# Neoadjuvant Therapy and the Effect of Nodal Downstaging in Pancreatic Adenocarcinoma

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### Background

#### • Pancreatic cancer is the third leading cause of cancer-related death in the US.

- Tumor resection is the only potential cure for pancreatic adenocarcinoma.
- Only 15-20% of tumors are resectable at the time of diagnosis.
- Use of neoadjuvant therapy prior to surgery has been show to increase resectability and improve survival.
- The effect of neoadjuvant therapy on nodal involvement is poorly understood.

# **Research Objectives**

- To understand the practice patterns in patients who received neoadjuvant therapy prior to surgery for pancreatic adenocarcinoma.
- To analyze rates and predictors of nodal downstaging in patients who underwent neoadjuvant chemotherapy versus chemoradiation.
- To compare survival in patients who were nodally downstaged after receiving neoadjuvant chemotherapy versus chemoradiation.

# Methods

- We used the National Cancer Database (NCDB) Pancreas Participant User File from 2004 - 2016.
- We included patients with underwent surgery for a confirmed diagnosis of pancreatic adenocarcinoma.
- We excluded patients with metastatic disease.
- We identified patients who received neoadjuvant chemotherapy alone versus chemoradiation, defined as patients starting chemotherapy and radiotherapy on the same date.
- Fisher's exact test, ANOVA, and log-rank test were used to identify statistical differences when applicable. Logistic regression was used to evaluate predictors of nodal downstaging.



n = 38,008	
No Therap	ру

#### Table 1. Patient Characteristics

	Chemother	apy (n = 3,311)	Chemoradia	tion (n = 1,226)	P-value
	n	%	n	%	
Age (IQR)	65 (14)		65 (14)		0.893
Sex					0.812
Male	1,720	51.95%	632	51.55%	
Race					<0.001
White	2,737	82.66%	997	81.32%	
Black	253	7.64%	121	9.87%	
Hispanic/Latino	129	3.90%	32	2.61%	
Asian/Pacific Islander	81	2.45%	16	1.31%	
Other/Unknown	111	3.35%	60	4.89%	
Clinical Node Stage					0.006
cN0	2,060	62.22%	783	63.87%	
cN1	939	28.36%	305	24.88%	
Tumor Size, mm (IQR)	32 (16)		32 (17)		0.992
Regional Nodes Examined (IQR)	17 (14)		12 (13)		<0.001
Grade					0.051
1	223	6.74%	100	8.16%	
2	1,186	35.82%	442	36.05%	
3	692	20.90%	275	22.43%	

**Table 1:** Characteristics of patients who underwent

 neoadjuvant chemotherapy and chemoradiation analyzed by Fisher's exact test.

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#### Figure 1. Cohort Derivation

*Figure 1:* Derivation of the analyzed cohort.

#### Figure 2. Nodal Staging after Neoadjuvant Therapy



Figure 2: Migration of patients staged with clinically node positive disease.

#### Table 2: Nodal Downstaging

Univariable				
	Odds Ratio	Std. Err.	P-Value	[95% Conf. Interval]
Age	0.974	0.003	<0.001	0.968 - 0.979
Sex				
Male	1			
Female	0.971	0.059	0.625	0.861 - 1.094
Race				
White	1			
Black/African-American	0.972	0.104	0.793	0.788 - 1.200
Hispanic/Latino	0.905	0.140	0.517	0.669 - 1.224
Asian/Pacific Islander	0.842	0.183	0.430	0.549 - 1.290
Other/Uknown	0.789	0.114	0.099	0.595 - 1.046
Comorbidity Index				
0	1			
1	1.278	0.086	<0.001	1.120 - 1.459
2	1.230	0.157	0.105	0.958 - 1.581
3+	0.884	0.219	0.620	0.544 - 1.437
umor Size, mm	1.000	0.000	0.408	0.999 - 1.000
egional Nodes Examined	1.003	0.002	0.109	0.999 - 1.007
irade				
1	1			
2	0.794	0.095	0.053	0.628 - 1.003
3	0.727	0.091	0.011	0.569 - 0.931
Aultivariable				
lge	0.975	0.003	<0.001	0.969 - 0.980
Comorbidity Index				
. 0	1			
1	1.390	0.095	<0.001	1.217 - 1.589
2	1.429	0.185	0.006	1.110 - 1.841
3+	0.982	0.245	0.941	0.602 - 1.600
irade				
1	1			
2	0.798	0.095	0.058	0.631 - 1.008
3	0.733	0.092	0.014	0.573 - 0.938

Table 2: Logistic regression analysis evaluating for predictors of nodal downstaging after neoadjuvant therapy.

#### Figure 3. Nodal Downstaging



Figure 3: Kaplan-Meier survival analysis between patients who were downstaged after receiving neoadjuvant chemotherapy versus chemoradiation (logrank p<0.001).

#### Results

- The cohort derivation is illustrated in **Figure 1**. Patient characteristics of those who received neoadjuvant chemotherapy versus chemoradiation are demonstrated in Table 1.
- After surgery for clinically node-positive disease, 23.3% of patients who received neoadjuvant chemotherapy alone and 41.31% of patients who received chemoradiation were downstaged to node-negative disease on pathology (Figure 2).
- Median survival in patients who were downstaged after receiving neoadjuvant chemotherapy versus chemoradiation was 37.5 and 27.5 months, respectively (logrank p<0.001, **Figure 3**).
- Younger age, comorbidity status, and tumor grade were each found to independently predict nodal downstaging in patients who received neoadjuvant therapy (Table 2).

### Conclusions

- Patients who receive neoadjuvant chemotherapy are less likely to have nodal downstaging than those who receive neoadjuvant chemoradiation.
- Patients who were downstaged after neoadjuvant chemotherapy experienced improved survival compared to patients downstaged after chemoradiation, which may be attributed to chemoradiation being used on patients with greater disease burden.
- Patient factors, including age and comorbidity status, should be considered when determining the optimal neoadjuvant therapy.