

ORIGINAL ARTICLES

CORRELATION OF HISTOLOGICAL RISK ASSESSMENT/ SCORING SYSTEM WITH LYMPH NODE METASTASIS AND RECURRENCE/PROGRESSION OF DISEASE IN ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Objective: To correlate the scoring system using histopathologic parameters; worst pattern of invasion (WPOI), lymphocytic host response (LHR) and peri-neural invasion (PNI), with disease recurrence, overall survival and cervical lymph node metastasis in OSCC patients.

Study Design: Cross sectional.

Place and Duration of Study: Department of Histopathology, Shaukat Khanam Memorial Cancer and Research Hospital, Lahore in collaboration with Department of Histopathology, Armed Forces Institute of Pathology, Rawalpindi. Study completed in 2 years.

Material and Methods: A "Risk Scoring system" was applied to 50 cases of OSCC with 2 years follow-up data, based on histopathologic parameters WPOI, LHR and PNI. The cases were divided into High risk and Non-High risk categories according to the specified parameters and then correlated with disease recurrence, overall survival and cervical lymph node metastasis.

Results: There were 7 low risk, 17 intermediate risk and 26 high risk cases. No correlation was seen between the risk groups and disease recurrence, overall survival or cervical lymph node metastasis. However, when assessing the individual parameters, significant correlation was observed between PNI with disease recurrence ($p = 0.03$), and between WPOI and overall survival ($p = 0.02$) and cervical lymph node metastasis ($p = 0.005$).

Conclusion: The individual parameters, peri-neural invasion and worst pattern of invasion are observed to be significant prognostic indicators in OSCC patients. A study with a larger number of cases is required to truly assess the value of the scoring system in Pakistani patients.

Keywords: Oral squamous cell carcinoma, Peri-neural invasion, Worst pattern of invasion.

INTRODUCTION

Squamous cell carcinoma ranks as one of the top 10 cancers worldwide¹. It is also amongst the 10 most common malignancies in Pakistan, mostly involving the patients above the age of 50 years. The major risk factors in Pakistan are tobacco use (in the form of naswar, snuff and tobacco chewing)². Despite the recent advances in medicine, the overall 5 year survival rates for oral squamous cell carcinoma have shown very little improvement. The major cause of death in these patients is loco-regional

recurrence.

A number of factors, such as tumour size, malignancy grade, resection margin status, lymph node metastasis, peri-neural invasion, etc, influence loco-regional recurrence and overall survival for these patients. Standard histopathology does not predict the treatment response / prognosis very well. In routine practice, high stage (stage III/IV) patients are treated more aggressively and are offered multimodality treatments. On the other hand low stage (stages I/II) patients are given single modality treatments. In these patients there is 25-37% recurrence after single modality treatment¹. These patients are candidates for more aggressive therapy. In a study of risk assessment, various histological parameters and pattern of invasion, lymphocytic response and peri-neural invasion were found to be good

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predictors of aggressive behavior in patients. Subsequently these authors proposed a scoring system for determining the risk category of these patients. The scoring system gives a score of 0-9 to different tumours for purpose of risk assessment.

The rationale for present study was to assess the modified scoring system in identifying the low stage (stage I/II) patients who are at a high risk of disease progression, then these patients can be offered adjuvant chemo-radiotherapy in hope of improving their overall survival and reducing the chances of local recurrence, as patients with high stage disease are usually already given multimodality treatment.

MATERIAL AND METHODS

This cross section study was carried out at Department of Histopathology, Shaukat Khanam Memorial Cancer and Research Hospital, Lahore in collaboration with

collected from files (with at least 2 years follow-up). As per inclusion criteria 50 cases were recovered. All diagnosed cases of oral squamous cell carcinoma with neck dissection were included. All the patients who had received chemo/radiotherapy prior to surgery or had visceral metastasis were excluded from the study. Already prepared and new slides (where required) were stained with haematoxylin and eosin (H&E), and studied for the histological parameters. Following histological variables like Worst pattern of invasion (WPOI), Peri-neural invasion (PNI) and Lymphocytic host response (LHR) were studied. The cases were analysed by applying the Risk Model given in (table-1) adapted from³. The cases were divided into three categories according to the total points for each individual case as follows: Low risk = total point score 0 Intermediate risk = total point score 1 or 2 and High risk = total point score 3 or greater. The

Table-I: Risk scoring system (Adopted form Brandwein-Gensler et al, 2010).

Variable		Definition	Point assigned
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 tumour islands, 15 cells or fewer per island	+1
	Type 5	Tumour satellites, equal or greater than 1mm away from main tumour (20x) or next closest satellite	+3
LHR	Type 1 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	Tumour wrapping around nerves, <1mm diameter	+1
	Large nerves	Tumour wrapping around nerves, equal to or greater than 1mm diameter (20x)	+3

Department of Histopathology, Armed Forces Institute of Pathology, Rawalpindi. Tissue embedded samples of the patients were

data was entered and analysed using SPSS 20. Pearson correlation was applied to observe correlations between scoring system and lymph

node metastasis and also with recurrence or disease progression. A *p*-value of <0.05 was considered as statistically significant.

RESULTS

A total of 50 cases of oral squamous cell carcinoma along with their cell blocks of neck dissection specimens were included in this study. Neck dissections included radical neck, supra-omohyoid and modified neck dissections. The age range was 32-68 and mean age of the patients was 49.74 years. Thirty (60%) were male and 20 (40%) female patients. All patients

correlated. A strong LHR was seen in 21 (42%) cases, moderate LHR in 16 (32%) cases and weak in 13(26%) cases. This lymphocytic host response was also correlated with overall survival, disease recurrence and Lymph node status. The *p*-value for all these parameters showed insignificant correlation. Peri-neural invasion (PNI) of large nerves was seen in 3 (6%) of the total cases whereas, PNI of small nerves was found in 15 (30%) of the cases and 32 patients had no PNI. The PNI showed significant correlation with disease recurrence

Table-2: Showing association of worst pattern of invasion (WPOI) with survival, recurrence and lymph node status.

Types of WPOI	Alive	Recurrence	Lymph node involvement
Type 1	1 (100%)	0 (0%)	0 (0%)
Type 2	1 (100%)	0 (0%)	1 (100%)
Type 3	10 (67%)	9 (33%)	9 (60%)
Type 4	20 (77%)	10 (23%)	15 (58%)
Type 5	6 (86%)	1 (14%)	3 (43%)
<i>p</i> -Value	<i>p</i> =0.0209 (significant)	<i>p</i> =0.097 (not significant)	<i>p</i> =0.005 (significant)

had primary carcinoma of tongue. The size of the tumour ranged from microscopic (0.2 cm) to 4.5 cm with average size of 3.8 cm. Twelve cases (24%) had well-differentiated, 31 (62%) moderately differentiated and 7 (14%) patients had poorly differentiated squamous cell carcinoma. Out of 50 patients, 38 (76%) patients were alive at the date of last follow up and 12 (24%) patients were dead. Recurrence of disease was observed in 20 cases out of 38 patients who were alive at the time of last follow up. From the neck dissection specimens of 50 patients, 28(56%) showed lymph node involvement by the tumour, whereas 22 (44%) were lymph node negative. Out of the total 50 cases, stage I disease was seen in n=18 (36%) of the cases, stage II in 27 (54%), stage III in 3 (6%) and stage IV in 2 (4%) of the cases

On analysis of worst pattern of invasion (WPOI), majority of the patients had type 3 and 4 pattern (type 3 in 15 (30%) and type 4 in 26 (52%) cases). The relationship of WPOI with survival and disease recurrence is given in Table-II and it was statistically significantly

(*p*-value=0.038), whereas correlation with overall survival and lymph node metastases was insignificant. On risk analysis as per table-I, seven cases (14%) fell in to low risk group, 17 (34%) in intermediate and 26 (52%) in high risk group. Categorization in these groups did not show any significant correlation with overall survival, lymph node metastases or recurrence.

DISCUSSION

Treatment of oral SCC is usually based on TNM staging and grade of the tumour⁴. Stage I and II patients being treated through surgery or radiation therapy alone as survival rates for both modalities are considered to be the same^{3,5}. A more aggressive treatment approach is usually opted for patients with stage III or IV disease. It is found that 25-37% of low stage (stage I and II) patients may develop loco-regional recurrence and requires multi-modality treatment approach³. Various clinical and histopathological variables have been studied in an attempt to predict the biological behavior and prognosis in OSCC patients. These include tumor size and thickness⁵,

resection margin status⁷, lymph node metastasis⁸, peri-neural invasion⁷, inflammatory cell infiltrate and lymphocyte host response⁷, and pattern of tumor invasion etc⁹. Over the last few years various scoring systems or models have been proposed, based on factors such as micro-vascular invasion, tumour thickness, inflammatory infiltration and peri-neural spread. Multi parameters model has been found to be more successful¹⁰.

In present study the worst pattern of tumor invasion, (WPOI) showed significant association with survival and lymph node metastases and same was observed earlier. The percentages of different types (Type-IV maximum) of WPOI was also same^{11,12} contrary to the study done by Bryne et al (1995)¹³. Disease recurrence with WPOI type-3 was found in majority of the cases in present series contrary to earlier observation where it was more in type-511. These results can be attributed to small number of cases in the present series.

Lymphocytic host response (LHR), of the category of strong moderate and weak, found in this series was same as reported earlier¹⁴. It was insignificantly associated with different parameters but the highest number of disease recurrence (46%) was seen in those cases with a weak LHR and same was supported by earlier observations¹¹. In the present study no significant correlation was found between LHR and cervical lymph node metastasis. Conversely other studies have shown LHR as part of a multivariate analysis to be significantly correlated to cervical lymph node metastasis^{11,12}. This difference in the results may be attributed to the more number of cases studied in other study series.

Extensive studies have been carried out in order to identify the importance of peri-neural invasion (PNI). Variable results have been reported. In the present study, peri-neural invasion (PNI) was seen in 36% cases as compared what was reported earlier showing wide variation from 10-60%¹⁵⁻¹⁷. In the present study a significant correlation ($p=0.03$) was found between PNI and recurrence of disease

and same was observed earlier. The size of nerve involvement is also important¹⁵. The results in the present study as others showed that PNI is a reliable indicator of disease recurrence¹⁸. The overall survival with peri-neural invasion was found similar as reported earlier¹⁵.

The division of cases in to non-high risk (including both low and intermediate risk group) and the high risk group was similar as found earlier¹¹. In another study 76% of the cases were found in high risk group. Although high risk groups showed more recurrence but it was not statistically significant. Same higher recurrence rate was observed in the high risk group in earlier studies. The correlation of scoring system with cervical lymph node metastasis showed no significant correlation¹¹⁻¹³.

CONCLUSION

Correlation of the individual parameters included in the scoring system showed Peri-neural invasion (PNI), worst pattern of tumour invasion (WPOI) to be significantly correlated to disease recurrence in OSCC patients. Although high risk groups and patients with low LHR showed more disease recurrence and lymph node metastasis but it was not statistically significant. Preferably more such studies are required to further validate this scoring system in our set up.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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AUTHORS CONTRIBUTION

Marya Batool, case selection, Interpretation & analysis, Sajid Mushtaq, verification of findings, Shahid Jamal, supervision, write up, concept, Asif Loya, slides reviewed.