

Pre-treatment pain is associated with cancer site and peripheral nerve presence in patients with head and neck squamous cell carcinoma



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INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) causes severe pain and reduced quality of life (QOL). The presence of pre-treatment pain as well as histologic evidence of perineural invasion (PNI), are independently thought to be a poor prognostic indicator of survival in HNSCC. In this retrospective study, we examined the prevalence of pain and overall QOL in head and neck cancer patients prior to treatment.

MATERIALS & METHODS

Table 1: Clinical Demographics

Variables	M±SD
Age, years	60.94±11.1
Sex	n(%)
Male	202(69.18)
Female	90(30.82)
Race	
White	283(97.25)
Other	8(2.75)
Nodal Stage	
N0-N1	154(52.7)
N2-3	117(40.07)
NX	21(7.19)
Tumor Stage	
T1	111(38.01)
T2	83(28.42)
T3	32(10.96)
T4	66(22.61)
Metastasis	
M0	33(11.30)
MX	259(88.70)
Site	
Oropharynx	89(30.48)
HPV	
Neg	7(7.87)
Pos	82(92.13)
Oral cavity	126(43.15)
Mandible	34(11.64)
Larynx	43(14.73)
Smoking	
No	76(26.03)
Yes	216(73.97)
Alcohol	
No	88(30.14)
Yes	204(69.86)
Perineural invasion (PNI)	
No	190(65.07)
Yes	102(34.93)
Extracapsular spread (ECS)	
No	94(32.19)
Yes	87(29.79)
Not Evaluated	111(38.02)
Opioid usage	
No	214(73.29)
Yes	78(26.71)
Beta Blocker usage	
No	233(79.79)
Yes	59(20.21)

- A retrospective analysis of HNSCC patients who underwent surgical resection at the University of Pittsburgh Medical Center between 2015-2018.
- Pretreatment pain and QOL were assessed at least 1 week before surgery using the Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N).
- Demographics, clinical characteristics, and concomitant medications were obtained from medical records.
- Differences in the distribution of trismus were examined using Fisher exact test, chi-square test, and t-test for categorical variables and continuous variables
- Multiple linear regression analysis was performed to investigate the association between FACT scores while controlling for other variables, (e.g., sex, tumor site, T stage, opioid usage).

RESULTS: HNSCC patients with oropharynx tumors report less pretreatment pain and have improved QOL

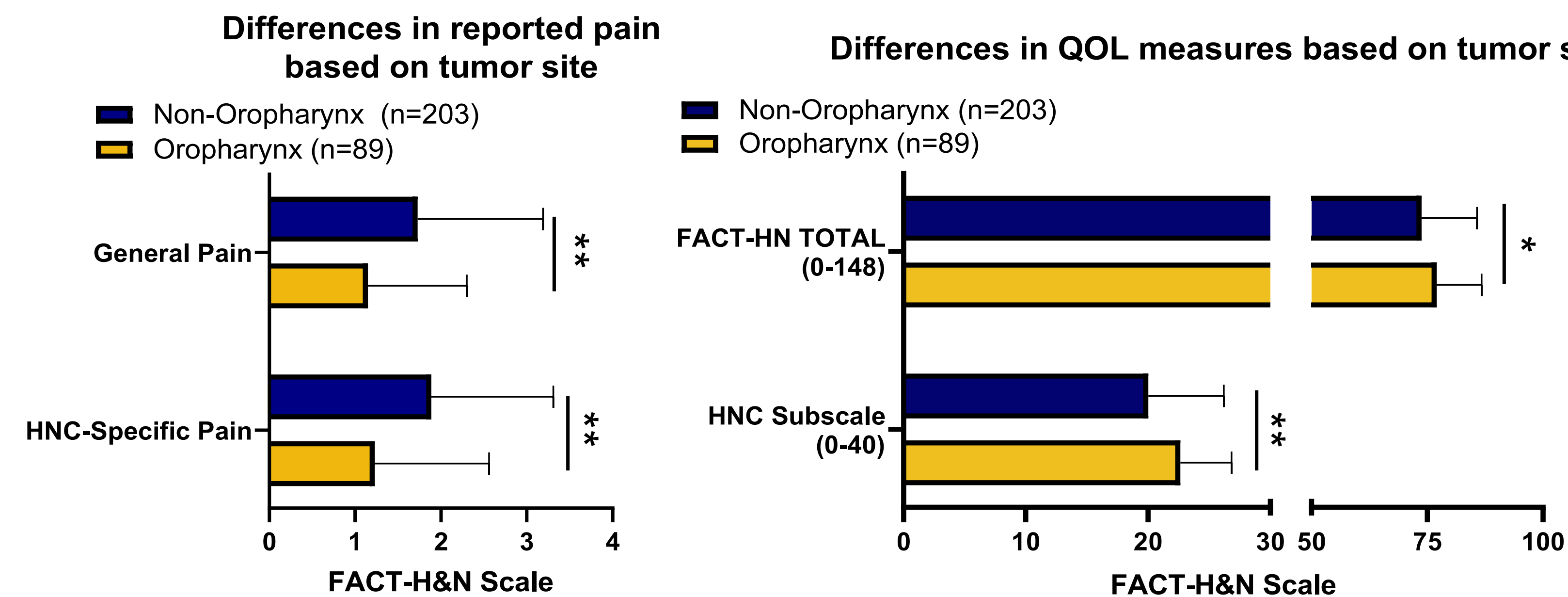


Figure 1: Reported pain in HNSCC patients by tumor site. A) Patients with HNSCC in the oropharynx region reported significantly less general pain and head and neck regional pain compared to patients with tumors in non-oropharynx regions (e.g., oral cavity). Pain was scored on a 0-4 scale with 4 indicating "very much". Welch Two Sample t-test **p<0.01. B) Patients with HNSCC in the oropharynx region reported significantly higher quality of life (QOL) scores overall and specific to the head and neck region compared to patients with tumors in non-oropharynx regions. Welch Total QOL was scored on a 0-148 scale and HNC-specific was scored on a 0-40 scale; higher values indicate better QOL. Two Sample t-test *p<0.05 **p<0.01.

RESULTS: PNI is a predictor of pretreatment pain & reduced QOL in HNSCC patients

Table 2: Multivariable Linear Regression Models for Patients with Cancer at the Oropharynx Site

Variable	General Pain		HNC-specific		FACT-HN TOTAL		HNCS	
	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value
PNI								
No	(Baseline)	0.00066*	(Baseline)	0.00017*	(Baseline)	0.62	(Baseline)	0.67
Yes	1.02 (0.45, 1.59)		1.33 (0.66, 2.00)		-1.30 (-6.56, 3.95)		0.50 (-1.83, 2.83)	
Opioid								
No	(Baseline)	0.0012*	(Baseline)	0.078	(Baseline)	0.053		
Yes	0.98 (0.40, 1.56)		0.61 (-0.07, 1.29)		-5.27 (-10.61, 0.08)			

Table 3: Multivariable Linear Regression Models for Patients with Cancer at the Non-Oropharynx Site

Variable	General Pain		HNC-specific		FACT-HN TOTAL		HNCS	
	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value	Coefficient (95% CI)	p-value
Sex								
Female	(Baseline)	0.011*	(Baseline)	0.0019*	(Baseline)	0.21		
Male	-0.48 (-0.86, -0.11)		-0.60 (-0.98, -0.23)		-2.29 (-5.87, 1.28)			
PNI								
No	(Baseline)	0.004*	(Baseline)	0.0014*	(Baseline)	0.35	(Baseline)	0.039*
Yes	0.60 (0.20, 1.00)		0.64 (0.25, 1.03)		-1.78 (-5.52, 1.96)		-1.95 (-3.79, -0.10)	
T Stage								
T1			(Baseline)		(Baseline)		(Baseline)	
T2			0.12 (-0.38, 0.63)	0.63	1.72 (-3.13, 6.56)	0.49	0.56 (-1.79, 2.91)	0.64
T3			0.17 (-0.41, 0.76)	0.56	-6.52 (-12.72, -0.33)	0.039*	-4.75 (-7.76, -1.73)	0.0022*
T4			0.40 (-0.08, 0.88)	0.10	-3.91 (-9.38, 1.54)	0.16	-3.29 (-5.97, -0.61)	0.017*
Opioid								
No	(Baseline)	<0.0001*	(Baseline)	<0.0001*				
Yes	1.07 (0.68, 1.47)		1.04 (0.63, 1.44)					
Betablocker								
No	(Baseline)	0.50			(Baseline)	0.022*	(Baseline)	0.04*
Yes	-0.15 (-0.58, 0.28)				4.69 (0.68, 8.70)		2.06 (0.09, 4.03)	

RESULTS: PNI in patient tumor tissue

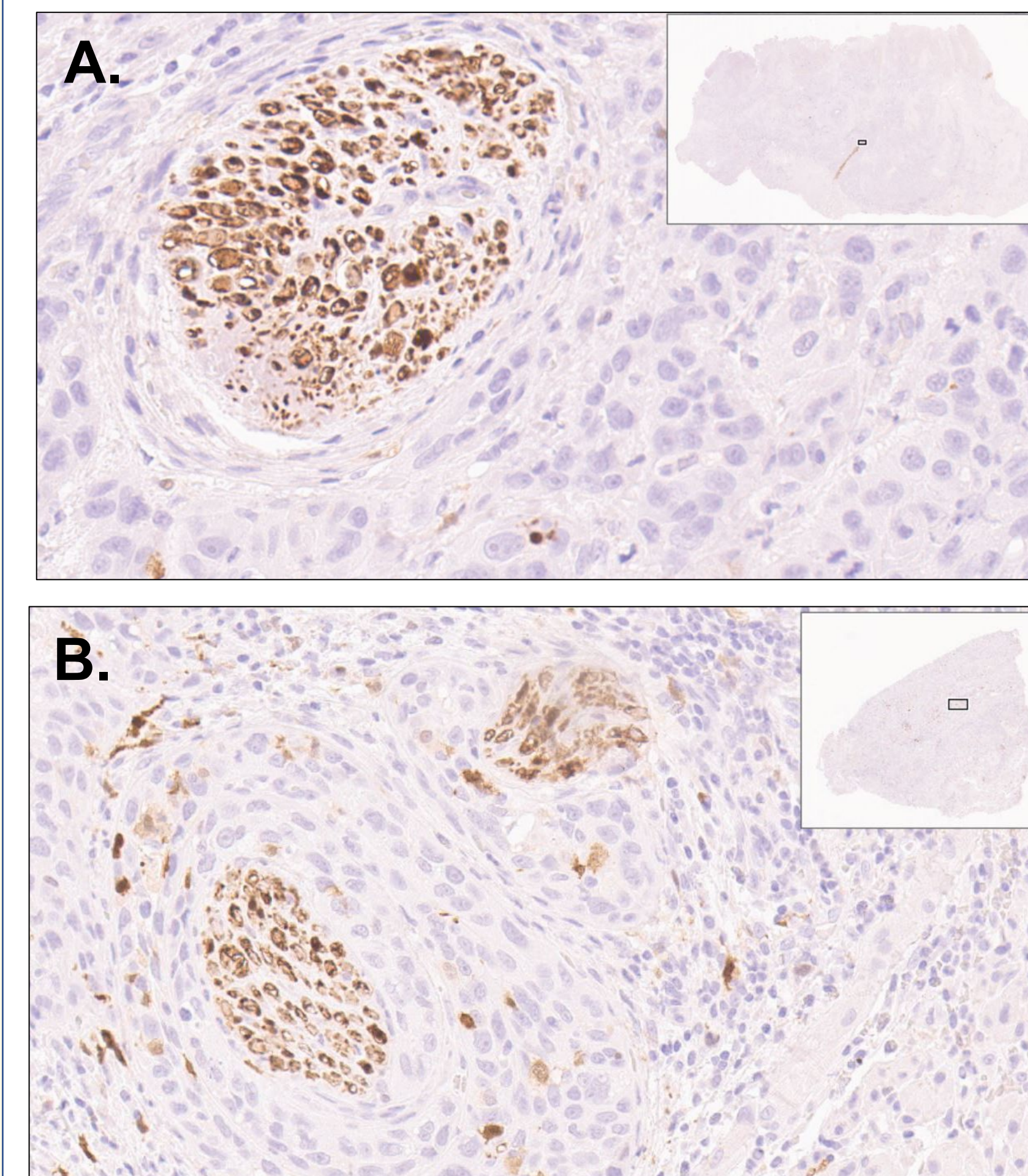


Figure 2: PNI in HNSCC tumors. Representative images of S100-positive staining with hematoxylin counterstain to identify nerve presence and subsequently PNI in 5µm sections from paraffin-embedded tumor specimen. Both (A) and (B) are from male patients with HPV-negative T4 tongue squamous cell carcinoma with pathologically identified PNI.

RESULTS: PNI is more prevalent in patients with late-stage oral cavity tumors

Table 3: PNI distribution by demographic and clinical characteristics

Variables	No PNI (n=190)	With PNI (n=102)	p-value
Age, y ^a	61.68 (11.99)	59.56 (11.13)	0.12
Sex			0.58
Male	134 (45.89)	68 (66.67)	
Female	56 (54.11)	34 (33.33)	
T Stage			<0.0001
T1	94 (49.47)	17 (16.67)	
T2	54 (28.42)	29 (28.43)	
T3	13 (6.84)	19 (18.63)	
T4	29 (15.26)	37 (36.27)	
Site			0.00051
Oropharynx	73 (38.42)	16 (15.69)	
HPV			0.60
Negative	5 (6.85)	2 (12.5)	
Positive	68 (93.15)	14 (87.5)	
Oral cavity	74 (38.95)	52 (50.98)	
Man	18 (9.47)	16 (15.69)	
Larynx	25 (13.16)	18 (17.64)	
Smoking			1
No	49 (25.79)	27 (26.47)	
Yes	141 (74.21)	75 (73.53)	
ECS			0.00011
No	62 (32.63)	32 (31.37)	
Yes	42 (22.11)	45 (44.12)	
Not Evaluated	86 (45.26)	25 (24.51)	
Opioid			0.0044
No	150 (78.95)	64 (62.75)	
Yes	40 (21.05)	38 (37.25)	
Beta Blocker			1
No	152 (80.0)	81 (79.41)	
Yes	38 (20.0)	21 (20.59)	

CONCLUSIONS

- Pretreatment pain and reduced QOL is associated with tumor progression, PNI, cancer site, opioid use, and sex.
- PNI is more prevalent in late-stage tumors in non-oropharynx sites
- These data support the demand for additional research into molecular mechanisms to further understand the complex relationship between pretreatment pain and QOL and disease progression.

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