Perineural invasion in sinonasal malignancies: Analysis of incidence, predictive factors and prognostic implications

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INTRODUCTION

- Perineural invasion (PNI) is recognized as one of the significant modes of tumor spreading various malignancies including head and neck tumors
- Presence of PNI represents an adverse prognostic marker with increased risk of locoregional recurrence
  - Therefore, it is an indication that the underlying malignancy is inherently aggressive
- It is important to identify presence of PNI when assessing head and neck malignancies in general
  - Due to a lower incidence of sinonasal malignancy (SNM), the impact of PNI on survival outcomes in in this specific group is unclear.
  - SNM are distinct from other head and neck tumors with a variety of histopathologic subtypes, increased proximity to critical neurovascular structures and variable morbidity and mortality
- **Objective:** To assess incidence rates, characterize predictors, and analyze survival outcomes in SNM patients with PNI

METHODS

- Retrospective Chart Review
  - **Inclusion Criteria**:
    - Patients with non-cutaneous SNM that were treated between 2012 and 2019
    - Patients who underwent surgical treatment with a curative intent
  - **Exclusion Criteria**
    - Treatment with a palliative intent
- Primary independent variable of interest: PNI status
  - Other variables: Demographics, TNM classification, tumor type (primary vs recurrent), extrasinonasal extension, pathologic grade, lymphovascular invasion, post-surgical margins.
- **Statistical Analysis**
  - Association between PNI status, patient, tumor and treatment characteristics was conducted using chi square and fisher's exact tests.
  - Kaplan Meier survival curve was plotted to assess correlation between PNI status and survival

RESULTS

All patients of sinonasal malignancies treated during study period (N=233)

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Patients who underwent surgical modality of treatment with curative intent (N=204)

↓

Patients who had PNI reported in the final surgical pathology report (N=195)

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Patients with PNI (N=54)
Patients without PNI (N=141)

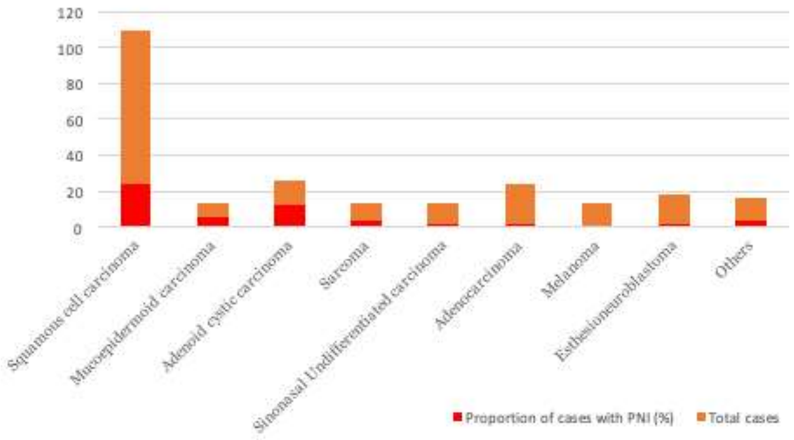
Demographics:
N= 195 patients

Mean age at surgery: 63.7 + 15.2 years

58% Males (n=114)
76% Caucasian (n=148)

59% with history of smoking (n=116)

Proportion of Cases with Perineural Invasion based on Histopathological Diagnosis

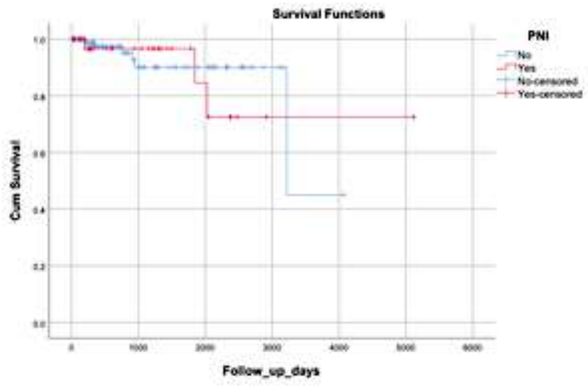


Significant predictive factors and prognostic implications for PNI

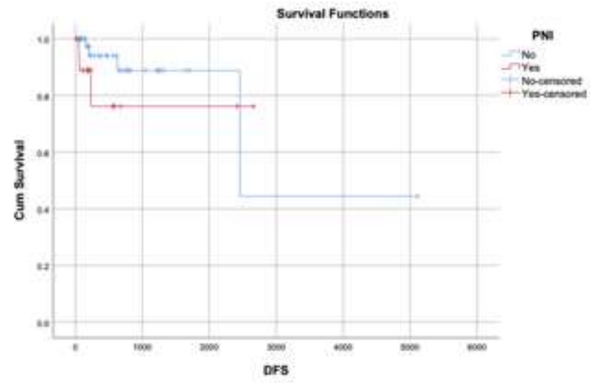
	Perineural invasion (n (%))		P value	OR (95% CI)
	Absent	Present		
T classification				
T1 or T2	15 (93.8)	01 (6.3)	0.012	9.71 (1.20-78.79)
T3 or T4	34 (60.7)	22 (39.3)		
N classification				
N_0	43 (74.1)	15 (25.9)	0.05	3.82 (1.14-12.83)
Any N+	06 (42.9)	08 (57.1)		
TNM staging				
Stage I or II	18 (94.7)	1 (5.3)	0.002	14.72 (1.79-121.2)
Stage III or IV	22 (55.0)	18 (45.0)		
Extra-sinonasal extension				
No	38 (82.6)	08 (17.4)	0.02	3.17 (1.18-8.53)
Yes	24 (60.00)	16 (40.00)		
Skull base involvement				
No	52 (77.6)	15 (22.4)	0.04	3.12 (1.07-9.08)
Yes	10 (52.6)	09 (47.4)		
Orbit involvement				
No	46 (80.7)	11 (19.3)	0.021	3.40 (1.27-9.09)
Yes	16 (55.2)	13 (44.8)		
Neck dissection				
No	44 (83.0)	9 (17.0)	0.004	4.07 (1.51-10.98)
Yes	18 (54.5)	15 (45.5)		
Surgical approach				
Endoscopic	35 (85.4)	06 (14.6)	0.009	0.26 (0.09-0.74)
Non-endoscopic	27 (60.0)	18 (40.0)		
Duration of hospital stay				
Mean (in days)	3.05	7.21	0.0001	
Standard deviation (in days)	3.31	5.93		

- Patients with and without PNI were found to be comparable in terms of age, gender, race, preoperative BMI, smoking status, and duration of follow up
- With regards to treatment, cases with PNI were 3.2 [95% CI 1.45-7.06] times more likely to undergo adjuvant radiotherapy (p=0.003) than cases without invasion
- Recurrence (time to recurrence and recurrence rates), long term survival outcomes, and 30 day readmission were found to be comparable between patients with and without PNI
- Through univariate analysis tumor laterality and recurrence were found to be significant, however upon multivariate analysis it was noted that none of the variables retained their significance

Overall Survival Outcomes in Patients with and without PNI



Disease Free Survival in Patients with and without PNI



- 70% (N=137) of patients had documented completion their respective cancer treatment and were included for survival analysis
- Both overall (p=0.795) and disease free log survival (p=0.261) between patients with and without PNI was comparable.

DISCUSSION

- The frequency of perineural invasion in sinonasal malignancies is lower than that of other head and neck sites, however this varies with histologic subtype
  - Our study demonstrates that overall, adenoid cystic carcinoma and mucoepidermoid carcinoma have high propensity for PNI, whereas melanoma and adenocarcinoma rarely invade nerves
- Perineural invasion in sinonasal malignancies is not a significant predictor of survival or recurrence provided adjuvant radiotherapy is utilized.
  - In patients with PNI, salvage surgery for recurrent disease can help achieve survival rates that are comparable to those without PNI.

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