Exploring the Mediating Effects of BMI on the Association between Social Deprivation and Neoadjuvant Chemotherapy Response in Pancreatic Cancer Patients

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Background

- It has been reported that risk factors and health care inaccessibility associated with low SDOH status can not fully explain the persistent disparities in cancer incidences and outcomes for populations living in underserved communities.
- Researchers have hypothesized that SDOH disparities can impact cancer outcomes through biological effectors, such as anxiety and inflammation, which may cause epigenetic changes that can be passed down through generations.
- Obesity, a known risk factor for many types of cancers (including pancreatic cancer), is also a health condition that can be driven by biological effectors associated with low SDOH status.
- This study explores how the biological effectors of SDOH can impact, with obesity as a mediating factor, treatment responses for neoadjuvant chemotherapy (NAC) in pancreatic cancer patients.

Methods

Study Participants

- A group of patients (n=137) with localized pancreatic ductal adenocarcinoma who received NAC with either mFOLFIRINOX, gemcitabine/abraxane, or both and underwent pancreatectomy between July 2015 and October 2022 at Sylvester Comprehensive Cancer Center in South Florida were enrolled in this study.

Responses to NAC

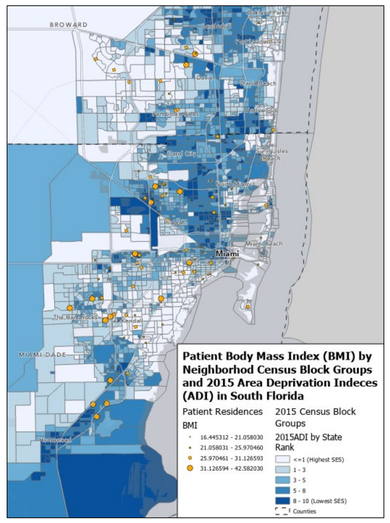
- 0=Complete Response, 1=Near-Complete Response, 2=Partial Response, and 3=Poor or No Response.
- Neutrophil to Lymphocyte Ratios (NLR), reflecting levels of inflammation, at diagnosis and before pancreatectomy were also recorded.

Area Deprivation Index (ADI):

- Patients' addresses were geocoded to Census block groups to identify the 2015 ADIs, a measure of neighborhood SDOH status obtained from the Neighborhood Atlas of University of Wisconsin, for the patients' residential neighborhoods.

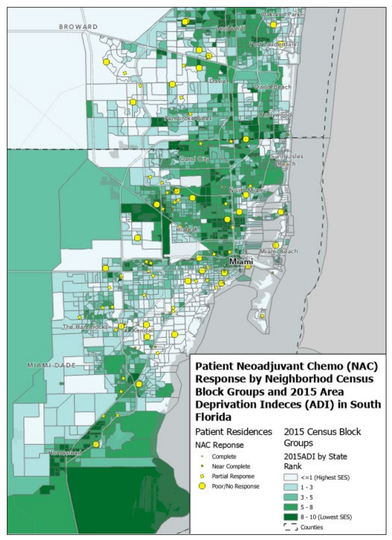
Results

1. Patient BMI and 2015 ADIs by Block Groups



- Neighborhoods with high ADI in northcentral Miami-Dade County are recognized by US Census as persistent poverty areas (more than 25% poverty rate for over 30 years).
- Consistent with known association between low SDOH and prevalence of obesity, pancreatic cancer patients with higher BMI (larger circle) tend to be found in block groups with higher ADI (darker blue).

2. Patient NAC Responses and 2015 ADIs by Block Groups



- In general, patients with worse NAC responses (larger yellow circle) tend to be found in block groups with higher ADIs (darker green).
- The contingency table below demonstrates that the percentage of patients with complete or near-complete response decreases for those living in higher ADIs (lower SDOH).

ADI State Rank Categories	NAC Response			
(1-10, lowest-highest deprivation)	Complete and Near Complete	Partial and Poor/No Response	(Missing)	Grand Total
1	8 (20.5%)	31 (79.5%)		39 (100%)
2.5	7 (11.5%)	53 (86.9%)	1	61 (100%)
6-10	3 (9.7%)	28 (90.3%)		31 (100%)
(Missing)	1	5		6
Grand Total	19	117	1	137

3. BMI, Age at Diagnosis, and NAC Response

	NAC Responses					
Age Group	Complete and Near Complete		Partial and No Response		Grand Total	
BMI Levels	Number of Patients	Percentage	Number of Patients	Percentage	Number of Patients	Percentage
1 (=<55)	0	0%	17	100%	17	100%
Normal	0	0%	8	100%	8	100%
Overweight	0	0%	5	100%	5	100%
Obese	0	0%	4	100%	4	100%
2 (56-65)	4	10%	38	90%	42	100%
Normal	0	0%	13	100%	13	100%
Overweight	3	16%	16	84%	19	100%
Obese	1	10%	9	90%	10	100%
3 (66-75)	10	22%	35	78%	45	100%
Normal	5	26%	14	74%	19	100%
Overweight	4	25%	12	75%	16	100%
Obese	1	10%	9	90%	10	100%
4 (>=76)	5	19%	25	78%	30	100%
Normal	1	7%	14	93%	15	100%
Overweight	1	13%	7	88%	8	100%
Obese	3	38%	4	50%	7	100%
Grand Total	19	14%	115	85%	134	100%

- Patients diagnosed at age =<65 all showed worse NAC response, while those at age >65 showed better response.
- No consistent relationship is found between BMI and NAC responses. However, for patients aged 66-75, being obese is associated with worse NAC responses.

4. ADI, BMI, and Age at Diagnosis

	Average Age			
ADI State Rank Categories	BMI Levels			
(1-10, lowest-highest deprivation)	Normal	Overweight	Obese	Grand Total
1	68.3	68.8	67.9	68.5
2-5	66.5	63.3	68.1	65.7
6-10	65.9	63.6	63.8	64.9
Grand Total	67.1	65.0	66.8	66.3

- Patients from neighborhoods of higher deprivation were often diagnosed at younger ages, regardless of BMI level.

5. ADI and Neutrophil-to-Lymphocyte Ratios at Diagnosis and prior to Surgery

ADI State Rank Categories	Complete and Near-Complete NAC Response			Partial and No Response		
(1-10, lowest-highest deprivation)	Average NLR at Diagnosis	Average NLR prior to Surgery	Average NLR Change	Average NLR at Diagnosis	Average NLR prior to Surgery	Average NLR Change
1	2.54	2.70	0.17	3.56	4.13	0.57
2-5	2.47	2.13	-0.34	3.74	3.30	-0.44
6-10	3.07	2.43	-0.64	2.97	3.02	0.04
Grand Total	2.70	2.50	-0.20	3.56	3.49	-0.07

- Patients showing worse NAC responses have higher average NLR ratios at diagnosis and less NLR reduction prior to surgery than those with better responses.

Conclusions

- Our study shows that social deprivation has a negative impact on NAC responses.
- Patients from areas with higher ADI were more likely to be diagnosed at younger ages and showed worse NAC outcomes.
- No consistent relationship is found between BMI and NAC responses.
- Patients with worse NAC responses showed higher NLR at diagnosis and less NLR reduction prior to surgery, suggesting that NLR can be a predictor of NAC outcomes.
- Our study is limited by patient sample size and skewness toward lower ADIs.
- Future extension of this study will expand the sample size and geographic coverage (more ADI variations) as well as focus on patients diagnosed at younger ages for exploration of biological effectors that impact their NAC responses.