# Weight Loss During Neoadjuvant Chemotherapy Increases Postoperative Complications in Pancreatic Cancer Resection

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## Background

- Neoadjuvant chemotherapy (NAC) is a standard preoperative treatment for localized pancreatic cancer.
- Preoperative weight loss has been shown to increase postoperative complications for complex surgery in the literature.
- However, the specific effects of NAC-associated weight loss on postoperative complications have not been extensively studied.

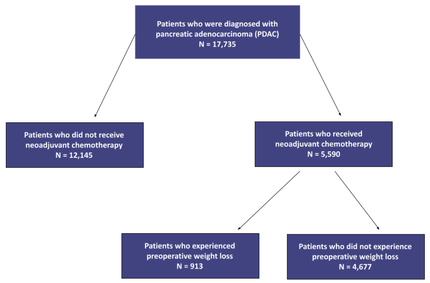
## Research Objectives

- To understand NAC practice patterns and its correlation with NAC-associated weight loss.
- To evaluate effects of weight loss during NAC on postoperative complications in patients who underwent pancreatectomy for pancreatic cancer.
- To determine if weight loss is an independent predictor of a postoperative complication.

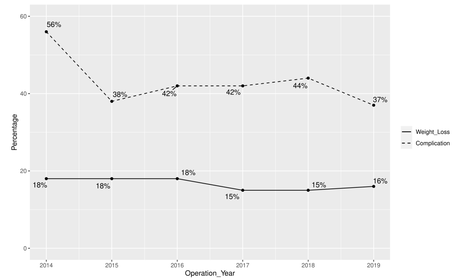
## Methods

- The National Surgical Quality Improvement Program (NSQIP) database was used from 2014 to 2019.
- Patients who were diagnosed with pancreatic adenocarcinoma (PDAC) and received NAC were included in the analysis.
- Preoperative weight loss was defined as >10% weight loss in the six months prior to surgery in patients undergoing NAC.
- Fisher's exact test and Pearson's chi-squared test were applied to establish significance between variables, and logistic regression was used to identify independent predictors of a postoperative complication.

## Figure 1. Population Derivation




## Figure 2. NAC Trends




## Table 1. Demographic Characteristics

| Characteristic | No Weight Loss, N = 4,677[1] | Weight Loss, N = 913[1] | p-value[2] |
|---|---|---|---|
| Age | 66 (59, 72) | 66 (60, 72) | 0.14 |
| Sex | | | 0.009 |
| female | 2,253 (48%) | 483 (53%) | |
| male | 2,424 (52%) | 430 (47%) | |
| Smoker | 784 (17%) | 207 (23%) | <0.001 |
| Diabetes | 1,411 (30%) | 341 (37%) | <0.001 |
| Race | | | 0.058 |
| American Indian or Alaska Native | 9 (0.2%) | 4 (0.4%) | |
| Asian | 152 (3.2%) | 23 (2.5%) | |
| Black or African American | 385 (8.2%) | 71 (7.8%) | |
| Native Hawaiian or Pacific Islander | 3 (<0.1%) | 0 (0%) | |
| Unknown/Not Reported | 368 (7.9%) | 51 (5.6%) | |
| White | 3,760 (80%) | 764 (84%) | |
| Hispanic Ethnicity | | | 0.007 |
| No | 4,203 (90%) | 845 (93%) | |
| Unknown | 306 (6.5%) | 35 (3.8%) | |
| Yes | 168 (3.6%) | 33 (3.6%) | |
| History of COPD | 155 (3.3%) | 41 (4.5%) | 0.077 |
| Hypertensive Medication Use | 2,289 (49%) | 459 (50%) | 0.5 |

[1]Median (IQR); n (%)

[2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

## Table 2. Postoperative Complication Rates

| Characteristic | No Weight Loss, N = 4,677[1] | Weight Loss, N = 913[1] | p-value[2] |
|---|---|---|---|
| Organ/Space SSI | | | >0.9 |
| No Complication | 4,200 (90%) | 820 (90%) | |
| Organ/Space SSI | 477 (10%) | 93 (10%) | |
| Wound Disruption | | | 0.038 |
| No Complication | 4,628 (99%) | 910 (100%) | |
| Wound Disruption | 49 (1.0%) | 3 (0.3%) | |
| Pneumonia | | | 0.064 |
| No Complication | 4,563 (98%) | 881 (96%) | |
| Pneumonia | 114 (2.4%) | 32 (3.5%) | |
| Unplanned Reintubation | | | 0.004 |
| No Complication | 4,573 (98%) | 878 (96%) | |
| Unplanned Intubation | 104 (2.2%) | 35 (3.8%) | |
| Pulmonary Embolism | | | 0.4 |
| No Complication | 4,633 (99%) | 907 (99%) | |
| Pulmonary Embolism | 44 (0.9%) | 6 (0.7%) | |
| Ventilator >48 Hours | | | <0.001 |
| No Complication | 4,595 (98%) | 879 (96%) | |
| On Ventilator greater than 48 Hours | 82 (1.8%) | 34 (3.7%) | |
| Progressive Renal Insufficiency | | | 0.013 |
| No Complication | 4,667 (100%) | 906 (99%) | |
| Progressive Renal Insufficiency | 10 (0.2%) | 7 (0.8%) | |
| Urinary Tract Infection | | | 0.044 |
| No Complication | 4,571 (98%) | 882 (97%) | |
| Urinary Tract Infection | 106 (2.3%) | 31 (3.4%) | |
| CVA/Stroke with Neurological Deficit | | | 0.2 |
| No Complication | 4,670 (100%) | 910 (100%) | |
| Stroke/CVA | 7 (0.1%) | 3 (0.3%) | |
| Cardiac Arrest Requiring CPR | | | 0.055 |
| Cardiac Arrest Requiring CPR | 40 (0.9%) | 14 (1.5%) | |
| No Complication | 4,637 (99%) | 899 (98%) | |
| <30 Days from Operation to Death | 58 (1.2%) | 14 (1.5%) | 0.5 |
| Sepsis | | | 0.068 |
| No Complication | 4,343 (93%) | 832 (91%) | |
| Sepsis | 334 (7.1%) | 81 (8.9%) | |
| Septic Shock | | | <0.001 |
| No Complication | 4,592 (98%) | 877 (96%) | |
| Septic Shock | 85 (1.8%) | 36 (3.9%) | |
| Reoperation | 203 (4.3%) | 55 (6.0%) | 0.027 |
| Pancreatic Fistula | | | 0.4 |
| Biochemical Leak only | 64 (1.4%) | 9 (1.0%) | |
| No | 4,190 (90%) | 833 (91%) | |
| Unknown | 24 (0.5%) | 6 (0.7%) | |
| Yes | 399 (8.5%) | 65 (7.1%) | |
| Pancreatic Drain | 4,127 (88%) | 833 (91%) | 0.009 |
| Delayed Gastric Emptying | | | 0.2 |
| No | 4,120 (88%) | 785 (86%) | |
| Unknown | 18 (0.4%) | 4 (0.4%) | |
| Yes-no oral intake by POD 14 | 51 (1.1%) | 15 (1.6%) | |
| Yes-tube to external drainage/NG tube present/reinserted | 488 (10%) | 109 (12%) | |
| Percutaneous Drain | 407 (8.7%) | 81 (8.9%) | 0.9 |
| Drain Still Present 30 Days After Operation | 265 (5.7%) | 55 (6.0%) | 0.7 |
| Unplanned Readmission | 712 (15%) | 140 (15%) | >0.9 |

[1]n (%)

[2]Pearson's Chi-squared test; Fisher's exact test

## Table 3. Regression Analysis

| Characteristic | N | Univariate Analysis exp(Beta) | 95% CI[1] | p-value | Multivariate Analysis OR[1] | 95% CI[1] | p-value |
|---|---|---|---|---|---|---|---|
| Weight Loss | 5,590 | | | | | | |
| No | | — | — | | — | — | |
| Yes | | 1.03 | 1.00, 1.07 | 0.053 | 1.17 | 1.01, 1.36 | 0.031 |
| Age | 5,590 | 1.00 | 1.00, 1.00 | 0.2 | | | |
| Sex | 5,590 | | | | | | |
| female | | — | — | | — | — | |
| male | | 1.06 | 1.03, 1.08 | <0.001 | 1.26 | 1.13, 1.40 | <0.001 |
| Smoker | 5,590 | | | | | | |
| No | | — | — | | — | — | |
| Yes | | 1.01 | 0.98, 1.04 | 0.5 | | | |
| Diabetes | 5,590 | | | | | | |
| No | | — | — | | — | — | |
| Insulin | | 0.99 | 0.96, 1.02 | 0.6 | | | |
| Non-Insulin | | 1.03 | 0.99, 1.07 | 0.10 | | | |
| Race | 5,590 | | | | | | |
| American Indian or Alaska Native | | — | — | | — | — | |
| Asian | | 0.80 | 0.61, 1.05 | 0.11 | | | |
| Black or African American | | 0.83 | 0.63, 1.08 | 0.2 | | | |
| Native Hawaiian or Pacific Islander | | 0.75 | 0.41, 1.39 | 0.4 | | | |
| Unknown/Not Reported | | 0.88 | 0.67, 1.15 | 0.3 | | | |
| White | | 0.79 | 0.61, 1.03 | 0.083 | | | |
| Hispanic Ethnicity | 5,590 | | | | | | |
| No | | — | — | | — | — | |
| Unknown | | 1.06 | 1.00, 1.12 | 0.034 | | | |
| Yes | | 1.05 | 0.98, 1.12 | 0.2 | | | |
| History of COPD | 5,590 | | | | | | |
| No | | — | — | | — | — | |
| Yes | | 1.09 | 1.02, 1.17 | 0.012 | 1.38 | 1.03, 1.83 | 0.030 |
| Hypertensive Medication Use | 5,590 | | | | | | |
| No | | — | — | | — | — | |
| Yes | | 1.05 | 1.02, 1.07 | <0.001 | 1.20 | 1.08, 1.34 | <0.001 |
| Pancreatic Duct Size | 5,590 | | | | | | |
| <3 mm | | — | — | | — | — | |
| >=3 mm | | 0.96 | 0.93, 1.00 | 0.032 | 0.88 | 0.76, 1.03 | 0.11 |
| Unknown | | 0.95 | 0.92, 0.99 | 0.011 | 0.80 | 0.67, 0.95 | 0.013 |
| Pancreatic Gland Texture | 5,590 | | | | | | |
| Non-Soft | | — | — | | — | — | |
| Soft | | 1.06 | 1.03, 1.10 | <0.001 | 1.28 | 1.10, 1.49 | 0.001 |
| Unknown | | 1.02 | 0.99, 1.05 | 0.3 | 1.18 | 1.01, 1.37 | 0.032 |

[1]CI = Confidence Interval, OR = Odds Ratio

## Results

- Of the 17,735 patients diagnosed with PDAC, 5,590 received NAC. Of this subpopulation of NAC recipients, 913 experienced preoperative weight loss **(Figure 1).**
- The percentage of individuals who experienced weight loss from NAC has stayed stable from 2014 to 2019, but the percentage of individuals who experienced weight loss and a postoperative complication has slightly declined in the same time frame **(Figure 2)**.
- NAC patients who experienced weight loss were most often female and were more likely to be smokers and have a diagnosis of diabetes. Of note, there was no statistically significant difference in age between the two groups **(Table 1)**.
- NAC-associated weight loss was associated with a higher rate of severe complications such as unplanned intubation (3.8% vs. 2.2%), ventilator use for >48 hours (3.7% vs. 1.8%), and septic shock (3.9% vs. 1.8%) **(Table 2)**.
- NAC-associated weight loss, sex, history of COPD, hypertensive medication use, and pancreatic gland texture were independent predictors of a postoperative complication **(Table 3)**.

## Conclusions

- Despite the increasing use of multi-agent NAC regimens over the past several years, NAC-associated weight loss has not increased and management of those who do experience weight loss has improved.
- NAC patients who experienced significant weight loss experienced twice the rate of severe postoperative complications including prolonged ventilator use and septic shock.
- The use of prehabilitation during NAC may prevent significant weight loss, thus decreasing rates of severe complications after pancreatectomy.

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