Impact of Novel Histologic Risk Factors on Recurrence Rates for Oral Cavity Squamous Cell Carcinoma

Maxwell P. Kligerman[1] MD, MPH; Peter Moon[2] BA; Mahbuba Tusty[2], BA; Jeffrey M Cloutier[2], MD, PhdD; Christopher F. Holsinger[1], MD; Vasu Divi[1], MD

1. Department of Otolaryngology, Stanford University, Palo Alto, CA; 2. School of Medicine, Stanford University, Palo Alto, CA; 3. Department of Pathology, Stanford University, Palo Alto, CA

ABSTRACT

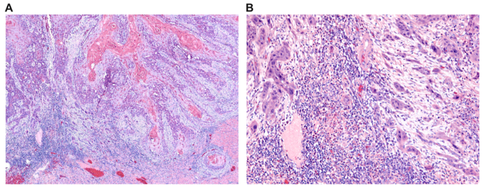
- This study assesses the impact of novel adverse histologic risk factors on recurrence rates for patients with early stage oral cavity squamous cell carcinoma (OCSCC)
- The analysis focuses on the impact of tumor budding (TB), Predominant Pattern of Invasion (PPOI), and Tumor Infiltrating Lymphocytes (TILS)
- Retrospective chart review was performed at a single institution
- 161 patients met criteria and were included in the analysis
- TB was the strongest predictor of recurrence and a stronger predictor than established risk factors like depth of invasion
- PPOI trended towards significance on bivariable analysis but on multivariable analysis was not significant
- TILS was not significantly associated with recurrence

BACKGROUND

- Early stage OCSCCs that are excised with five millimeter margins still face recurrence rates ranging from 10-30%[1]
- The etiology for this high rate of failure remains unclear
- Previously unappreciated, adverse histologic factors confer increased risk of recurrence despite adequate margins
- Factors like worst pattern of invasion (WPOI), predominant pattern of invasion (PPOI), tumor budding (TB), and tumor infiltrating lymphocytes (TILS), may be independently linked to local recurrence or distant spread

KEY TERMS

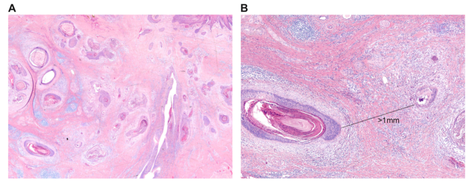
TERM	DEFINITION
Pattern of Invasion (POI)	Histologic appearance of the host/tumor interface[2]
POI 1	tumors that invade in a broad, pushing manner
POI 2	tumors that invade with broad pushing fingers or those with separate stellate appearing large tumor islands
POI 3	tumors with invasive islands of greater than 15 cells per island
POI 4	tumors with invasive islands smaller than 15 cells per island (including single cell invasion)
POI 5	tumors with satellites of tumors of any size with 1 mm or greater of intervening normal tissue at the tumor/host interface
Worst Pattern of Invasion (WPOI)	highest grade POI visualized
Predominant Patter of Invasion (PPOI)	most prevalent pattern of invasion
Tumor Infiltrating Lymphocytes (TILS)	lymphocyte response at the host/tumor interface[2]
TILS 1	weak reaction characterized by dense collections of lymphocytes in some but not all 4x magnification fields
TILS 2	intermediate response with dense collections of lymphocytes present in all 4x magnification fields
TILS 3	complete host response with lymphocytes rimming the invasive front of the tumor
Tumor budding (TB)	Single tumor cell or a cluster of 5 or fewer tumor cells at the host/tumor interface[4]
Present	Tumor budding present
Absent	Tumor budding absent
Total number	Total number of tumor buds at 20x magnification



Representative oral cavity squamous cell carcinoma with numerous tumor buds at the invasive tumor front. The tumor is also associated with a brisk inflammatory response. (A, 40x; B, 200x).

METHODS

- Retrospective chart review was performed at a single institution to identify patients with OCSCC who underwent surgical excision with or without elective neck dissection
- Inclusion criteria included T1-T2 stage disease based on AJCC 7th edition guidelines, no cervical lymph node involvement, no perineural invasion (PNI), no lymphovascular invasion (LVI), no post-operative adjuvant radiation therapy, and cancer involving only the oral tongue or floor of mouth
- Patients were excluded if they had positive final margins
- A subset of 35 patients were selected for additional histologic review to determine WPOI, PPOI, TB, and TILS
- Bivariable and multivariable cox analysis was performed to determine variables that were significantly associated with recurrence



Representative oral cavity squamous cell carcinoma with a high grade pattern of invasive (POI 5), characterized by islands of tumor separated by > 1mm of stroma at the invasive tumor front. (A, 10x; B, 40x)

RESULTS

- 161 patients met criteria and were included in the analysis
- Variables that were significantly associated with recurrence on bivariable analysis included tumors with high risk PPOI (groups 4 and 5; p=0.021), TB with ten or more buds (p=0.021), T-stage (p=0.001), neck dissection (p=0.03), and depth of invasion (DOI) >4 mm (p= 0.044)
- Multivariable cox proportional hazards model were run in a step-wise fashion
- The final model identified T-stage (HR: 6.40; p=0.007), neck dissection (HR: 0.23; p=0.023), and TBs (HR: 1.17; p=0.006) as significantly associated with recurrence

CONCLUSIONS

- Tumor budding is the strongest predictor of recurrence and is a stronger predictor even than depth of invasion
- While PPOI trended towards significance on bivariable analysis, on multivariable analysis it was ultimately not significant
- TILS was not significantly associated with recurrence
- These novel histologic risk factors may help further guide recurrence prognostication and/or treatment in the future for patients with OCSCC

References

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