

Impact of perineural invasion on oncologic outcomes in early-stage oral cavity squamous cell carcinoma. A seven-institution analysis of 532 patients.

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INTRODUCTION

- Early-stage oral cavity squamous cell carcinoma (OCSCC) demonstrates variable clinical behavior, ranging from indolent to aggressive
- Perineural invasion (PNI) has been associated with worse outcomes in OCSCC in studies of small or heterogeneous patient populations¹⁻⁷

Hypotheses:

1. PNI has an independent association with poor oncologic outcomes
2. Adjuvant radiotherapy (XRT) mitigates the adverse effects of PNI

METHODS

- Retrospective series from seven tertiary medical centers
- Inclusion criteria - Adult patients (≥18-19 by state law); nonrecurrent clinical stage T1-2N0M0 OCSCC; primary surgical treatment
- Kaplan-Meier estimates and Cox proportional hazards models (CPHM) constructed to investigate overall survival (OS), disease-free survival (DFS), and locoregional control (LRC). All cases censored at 60 months of follow-up
- PNI status derived from pathology report as binary variable
- Subset analysis included patients with PNI positive tumors that were AJCC7 pathologic stage T1-T2N0, lymphovascular invasion negative, with negative surgical margins

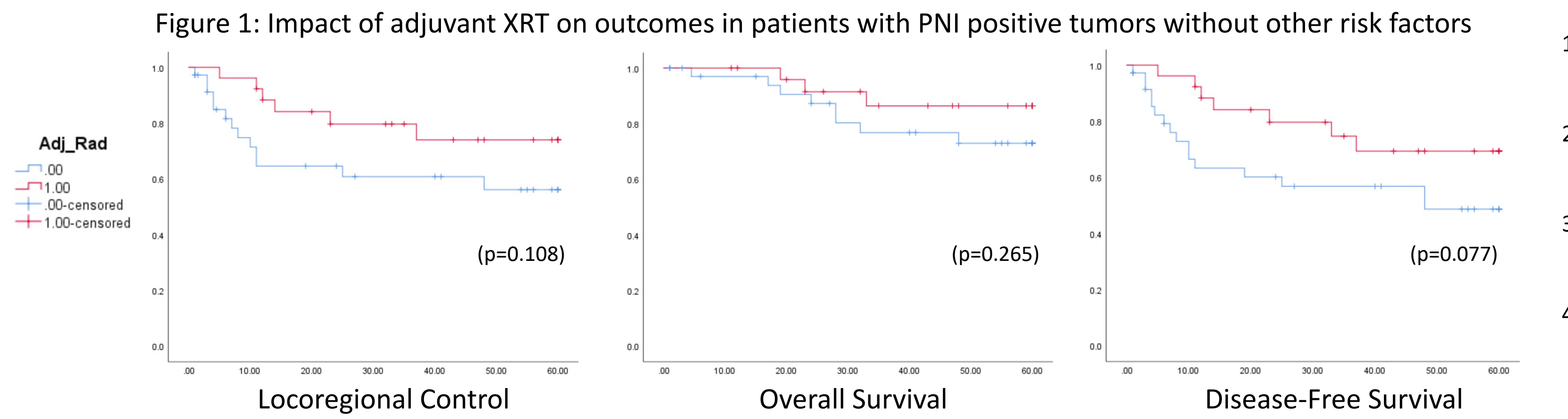
RESULTS

- 587 patients treated from 2000 to 2018, 532 included in survival analyses
- Median follow-up 48 months (Range 0-60), 156 patients had 5-year follow-up
- Clinical and pathologic characteristics in tables 1-2

Table 1: Clinical characteristics		
Variable	Category	n= (%)
Age	Mean (SDV)	61.5 (13.6)
Sex	Male	330 (56.2)
	Female	257 (43.8)
BMI	Mean (SDV)	27.3 (5.8)
Smoking Status	Current	141 (24.9)
	Former	203 (35.8)
	Never	223 (39.3)
Tumor Site	Cheek	30 (5.1)
	Floor of mouth	69 (11.8)
	Alveolar ridge	30 (5.1)
	Hard palate	14 (2.4)
	Lip	10 (1.7)
	Mouth NOS	17 (2.9)
	Retromolar trigone	18 (3.1)
	Tongue	399 (68.0)
cT Classification	T1	358 (61.0)
	T2	229 (39.0)
cN Classification	N0	587 (100)

Table 2: Pathology and treatment characteristics		
Variable	Category	n= (%)
pT Classification	T1	408 (69.5)
	T2	167 (28.4)
	≥T3	12 (2.0)
Grade	1	239 (41.0)
	2	302 (51.8)
	3	42 (7.2)
DOI/TT	Mean (SDV)	5.5 (4.5)
	Yes	64 (11.4)
LVI	No	499 (88.6)
	Yes	123 (21.7)
PNI	No	445 (78.3)
	Yes	36 (6.2)
Positive Margins	No	542 (93.8)
	Yes	36 (6.2)
pN Classification	Nx	191 (32.5)
	N0	310 (52.8)
	N1	51 (8.7)
Adjuvant XRT	N2b	35 (6.0)
	Yes	124 (21.1)
	No	463 (78.9)
Adjuvant Chemo	Yes	53 (9.0)
	No	534 (91.0)
Neck Dissection	Yes	391 (66.6)
	No	196 (33.4)

- Oncologic Outcomes
 - Among all patients at 2 and 5 years respectively, OS was 90.6% and 83.3%, DFS was 78.0% and 69.5% and LRC was 83.1% and 77.9%
- Univariate analyses
 - PNI associated with worse OS (p=0.021), DFS (p<0.01), and LRC (p<0.01)
 - Among all PNI positive patients, adjuvant XRT not associated with differences in OS (p=0.597), DFS (p=0.984), or LRC (p=0.779)
 - Among patients with PNI as an isolated risk factor (n=62), patients receiving XRT did not experience significantly improved LRC (p=0.108), OS (p=0.265) or DFS (p=0.077) although clinical differences in 2-year LRC (77.3% vs 60.7%) and 2-year LRC (77.3% vs 58.1%) may be meaningful



- Multivariate analyses
 - Associations with worse OS included AJCC7 pN classification ≥N1 (HR 2.55, CI 1.33-4.90), adjuvant XRT (HR 1.95, CI 1.18-3.22), advanced age (HR 1.05, CI 1.03-1.07), and higher depth of invasion (DOI) / tumor thickness (TT) (HR 1.05, CI 1.02-1.08)
 - Associations with worse DFS included adjuvant chemotherapy (HR 2.72, CI 1.81-4.07), advanced age (HR 1.01, CI 1.00-1.03), and higher DOI/TT (HR 1.04, CI 1.02-1.07)
 - Associations with worse LRC included PNI (HR 1.63, CI 1.05-2.53), adjuvant chemotherapy (HR 2.51, CI 1.54-4.09), higher DOI/TT (HR 1.04, CI 1.01-1.08), and no neck dissection (HR 1.66, CI 1.10-2.50)

CONCLUSION

- PNI is independently associated with worse LRC but not DFS or OS among 532 patients treated surgically for nonrecurrent clinical stage T1-2N0M0 OCSCC
- Adjuvant XRT not associated with improved outcomes among PNI positive patients in univariate analysis, possibly an indicator of more aggressive pathology in group receiving XRT
- Among patients with PNI as an isolated risk factor (n=62), XRT may offer clinical benefit in LRC or DFS, but these differences were not statistically significant
- PNI is rarely an isolated risk factor in OCSCC, and adjuvant therapy decisions remain a clinical challenge in this patient population

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