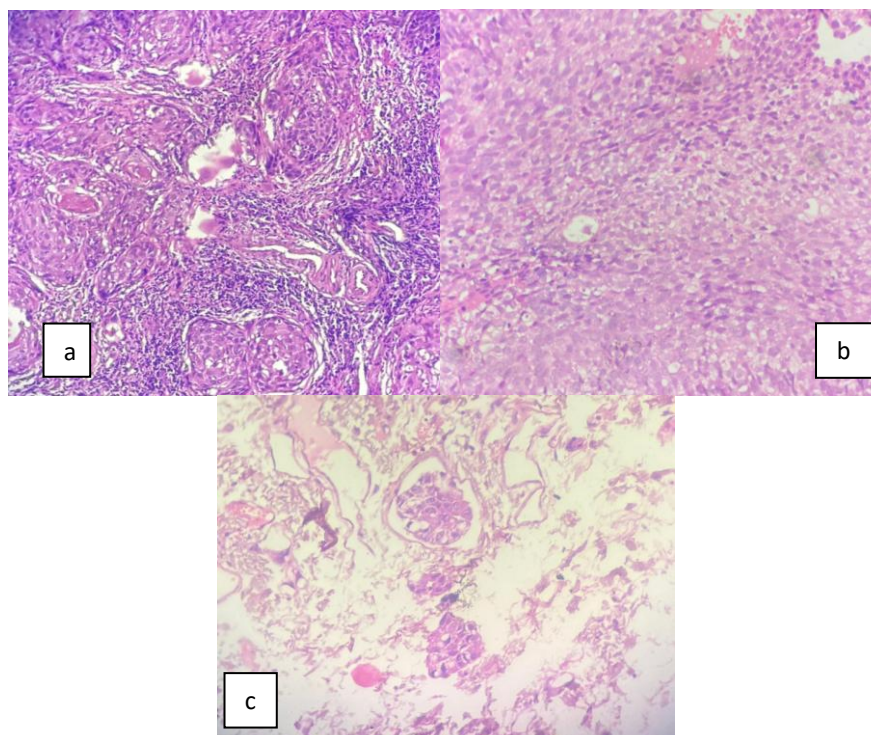
With photomicrographs showing a-Well differentiated squamous cell carcinoma (a,H and E ×400), b-Moderately differentiated squamous cell carcinoma (b,H and E ×400) OSCC.c-Lympho-vascular invasion(c,H and E ×400)

Discussion

Squamous cell carcinomas of oral cavity is one of the most common causes of morbidity in developing countries like India[6]. The recent guidelines recommend therapeutic resection of primary tumour with postoperative adjuvant therapy .The adjuvant therapy is based on the various histopathological details of the resected tumour[7]. The parameters which measure the prognosis of oral squamous cell carcinomas are clearly not defined. Several studies have described different parameters like histologic grade, tumour depth of invasion, lymphovascular invasion, perineural invasion, margin status, lymphocytic host response, worst pattern of invasion[8]. Among these histological parameters, lymphovascular invasion and perineural invasion are commonly noted in all the malignancies, so new parameters like tumour depth of invasion, margin status and worst pattern of invasion were examined in detailed in the present study.

In present study OSCC, showed the median age of 63.4 years with a male predominance of 32 (57.2%) and females 24 (42.8%) cases shown in table 2. The study done by Hori et al.[9]and Li et al[10]. had similar findings of median age of 61 and 63 years with a male predilection of 69% and females 56% respectively.

T1 and T2 stage tumors in the present study constituted 17.8% and 67.8% cases respectively shown in table 3. T1 and T2 tumors in the studies done by Hori et al[9].Li et al[10]. and Almangush et al[11].constituted 56% and 44%, 61% and 39%, 44.3% and 55% respectively.

Previous studies done on early stage OSCC were predominantly conducted on unknown pathological nodal status, or without nodal status correlation.In the present study data on nodal metastases was analyzed and which was not statistically significant predictor of LRR. Univariate analysis identified LVI(P=0.627), DOI(P=0.116), nodal involvement (P =0.107), WPOI (P=0.084), LHR (P = 0.280) were not statistically significant and only Brandwein-Gensler risk model (P< 0.001) showed statistically significance shown in table 4. Similarly risk factors for LRR was done by   Hori et al.[9]identified blood vessel invasion (P = 0.03), lymphatic invasion (P < 0.001), WPOI (P < 0.001), and tumor budding and depth (P < 0.001) as histopathological risk factors for lymph node recurrence, and lymphatic invasion (P = 0.001), WPOI (P < 0.001), and tumor budding and depth (P

< 0.001) as predictive factors for DFS. Li et al.[10]identified WPOI (P = 0.0002), LHR (P = 0.0297) and Brandwein-Gensler risk model (P = 0.0012) as histological risk factors for LRR [Table 4]. The present study showed DOI, WPOI, LVI, nodal metastases, LHR were not statistically significant because of less number of cases.Only risk category was statistically significant .

CONCLUSION
Early stage OSCC is associated with a heterogeneous prognosis. DOI, WPOI, LVI, nodal metastases, LHR were not statistically significant because of less number of cases and more study is required in the present study .Only risk category was statistically significant . Adequate assessment of simple parameters on routine H and E by incorporating Brandwein-Gensler histological risk scoring model at the initial presentation can help in the prognosis and predict LRR and select patients for post surgical adjuvant therapy.

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