

## Prediction of Early Oral Squamous Cell Carcinoma Recurrence Based on the Histological Risk Score

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### Abstract:

**Introduction:** In 2018, 177,384 people died and 354,864 were diagnosed with oral cancer. There's a dispute over prognoses for young and elderly patients, as well as smoking and alcohol consumption. The prognosis depends on histological findings and grading systems. A novel risk assessment model, the Brandwein-Gensler model considers perineural invasion, host response, and whole-body invasion.

**Aims and Objectives:** This research aims to create a histological risk score for early oral squamous cell carcinoma to predict recurrence and enable more effective treatment treatments..

**Methods:** This retrospective analysis examined individuals diagnosed with T1/2 "oral squamous cell carcinoma (OSCC)" at an early stage, as defined by the 8th AJCC edition. It was carried out from September 2022 through August 2023 and came after surgical resection was used as the major therapy up to January 2020. With a particular emphasis on the efficacy of surgical resection, it examines the long-term results and prognostic variables.

**Results:** Table 1 shows the Brandwein-Gensler risk model, which scores elements to assess OSCC risk. Variables WPOI, lymphocytic host response (LHR), and Perineural Invasion (PNI). The overall score classifies patients as low (0), moderate (1 or 2), or high risk (3+). This model helps OSCC patients choose therapy and prognosis. Table 2, "locoregional recurrence (LRR)" risk factors for 120 OSCC patients include males, tumor size, lymph node involvement, poorly differentiated tumors, lymphovascular invasion, depth of invasion, nodal involvement, specific WPOI types, high LHR, and perineural invasion.

**Conclusion:** The study has concluded that this method helps prognosticate LRR and identify patients who might benefit from post-surgical adjuvant treatment.

**Keywords:** "locoregional recurrence (LRR)", tumor size, WPOI types, high LHR.

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### Introduction

In many nations, oral Cancer is thought to be the main reason for mortality from oral disorders, making it a serious health concern. According to recent estimates, there were 177,384 fatalities and 354,864 new cases worldwide in 2018. Traditional oral cancer risk factors include smoking and alcoholism [1]. Oral squamous cell carcinoma, a kind of head and neck cancer, is one of the most prevalent types (OSCC), which has become more widespread worldwide, particularly in younger age groups. It is still debatable if young and senior OSCC patients have differing prognoses. Recent investigations comparing the features of OSCC in both elderly and young individuals found no appreciable changes in tumour stage or grade. According to a recent review of the Surveillance, Epidemiology, & End Results (SEER) database, the oral tongue is the most prevalent subsite and is

linked with increased mortality since OSCC occurs in multiple subsites (including the bottom of the mouth, gingivae, as well as retromolar trigone) [2].

evaluation regarding the tumour's anatomic dimensions, clinical features, and relationship to host tissues all have an important influence on the risk of acquiring oral squamous cell carcinoma. Numerous studies highlight the need to include the histological features in oral cancer specimens which have undergone resection in pathology reports [3]. Although it is difficult to apply the prognostic influence of every core data item with absolute certainty if choosing methods of treatment in multidisciplinary meetings, it is recommended within the UK that information be collected synoptically in the RCPATH dataset format for histopathological stating of mucosal malignancies for the oral cavity [4]. which is supported by the best

available evidence. There have been several histological grading systems reported, however, there isn't universal agreement on a reliable, good prediction model. The Broders grading structure, which was developed by The WHO still recommends it, and it was perhaps the most well-known attempt at prognostication using grading of moderately as well as poorly differentiated and Important histological traits (such as mitotic activity, cellular pleomorphism, and degree of differentiation) are evaluated subjectively. Although widely accepted, this system's discriminatory power is in doubt considering that as many as ninety percent of oral tumours can differ to some extent [5].

Focusing on the relationship between the cancer & its surrounding tissue was Annoreth et al., taking into account elements including the pattern of invasion's degree, its stage, and leukocyte infiltration. Later, the intrusive front grading (IFG) system, which includes host reaction as one of five histological features was developed by Bryne et al [6]. Due to the assessment of several specimen kinds (biopsies and resection specimens), limited sample sizes, and a variety of tumour sites alone), these models have not proven successful. In more recent research, Woolgar et al. investigated prognostic indicators for lymph node metastasis, distant metastasis, and local regional recurrence. Many of the key data parameters that the UK RCPATH produced in 1998 in addition to the standard minimum dataset proforma are backed by data from investigations carried out by Woolgar [7].

A histologic risk assessment model that It was claimed that the 2005 proposal by Brandwein-Gensler and colleagues had greater prognostic value than previously mentioned techniques. The three main histology Worst patterns are “perineural invasion (PNI)”, the “lymphocytic host response (LHR)”, & the “whole-body invasion (WPOI)”. characteristics are evaluated cumulatively to form the basis of the model [8]. The three factors' combined points are added after scoring each of the three factors. When the overall score is 0, it is deemed low risk, when it is one or two, it is deemed intermediate risk, and when it is three or more, it is deemed high risk [9].

The oral cavity (OSCC) sub-entity type About 300,000 people worldwide develop head and neck squamous cell cancer (HNSCC) cases and 145,000 fatalities per year globally. The sixth most common malignancy is HNSCC overall [10]. There is no agreement on the schedule There is no established norm for examination, frequency of appointments, or both procedures, even though several Options for an OSCC follow-up regime are provided by national and international standards as well as recommendations from various working groups. In the first two years, even symptom-free patients are encouraged to have follow-up appointments every

three months, and after three to five years, every six months [11]. Even yet, diagnosis of recurrence was made in up to 78% of instances due to largely symptoms that patients with OSCC self-report having and lack of identification during routine follow-up visits. Accordingly, scant data is supporting the efficacy after initial OSCC therapy, of follow-up, and there is also scant evidence that careful follow-up can enhance oncologic outcomes. Therefore, Research in the future should focus on risk stratification to establish evidence-based follow-up recommendations following OSCC [12].

## Method

### Research Design

This retrospective study examined early-stage T1/2 “oral squamous cell carcinoma (OSCC)” patients defined by the 8th edition of the AJCC. The study considered patients who visited the hospital from September 2022 to August 2023. Surgical resection was the primary treatment for primary “oral squamous cell carcinoma (OSCC)” patients in the trial, which followed them until January 2020. This study examines early-stage “oral squamous cell carcinoma (OSCC)” patients' long-term outcomes and prognostic factors, with a focus on surgical resection efficacy. This study will retrospectively review medical data and follow-up information to gather insights into illness progression, treatment outcomes, and survival rates. This study aims to improve our understanding of early-stage “oral squamous cell carcinoma (OSCC)” therapy.

Brandwein-Gensler risk model gives points to factors to estimate oral squamous cell carcinoma risk. WPOI, LHR, and PNI are variables. Assigning WPOI points depending on tumor development type, smaller tumor islands and satellites have higher risk. A weaker host immune response scores higher in LHR. Larger nerves increase PNI risk. Adding these factors' scores yields a total score, which classifies patients as low risk (0), moderate risk (1 or 2), or high risk (3 or more). OSCC patients' prognoses and treatment choices are guided by this risk model.

### Inclusion and Exclusion Criteria

#### Inclusion

- Early-stage T1/2 OSCC patients according to the 8th edition of AJCC staging.
- Primary surgical resection patients.
- Patients have documentable follow-ups till January 2020.
- Patient ages are not limited.
- All genders and ethnicities are treated.

#### Exclusion

- Patients with advanced OSCC (beyond T1/2) according to 8th edition AJCC staging.
- Non-surgical resection patients.

- Patients with oral or other cancer histories.
- Children under a certain age.
- Patients having coexisting diseases or contraindications that potentially affect research results.

**Table 1: Brandwein-Gensler risk model**

Variable	Definition	Point assignment
Worst pattern of invasion		
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		
Type 1	Strong	0
Type 2	Intermediate	1
Type 3	Weak	3
PNI		
None	None	0
Small nerves	Small nerves	1
Large nerves	Large nerves	3
Total score Low risk=0, Intermediate risk=1/2, High risk = $\geq 3$		

### Statistical Analysis

Descriptive statistics were employed to provide a summary of the histological characteristics of patients and the classification of the disease at the time of diagnosis. All pertinent data was inputted into the Microsoft Excel spreadsheet. The statistical software SPSS, specifically version 21.0, was utilized for the analysis. Log-rank tests were utilized to conduct a univariate analysis of the risk factors associated with the local recurrence of the disease. A P value less than 0.05 was deemed to be statistically significant.

### Result

Table 2 shows a complete study of “locoregional recurrence (LRR)” risk factors in 120 “oral squamous cell carcinoma (OSCC)” patients. Male patients (M) were more likely to develop LRR than females (F) based on demographic and clinical factors. Clinical staging showed that tumor size and lymph node involvement affect recurrence, as T1N0M0 patients had a greater risk than T2N0M0 cases. “Poorly differentiated (PD)” tumors had a much greater LRR risk than WD tumors. “Lymphovascular invasion (LVI)”, DOI greater than 5 mm, nodal involvement, WPOI types 4 and 5, high LHR, and perineural invasion (PNI) were all significantly associated with LRR. Clinical and histological criteria are crucial to risk assessment, as shown by these data. A risk-scoring model showed that 'high-risk' patients had a far greater LRR incidence than 'mid' and 'low-risk' individuals. The need for complete risk assessment in OSCC therapy and monitoring is highlighted by these findings.

### Discussion

Research in the future should focus on risk stratification agreement on the follow-up period. The purpose of the study was to examine the recurring pattern, detection technique, and related characteristics to determine potential risk classification. Retrospectively collected histopathological and epidemiological characteristics were linked with tumour recurrence, the overall prognosis, lymph node metastases, and distant metastases [13]. There were 760 patients altogether, 216 of whom had tumour recurrence. 24% of all recurrences were discovered during the first 12 months. Clinical examination served as the main means of detection. Lymph node metastases and advanced histopathological grading were substantially linked with tumour recurrence. Recurrence of the tumour was common. The primary technique of identification was clinical examination, and the likelihood of manifestation during the initial 6–12 months was high. For risk classification, the level of histopathological grading could be helpful [14].

With death rates of up to 92%, tumour recurrence continues to be one of the key issues in oral squamous cell carcinoma (OSCC) treatment. The prognosis is poorer for early recurrences than for late relapses. The impact However, there has not been much discussion in the literature on the impact of clinicopathological variables on the period of recurrence & patient survival [15]. The effectiveness of a salvage therapy, extracapsular dispersion, border status, and time to recurrence all of them are independent prognostic factors for overall survival. in patients who have recurrent OSCC. Additionally, there is a strong correlation between the main tumor's grade, when the lymph node ratio, margin state, and recurrence. With this knowledge,

personalised monitoring programmes may be created, which will lead to a quicker diagnosis and a greater likelihood of a second treatment in the event of a recurrence [16].

**Table 2: Various risk variables for LRR were analyzed using univariate analysis (log-rank tests).**

Variables	Total number of patient (120)	Recurrent cases (80)	P-value
Sex			
M	70	55	
F	50	25	
Clinical stage			
T1N0M0	65	51	
T2N0M0	55	29	
Differentiation			
Well differentiated	75	40	
Moderately differentiated	35	21	
Poorly differentiated	10	19	
Lympho-vascular invasion			
Present	51	49	<0.00001
Absent	69	31	
Depth of invasion			
<=5 mm	55	45	<0.00001
6-10 mm	65	35	
Nodal involvement			
Present	59	42	<0.00001
Absent	61	38	
Worst pattern of invasion			
Type 1,2,3 (Score 0)	71	32	<0.00001
Worst pattern of invasion 4 (Score 1)	31	22	
Worst pattern of invasion 5 (Score 3)	18	26	
Lymphocytic host response			
Type 1 (Score 0)	65	34	0.004
Type 2 (Score 1)	32	28	
Type 3 (Score 3)	23	18	
Perineural invasion			
None (Score 0)	52	39	0.012
Small nerves (Score 1)	40	21	0.004
Large nerves (Score 3)	28	20	
Risk scoring			
Low	12	40	
Intermediate	80	29	
High	28	11	

WD: Well differentiated, MD: Moderately differentiated, PD: Poorly differentiated, LVI: Lympho-vascular invasion, DOI: Depth of invasion, WPOI: Worst pattern of invasion, LHR: Lymphocytic host response,

The most frequent carcinoma impacting More than 90% of the mouth is oral squamous cell carcinomas (OSCC)", a kind of cancer found in the mouth cavity. A considerable percentage of "Loco regional recurrence (LRR)" is a complication of early-stage T1/T2 OSCC that lowers disease-free survival (DFS) & raises disease-related mortality. To evaluate the accuracy of the three factors that determine LRR in early-stage OSCC: lymphovascular invasion (LVI), depth of invasion

(DOI), & lymph node metastases [17]. The present investigation examined patients with initial stages of T1/2 OSCC who underwent surgical resection over two years and had follow-up information. Based on OSCC recurrence at the original site or in local lymph nodes, LRR was evaluated. Integrating the Brandwein-Gensler histological risk score model into the adequate evaluation of basic parameters on routine H and E at the first presentation can help in forecasting LRR, choosing patients who need post-surgical adjuvant therapy, and prognosticating treatment [18].

Stage I/II, or T1N0/T2N0, low-stage (oral squamous cell cancer) is typically treated surgically. A sizable portion Of individuals with oral cavity low-stage

carcinoma of squamous cells may have local recurrence & disease-related death, nonetheless. Based on an established histologic risk model, we divided 64 individuals were divided into high-, intermediate-, & low-risk groups for the present investigation with low-stage oral tongue and floor-of-mouth cancer [19]. These risk factors are determined by the presence and overall absence of perineural assault, the tumour-host junction's inspection for the worst invasion pattern, and lymphocyte host response. categories were created. Even after correcting We identified low-stage cavity squamous cell carcinoma individuals who are in the high-risk group for margin status and the T-stage group have a considerably greater chance for recurrence than patients with the group of low- or intermediate-risk. The morbidity and mortality linked to a recurrence may be reduced with adjuvant therapy for these individuals. Our findings suggest the histologic risk framework is a practical and easy-to-use method to evaluate Stage I and II oral squamous cell carcinoma recurrence risk [20].

'High-risk' tumours had a significant correlation likely because of the potential for aggressive traits like WPOI and PNI with distant metastasis. This was done to determine whether the Brandwein-Gensler risk model, as originally proposed, influences survival as well as development of the illness in individuals treated for oral squamous cell carcinoma (OSCC) [21]. As the T stage rises, High-risk characteristics are more frequently seen in primary tumours. characteristics. None of the 'low-risk' individuals passed away, which may indicate that These tumours have a very favourable prognosis and are an uncommon kind of OSCC [22].

To look at a collection of patients having oral cavity squamous cell carcinoma and the application of the histological risk model who received neck dissections simultaneously. Three pathologists came to a consensus on how to rate the primary tumours of 85 patients who had neck dissection and primary excision of the first and second-stage oral squamous cell carcinomas [23]. The conventional dataset values and risk score data were evaluated to look for any potential associations with extracapsular spread and nodal metastases. 62 individuals were labelled as having "high risk," while 72 patients were classified as having "low or intermediate risk." Nodal metastatic cases were statistically significantly different from the overall risk model score. according to a chi-squared test [24]. No metastasis was visible in any cancers with low risk ratings and had fewer head dissections, suggesting this the risk score might be a useful tool to identify a lack of metastasis. The existence or lack of metastases at presentation may be predicted by evaluation of risk initial tumours of oral squamous cell carcinoma at early stages. Making treatment decisions during multidisciplinary meetings may be

influenced by understanding the risk score and its component elements. Squamous cell carcinoma with minimal metastatic potential and great long-term survival may be an uncommon variety [25].

### Conclusion

The study has concluded that this method helps prognosticate LRR and identify patients who might benefit from post-surgical adjuvant treatment. Personalized risk assessment and treatment decision-making may improve early-stage OSCC management and results. In conclusion, early-stage "oral squamous cell carcinoma (OSCC)" has a variety of prognoses, and numerous key characteristics predict "locoregional recurrence (LRR)". This study emphasizes the importance of independent risk factors like "Depth of Invasion (DOI)", "Worst Pattern of Invasion (WPOI)", "Lymphovascular Invasion (LVI)", nodal metastases, LHR, PNI, and the Brandwein-Gensler risk model in assessing and predicting LRR. Additionally, including the Brandwein-Gensler histological risk grading model into regular H&E-stained sections at the first presentation is beneficial.

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