

A Multidisciplinary Approach to Explore the Intersection of Biology with Social Determinants of Health in the Development of Pain in Survivors of Head and Neck Cancer

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BACKGROUND

- Head and neck cancer (HNC) causes more debilitating functional pain than any other cancer^{1,2}
- Pretreatment pain is an independent predictor of survival in newly diagnosed HNC and is associated with recurrence within the first year^{3,4}
- Opioids are mainstay for pain relief in HNC as there are no recommended treatments for HNC-related pain¹
- Analgesic strategies overlook social and biological factors that may influence pain perception

PURPOSE

Explore drivers of HNC related pain in the context of social/demographic, and biological (transcriptome, methylome) factors

METHODS

- Men (n = 10) and women (n = 5) with squamous cell carcinoma of the oral cavity or oropharynx prior to definitive treatment enrolled into the Comprehensive Head & Neck Cancer Biorepository and Database at University Hospitals Seidman Cancer Center, Cleveland, OH
- The Brief Pain Inventory Worst Pain (BPI-WP) item was used to assess pain on a numeric scale of no pain (0) to worst pain (10)
 - BPI-WP score from 1 -3 considered mild pain and score ≥ 4 considered moderate/severe pain⁵

Data analysis:

- SPSS version 29 for univariate analysis
- R version 4.2.2 for bivariate analysis
 - T-tests and Tukey's HSD for comparisons

Area Deprivation Index (ADI):

- National ADI reported via the University of Wisconsin school of Medicine and Public Health ADI⁶ using nine-digit zip code
 - Ranking of neighborhoods including income, education, employment, and housing quality
 - "Neighborhood" is defined as Census block group
 - Higher ADI indicate greater disadvantage

Transcriptome and methylome data:

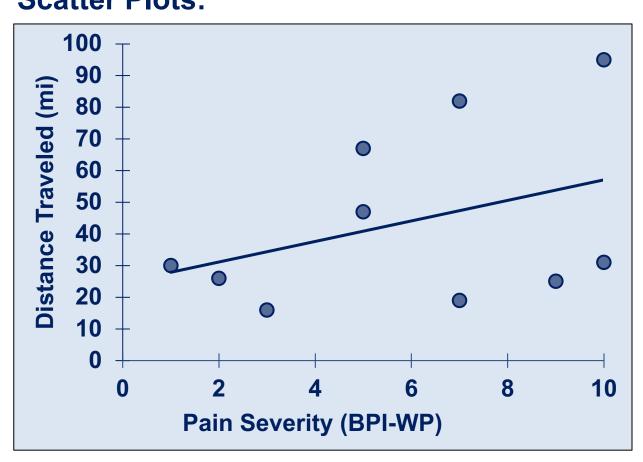
Peripheral blood samples currently undergoing analysis

RESULTS

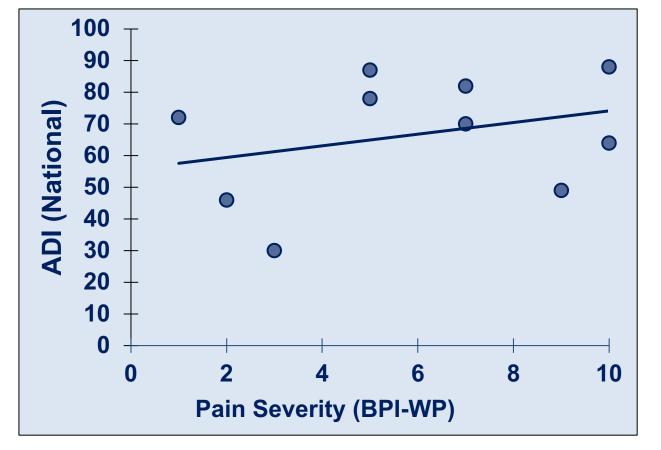
Participant Characteristics:

Characteristic (measure)	No Pain (n = 5) Mean ± SD or n (%)	Mild Pain (n= 3) Mean ± SD or n (%)	Moderate/Severe Pain (n = 7) Mean ± SD or n (%)
Age at Diagnosis (years)	66.4 ± 15.8	55.7 ± 15.0	60.6 ± 10.9
Race: White	5 (100)	3 (100)	7 (100)
Ethnicity: Non-Hispanic	5 (100)	3 (100)	7 (100)
Cancer site: Oral Cavity Oropharynx	0 (0) 5 (100)	2 (66.7) 1 (33.3)	6 (85.7) 1 (14.3)
Reported BPI-WP	0	2.0 ± 1.0	7.6 ± 2.1
Gender: Male Female	5 (100) 0 (0)	3 (100) 0 (0)	2 (28.6) 5 (71.4)
Tobacco Use: Yes No	3 (60) 2 (40)	2 (66.7) 1 (33.3)	6 (85.7) 1 (14.3)
Cancer Stage: Tumor - T1 T2 T3 T4 Node - N0 N1 N2 N3 Metastasis - MX M0	0 (0) 2 (40) 3 (60) 0 (0) 2 (40) 1 (10) 2 (40) 0 (0) 2 (40) 3 (60)	1 (33.3) 0 (0) 1 (33.3) 1 (33.4) 1 (33.3) 1 (33.4) 0 (0) 0 (0) 3 (100)	1 (14.3) 0 (0) 2 (28.6) 4 (57.1) 0 (0) 2 (28.6) 3 (42.8) 2 (28.6) 1 (14.3) 6 (85.7)
HPV P16: Positive Negative Not Tested	5 (100) 0 (0) 0 (0)	1 (33.4) 1 (33.3) 1 (33.3)	0 (0) 1 (14.3) 6 (85.7)
Perineural Invasion - Present Not Present	0 (0) 5 (100)	1 (33.3) 2 (66.7)	4 (57.1) 3 (42.9)
ADI (National)	64.2 ± 27.4	49.3 ± 21.2	74.0 ± 14.1
Distance Traveled to Cancer Center (miles)	22.6 ± 12.5	24.0 ± 7.2	52.3 ± 29.6

Scatter Plots:



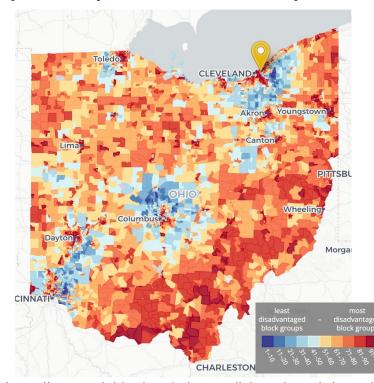
Relationship between Distance Traveled to Cancer Center and Pain Severity. There was no significant association between distance traveled to cancer center and pain severity in this sample. However, there was a trend toward significance in participants who reported moderate/severe pain (BPI-WP \geq 4).



Relationship between ADI and Pain Severity.
There was no significant association between ADI and pain severity in this sample.

RESULTS (cont.)

- More severe pain in participants diagnosed with oral cavity cancer (p = 0.004)
- Females experience more severe pain than males (p < 0.001)
- There was no association between PNI and pain severity.
 However, PNI was not present in participants with no pain
- There was a trend toward significance in the association between distance traveled by participant to reach the Cancer Center and pain severity (p = 0.09)
- There was no association between ADI and pain severity



nttps://www.neighborhoodatlas.medicine.wisc.edu/mapping

SUMMARY

Based on participant clinical and demographic factors, more severe pain was associated with:

- Female gender
- Cancer of the oral cavity
- Traveling a further distance to reach Cancer Center

Transcriptome and methylome data are pending

CONCLUSION/FUTURE DIRECTION

- Clinical and demographic factors may drive pain severity
- Further analysis will correlate transcriptome and methylome data with PNI status and pain scores as well as exploratory analyses involving ADI and neighborhood factors
- Study findings can be leveraged to construct predictive risk models, potential therapeutic targets, and strategies to ensure precision pain management to enable more pain free days, lessen morbidity and disability, and substantially improve quality of life

REFERENCES

- 1. Bossi et al., (2019). Crit Rev Oncol Hematol, 138:51-9.
- 2. Bossi et al., (2020). Support Care Cancer, 28(2):451-9
- 3. Reyes-Gibby et al., (2014). *J Pain*, 15(10):1015-22
- 4. Scharpf et al., (2009). Arch Otolaryngol Head Neck Surg, 135(8):789-94
- 5. NCCN (2024). Guidelines: Adult Cancer Pain
- 6. King et al., (2018). N Engl J Med, 378:2456-2458