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The Impact of Socioeconomic Deprivation on Clinical Outcomes for Pancreatic Adenocarcinoma at a High-Volume Cancer Center: A Retrospective Cohort Analysis

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Abstract

Objective: To assess the impact of a granular measure of socioeconomic deprivation on pancreatic surgical and cancer-related outcomes at a high-volume cancer center that employs a standardized clinic pathway.

Summary Background Data: Prior research has shown that low socioeconomic status leads to less treatment and worse outcomes for pancreatic adenocarcinoma. However, these studies employed inconsistent definitions and categorizations of socioeconomic status, aggregated individual socioeconomic data using large geographic areas, and lacked detailed clinicopathologic variables.

Methods: We conducted a retrospective cohort study of 1,552 pancreatic adenocarcinoma patients between 2008 and 2015. Patients were stratified using the Area Deprivation Index, a validated dataset that ranks census block groups based on socioeconomic deprivation (SED). Multivariable models were used in the curative surgery cohort to predict the impact of SED on 1) grade 3/4 Clavien-Dindo complications, 2) initiation of adjuvant therapy 3) completion of adjuvant therapy, and 4) overall survival

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Results: Patients from high SED neighborhoods constituted 29.9% of the cohort. Median overall survival was 28 months. The rate of Clavien-Dindo grade 3/4 complications was 14.2% and completion of adjuvant therapy was 65.6%. There was no evidence that SED impacted surgical evaluation, receipt of curative-intent surgery, postoperative complications, receipt of adjuvant therapy or overall survival.

Conclusions: While nearly one-quarter of curative-intent surgery patients were from high SED neighborhoods, this factor was not associated with measures of treatment quality or survival. These observations suggest that treatment at a high-volume cancer center employing a standardized clinical pathway may in part address socioeconomic disparities in pancreatic cancer.

Mini-Abstract

This study used a granular measure of socioeconomic deprivation (SED) to assess rates of surgical evaluation and post-operative outcomes for pancreatic cancer (PDAC). SED was not associated with treatment quality or survival. Treatment of PDAC at a high-volume center employing a standardized clinical pathway may positively impact socioeconomic disparities.

Keywords

pancreatic cancer; socioeconomic status; socioeconomic deprivation; cancer disparities; area deprivation index

Introduction

Surgical resection is the only potentially curative option for pancreatic cancer and remains a vital treatment to improve survival in patients with localized disease. With receipt of high-quality, multimodality treatment at high-volume centers there have been significant improvements in pancreatic cancer survival.[1] The distribution of these improvements, however, has been unequal; several studies show that low socioeconomic status leads to less treatment and worse outcomes for pancreatic cancer.[2–6]

The social determinants of cancer play a major role in the course of care for patients across the spectrum of oncologic disease.[7–9] Emphasizing the social context in which disease and treatment occur, this approach asserts that political and socioeconomic structures influence the factors that lead to disease and impact subsequent outcomes.[10] However, for pancreatic and other cancers, the measurement of social determinants has proved a challenge for multiple reasons. First, myriad definitions and categorizations of socioeconomic status/position have been deployed in the literature with socioeconomic status functioning as an umbrella term for various dimensions of social disadvantage (including race, insurance status, income, education level, poverty, housing/rent, and employment status).[11] This has resulted in difficulties making meaningful comparisons across studies and has the potential for information bias and misclassification of risk.[12] Second, reliance on national administrative datasets, which contain varying degrees of socioeconomic variables and often lack detailed clinicopathologic and treatment data that may serve as potential confounders, can also lead to bias.[13, 14] Finally, the paucity of individual-level socioeconomic data has led to large geographic units (zip codes or counties) being used for aggregate analysis of

socioeconomic variables. While census tract-level or smaller units for socioeconomic status geocoding is recommended, the use of larger area geocoding continues despite warnings about imprecision.[1, 4, 6, 15, 16]

Given these challenges, new and standardized approaches are needed to better assess the role of socioeconomic status in cancer outcomes. One detailed measure of socioeconomic deprivation (SED), the area deprivation index (ADI), has recently been updated and made publicly available. The ADI is a validated dataset that ranks census block groups (neighborhoods) on socioeconomic disadvantage based on US census and American Community Survey data that includes 17 variables such as income, education, employment, and housing quality data.[17] This index measure of SED allows for convenient comparison across populations and uses census block groups for aggregate socioeconomic data, avoiding the limitations of zip code or larger geocoding. To date no studies have assessed the impact of SED at the census block group level on pancreatic adenocarcinoma (PDAC) outcomes controlling for detailed clinicopathologic data and geographic distance from the treating facility. We therefore employed the ADI to 1) determine the degree of SED among PDAC patients treated at a high-volume comprehensive cancer center and 2) explore the relationship between SED and PDAC outcomes, including post-operative complications, initiation and completion of adjuvant therapy, and overall survival.

Methods

Study Cohort, Setting and Standardized Pathway

Moffitt Cancer Center (MCC) is the only National Cancer Institute designated Comprehensive Cancer Center in the state of Florida. Florida has the third largest population in the US and is ranked 49th in the US in overall health disparities with approximately 36% of the population living below 200% of the Federal Poverty Level.[18] Of the 29,488 incident cases of pancreatic tumors captured by the Florida Cancer Data System from 2008–2015, approximately 10% (2,867) were evaluated at MCC.

We performed a retrospective cohort study of patients diagnosed with PDAC from January 1, 2008 to December 31, 2015 at MCC. Patients were excluded if no ADI ranking was available, i.e., patients with PO box addresses, or if there was only a single visit (second opinion), identifying 1,552 patients. Surgical evaluation was defined as a completed surgical clinic appointment or documented presentation at multidisciplinary tumor board. Curative-intent surgical patients were then analyzed; patients who did not undergo a curative resection, e.g., palliative bypass, were excluded from the final analysis.

Of 307 curatively-resected PDAC patients who underwent surgery from 2008–2015, 289 patients had ADI data for analyses (289 had complication data, 283 had initiation of adjuvant therapy, 282 had completion of adjuvant therapy, 288 had overall survival and 256 had recurrence information). Treatment was provided in conjunction with a standardized clinical pathway based on multidisciplinary diagnosis and staging agreement (Supplemental Figure 1).[19] Patients with resectable disease underwent surgery as a first treatment and patients with borderline resectable disease underwent neoadjuvant treatment followed by surgery.[20] Surgery types included pancreatoduodenectomy, distal pancreatectomy with

or without splenectomy and total pancreatectomy; robotic-assisted and open cases were included. The institutional review board of MCC approved this protocol.

Predictor Variable: Area Deprivation Index

The ADI is a validated dataset that ranks census block groups (neighborhoods) on socioeconomic disadvantage, which comprises 17 variables, including income, education, employment, and housing quality data based on the 2013 American Community Survey (ACS).[21] US census block groups typically contain between 600 to 3,000 people and are statistical subdivisions within census tracts, which themselves are small, relatively permanent statistical groupings designed to be homogenous in demographic and socioeconomic characteristics.[22] Given the relative permanence of socioeconomic conditions, geographic-based measures of SED were developed and validated using US census measures through empirical linkage to mortality.[23] Using 2013 ACS data, the ADI was updated and made publicly available.[17]

For our cohort, state-level ADI decile was determined by patient address at diagnosis and divided into terciles of disadvantage (low, comprising rankings 1–3; moderate, comprising rankings 4–6; high comprising rankings 7–10) as previously described.[24] To visualize census block group data, Figure 1B shows the ADI by block group for Hillsborough and Pinellas Counties, FL alongside approximation of patient geographic residence at diagnosis according to zip code (Figure 1C). To highlight the greater sensitivity of census block group socioeconomic estimates, within the zip code 33602 which comprises downtown Tampa Bay, ADI rankings range from 1 to 10 with a mean of 4.27 and median of 3. While 9.1% of the zip code's population have a rank of 1, the lowest rank of socioeconomic disadvantage, 8.2% of the zip code's population has a rank of 10, indicating the highest level of socioeconomic disadvantage. For census block groups with a rank of 1, the range of median household income based on the 2013 ACS was US$ 116,146 to 117,542. For census block groups with a rank of 10, the range of median household income was US$ 9,515 to 20,500.

Outcome Variables

The outcome variables assessed in this study were 1) grade 3/4 Clavien-Dindo complication, 2) initiation of adjuvant therapy 3) completion of adjuvant therapy, and 4) overall survival. Clavien-Dindo grade 3/4 complications have been previously defined.[25] Complications assessed as possible grade 3/4 Clavien-Dindo complications included pancreatic-specific surgery complications (fistula, hemorrhage, delayed gastric emptying, biliary, and chyle leak) and non-pancreatic-specific surgical complications (surgical site infection, fascial dehiscence, pneumonia, deep vein thrombosis, pulmonary embolism, urinary tract infection, renal failure, cardiac arrest, sepsis, septic shock, Clostridium difficile infection, as well as mortality). Initiation of adjuvant therapy was defined as receipt of one or more cycles of chemotherapy with or without radiation. Completion of adjuvant therapy was defined as completion of intended adjuvant therapy course. The Moffitt clinical pathway for pancreatic cancer calls for all patients to receive adjuvant therapy regardless of receipt of neoadjuvant therapy. Therefore, the adjuvant therapy outcomes were analyzed as a separate covariate. Overall survival was defined as time from first treatment to death or last follow-up.

Covariates

Potential confounders were included as covariates. Preoperative variables included age, sex, race, insurance status (grouped as private, Medicare with private supplement, and government insurance, which included Medicare, Medicaid, and uninsured patients), BMI, pre-operative diagnosis of diabetes mellitus, Charlson Comorbidity Index (CCI), American Society of Anesthesiologists (ASA) score, presence of a biliary stent, and neoadjuvant treatment approach (defined as chemotherapy with or without chemoradiation). The Charlson age comorbidity index (CACI) was calculated to offer a comparison of comorbidity in our cohort to that of other published studies; CCI and age, however, were analyzed independently in regression models.[26] Distance to MCC was calculated in miles using the patient's address at diagnosis. Operative data included operation type, vascular resection, estimated blood loss, and operative time. Pathologic variables assessed included tumor stage, margin status, lymph node stage, presence of lymphovascular and perineural invasion. Additional postoperative variables included length of stay, 30-day mortality, and 90-day readmission.

Statistical Analyses

Patient characteristics were summarized using descriptive statistics including median and range for continuous measures and proportions and frequencies for categorical measures. When comparing characteristics to ADI the median and 25th and 75th percentiles are shown for continuous variables. The association between continuous variables and ADI were assessed using Kruskal-Wallis tests. The associations between categorical variables and ADI were evaluated using Chi-squared tests or Chi-squared permutation tests when the expected frequencies were less than 5 in some cells. Trend tests were also used when comparing variables to ADI (low to moderate to high). Categorical variable levels for overall survival were compared using the Log-rank test.

Logistic regression models were fit for the outcomes Grade 3 or 4 Clavien complication (no/yes), initiation of adjuvant therapy (no/yes), and completion of adjuvant therapy (no/yes), and Cox proportional hazard models were fit for overall survival. Unadjusted and adjusted (multivariable) models were run for ADI and covariates. Odds ratios (or hazard ratios for Cox models), with 95% confidence intervals, and p values are presented. For categorical variables with more than two levels, p values are presented for each level compared to a referent level, and also an overall p value using the type-III analysis-of-variance result for the respective model. For comparing ADI tercile group trends to the outcomes, the variable was converted to ordinal and Cox models fit. The proportional hazards assumption was assessed with Schoenfeld residuals. Due to the exploratory nature of this analysis p-values were not adjusted for multiple comparisons. All analyses were performed with R version 3.5.1

Results

Characteristics of the Study Population

Figure 1 provides a flowchart of MCC PDAC patients. The majority of patients with non-metastatic PDAC received surgical evaluation (94.7%). Of surgically treatable patients

(resectable and borderline cohorts), 99.6% and 98.9%, respectively, received surgical evaluation. There was no difference in surgical evaluation by SED group (p=0.144). Of surgically treatable patients, 33 (6.3%) were not surgical candidates. There was no difference in failure to receive curative-intent surgery by SED group (p=0.353).

Baseline characteristics of the 289 curative-intent surgical patients by SED tercile are shown in Table 1. Patients with low, moderate, and high SED comprised 117 (40.5%), 101 (34.9%) and 71 (24.6%) of the cohort, respectively. Preoperative resectability status showed that 189 (65.4%) were designated resectable and 100 (34.6%) were designated borderline resectable. Neoadjuvant therapy was given to 101 (34.9%) of patients, including all borderline resectable patients. Vascular venous reconstruction was performed in 36 (12.5%) patients in the cohort. The median time to recurrence was 13.3 months, with 185 recurrences (70.1%). The liver was the most common site of recurrence, occurring in 64 (24.4%) patients; 28 (10.7%) of patients recurred locally. We found no difference between SED and CCI at presentation or ASA score. We observed that the median CACI for our cohort was 6 [25th and 75th percentiles, 5;7] and was not associated with ADI in our cohort (p=0.718).

As shown in Table 1, we did not find evidence of a difference between SED and race, insurance status, comorbidity, resectability, pathology, post-operative complications, initiation of adjuvant therapy, completion of adjuvant therapy, or site of recurrence. Additionally, we did not find evidence of a difference between SED and geographic distance from MCC.

Grade 3 or 4 Clavien Complication

Grade 3 or 4 Clavien complications were identified in 41 (14.2%) of patients and grade B or C ISGPS pancreatic fistulae were identified in 37 patients (12.8%), similar to previously published rates from retrospective analyses and clinical trials.[27–29] After adjustment for potential confounders, moderate or high SED did not predict Grade 3 or 4 Clavien complications relative to low SED (Table 2). In the multivariable model, an ASA score of 3 increased the relative odds of a Grade 3 or 4 Clavien complication (OR, 3.52; 95% CI 1.36–10.05).

Initiation of Adjuvant Therapy

Adjuvant therapy was initiated in 231 (81.6%) patients. In univariable analysis, government insurance predicted the lowest relative odds of initiating adjuvant therapy (OR, 0.31; 95% CI, 0.12–0.72); higher age, CCI, and blood loss as well as ASA class 3 and Clavien grade 3/4 complication predicted decreased odds of initiating adjuvant therapy (Table 3). After adjustment for potential confounders, moderate or high SED did not drive initiation of adjuvant therapy relative to low SED. In the multivariable model, grade 3 or 4 Clavien complication conferred the lowest odds of initiating adjuvant treatment (OR, 0.22; 95% CI, 0.08–0.57). Male sex and increasing age were also associated with decreased relative odds of initiating adjuvant therapy.

Completion of Adjuvant Therapy

Adjuvant therapy was completed in 185 (65.6%) of patients, which is comparable to prior reports and clinical trials.[30] In univariable analysis, venous reconstruction was associated with the lowest relative odds of completing adjuvant therapy (OR, 0.42; 95% CI, 0.20–0.84); higher age, CCI and estimated blood loss as well as ASA class 3 and Clavien grade 3/4 complication predicted decreased odds of completing adjuvant therapy (Table 4). After adjustment for potential confounders, moderate or high SED did not predict completion of adjuvant therapy relative to low SED. In the multivariable model, Clavien grade 3/4 complication conferred the lowest odds of completing adjuvant treatment (OR, 0.33; 95% CI 0.14–0.77). Increasing age was also associated with decreased relative odds of initiating adjuvant therapy and other/unknown race predicted increased odds of completing adjuvant therapy.

Overall Survival

The median overall survival was 27.6 months with 215 deaths (74.4%). The 30-day mortality rate was 1.7% and the 90-day mortality rate was 3.1%, which are comparable to other high-volume centers.[31] There was no difference in survival probability by SED tercile rank (Figure 2). As shown in Table 5, in univariable analysis, the greatest decrease in hazard of death was predicted by completion of adjuvant therapy (HR, 0.42; 95% CI 0.32–0.56). Neoadjuvant therapy (HR, 0.59; 95% CI 0.44–0.79) also predicted decreased hazard of death; increasing age, higher T stage, and higher N stage predicted increased hazard of death. After adjustment for potential confounders, moderate or high SED did not predict hazard of death relative to low SED. In the multivariable model, completion of adjuvant therapy conferred the greatest decrease in hazard of death (HR, 0.38; 95% CI 0.25–0.58). Neoadjuvant therapy was also predictive of decreased hazard of death (HR, 0.54; 95% CI 0.36–0.80). Increasing N stage as well as T2 and T3 stage relative to CR/in situ disease were the greatest drivers of increased hazard of death. Increased operative time and length of stay also predicted increased mortality.

Discussion

This study used a publically-available, validated dataset at the census block group level to examine the impact of SED on PDAC post-operative outcomes and overall survival. Use of the ADI overcomes several obstacles in measuring and comparing SED and has broad applicability in surgical and oncologic research. We observed that nearly one-third of non-metastatic patients are from high SED neighborhoods. There was no evidence that SED was associated with receipt of surgical evaluation, curative-intent surgery or that SED predicts post-operative Clavien grade 3/4 complications, initiation or completion of chemotherapy, or overall survival. These results are in contrast to several studies that have observed low socioeconomic status is associated with worse post-operative outcomes and survival.[2, 3, 5, 6, 32–34]

In studies using national registries, low socioeconomic status has been predictive of higher operative mortality, worse post-operative outcomes, and decreased receipt of adjuvant therapy.[4, 35, 36] Reames (2014) observed that patients in the lowest quintile of

socioeconomic status had increased rates of complications, failure to rescue, and mortality for pancreatic cancer. The higher odds of failure to rescue persisted when controlling for patient characteristics, however, they were attenuated when adjusting for hospital characteristics, including volume. Low socioeconomic status has also been associated with decreased receipt of adjuvant therapy.[36] Dimou (2016) observed that patients with government insurance had decreased odds of multimodality PDAC treatment compared to those with private insurance.[1]

Several studies have evaluated the relationship between socioeconomic status and PDAC survival. Studies from the California Cancer Registry from the 1990s and 2000s at the census block group level found conflicting results; one study showed that high socioeconomic status was associated with improved survival while another did not, though the categorization of SES differed between the studies making comparison a challenge.[2, 32] Using the Florida Cancer Data System, Cheung (2010) observed that higher poverty predicted decreased overall survival after adjustment for potential confounders.[6] In a more contemporary cohort of resected patients, higher median income was predictive of improved survival.[3]

One explanation offered for these disparities is that high-volume centers are predisposed to do well because they treat higher socioeconomic status patients with better baseline comorbidity status.[4, 37] While we did not identify a difference in Charlson comorbidity score by SED in curative-intent surgery patients, the median CACI was 6 and not associated increased early mortality. These findings are in contrast with published data from other high-volume centers that observed a median CACI of 3 for resected PDAC patients and found that a score of 6 or higher led to increased early mortality.[38, 39]

Another potential explanation for our findings is that high-volume care in conjunction with adherence to clinical guidelines/pathways not only improves outcomes but may reduce socioeconomic disparities.[40–42] While the impact of high-volume care has been well-documented, few studies have explored the impact of guideline/pathway adherence. Visser (2012) showed that after controlling for facility volume, compliance with NCCN guidelines for pancreatic cancer decreased mortality. Furthermore, high-volume centers with NCCN compliant PDAC care had a greater than 10-month improvement in median survival compared to non-compliant high-volume centers. However, others have shown that disparities persist with pathway use.[43] While promising, clinical pathway implementation alone is unlikely to serve as a widely-applicable panacea and more research is needed to identify interventions and policy measures to reduce socioeconomic disparities.[43–45]

Finally, compared to national data and Florida demographics, our cohort was significantly more homogenous in terms of race/ethnicity and insurance status, which may contribute to the results observed. Our cohort consisted of 4.5% African-Americans and 4.5% had Medicaid or were uninsured compared to national rates of 9.3% for African Americans and 8.0% for Medicaid/uninsured patients undergoing surgery, respectively.[46] These elisions of patient diversity limit the external validitity of these findings. Consequently, generalizing from these homogenous data is fraught with challenges as they do not account for the

potentially compounding vulnerabilities that exist at the intersection of SED, race, and insurance status.

There are additional limitations to consider when interpreting these findings. Although the majority of patients are referred from other providers, our sample may have increased health-seeking behaviors and/or characteristics which may lead to improved outcomes. While we showed that our patients have similar characteristics across SED strata, we cannot exclude unmeasured selection bias that may have impacted our findings. Additionally, this measure of SED is a geocoded, aggregate measure that relies on census block group data and therefore has the potential for ecological fallacy, though this error is decreased compared to zip code level analysis. Finally, while we did not find a statistical difference between SED and outcomes, we cannot exclude that the study was underpowered.

Despite these limitations, our findings suggest that a granular measure of SED can be applied to studies of complex cancer care. Noting the revealing racial and insurance status disparities between MCC and more representative populations, our findings suggest that treatment of localized PDAC at a high-volume cancer center employing a standardized pathway can offer high rates of surgical evaluation, curative-surgery, and superior post-operative outcomes. While we have suggested that high fidelity to a standardized clinical pathway may contribute to these findings, this was not directly tested and it remains uncertain what factor or combination of factors (cohort homogeneity, high-volume center, teaching facility, standardized clinical pathway, clinical and social support services) contributed to these results. It is also unknown if these outcomes would persist if the number of patients from neighborhoods of high SED was increased at our institution, however, other studies have not shown that centralization diminishes outcomes.[47]

There have been prior calls for centralization of complex cancer care to improve outcomes.[48] Increasing the number of patients from areas of high SED receiving treatment at high-volume cancer centers with adherence to clinical guidelines may improve outcomes for this group. However, this remains a challenge particularly for low SED patients. Nearly 40% of US patients receive care at low-volume facilities and compliance with NCCN guideline care is less than 35%.[42, 49, 50] If the field of surgical oncology hopes to move toward achieving equity for cancer patients, it will involve critical examination of the social determinants of health and moving beyond descriptive studies of disparities. This necessitates accurate measurement of SED that allows for convenient comparison across populations. This transition to a more local/regional analytic approach, focused on actionable efforts to improve access and quality of care, may lead to improved outcomes for patients from even the most socioeconomically deprived neighborhoods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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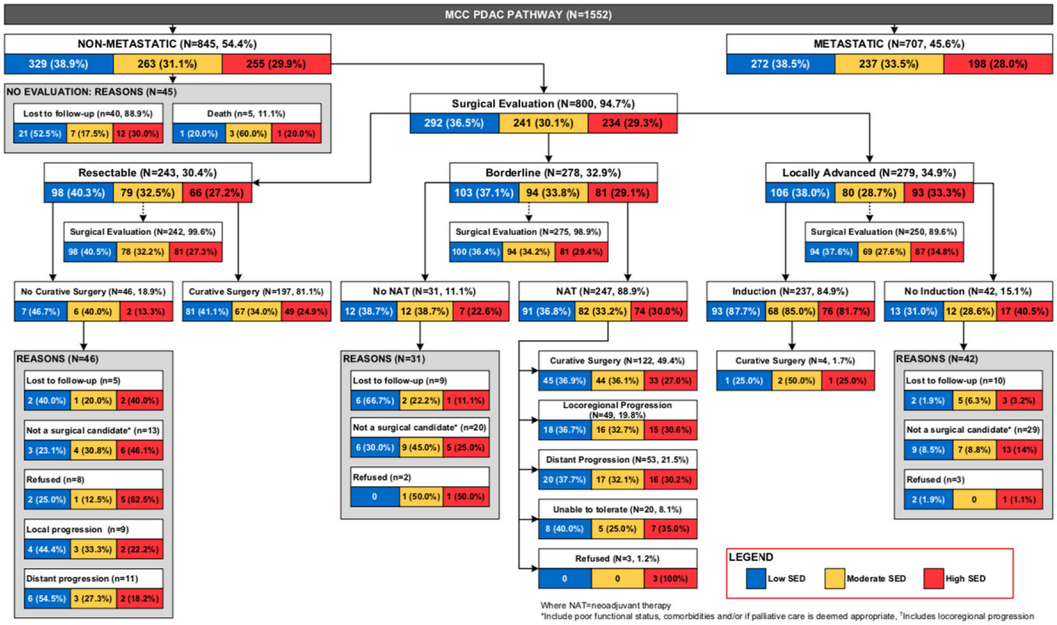
A.



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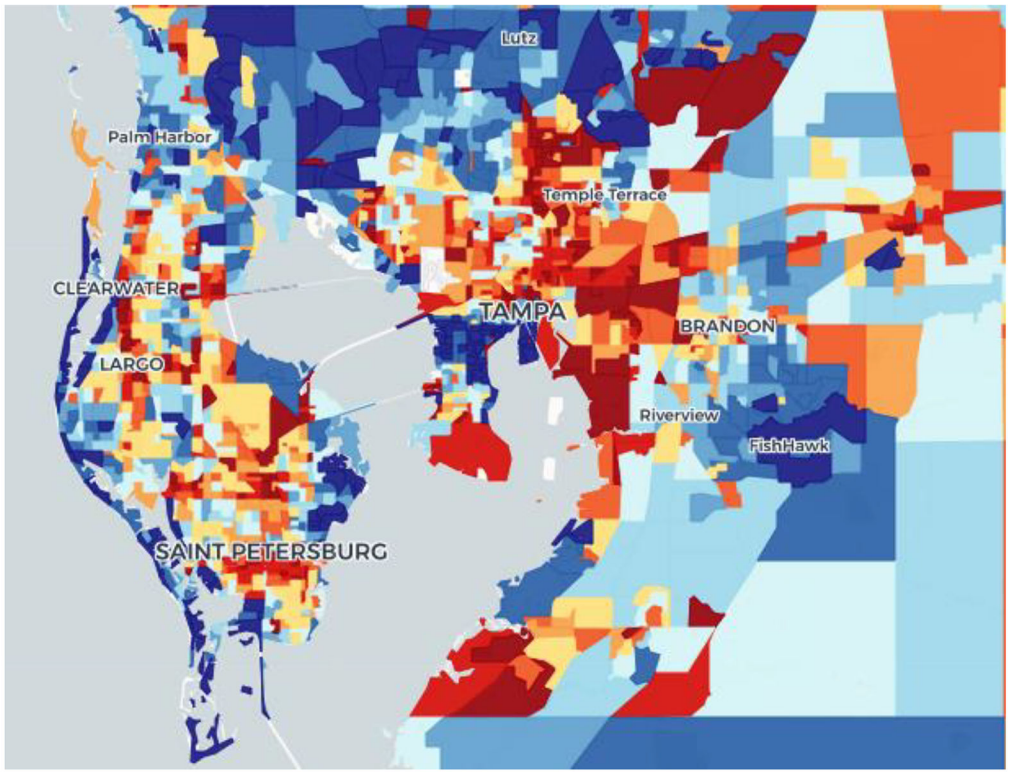

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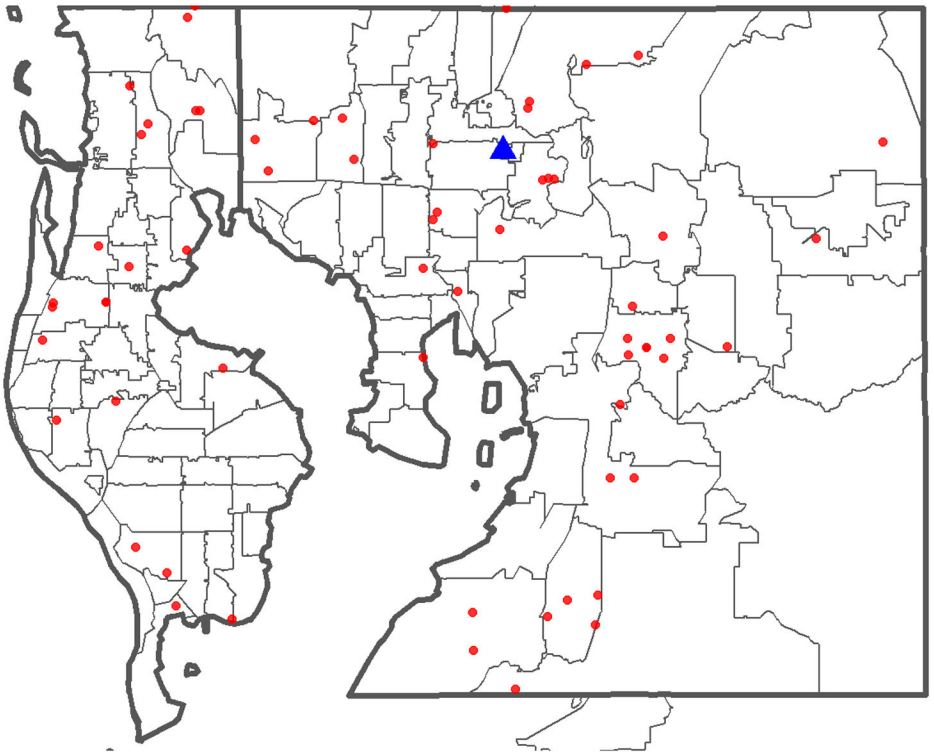

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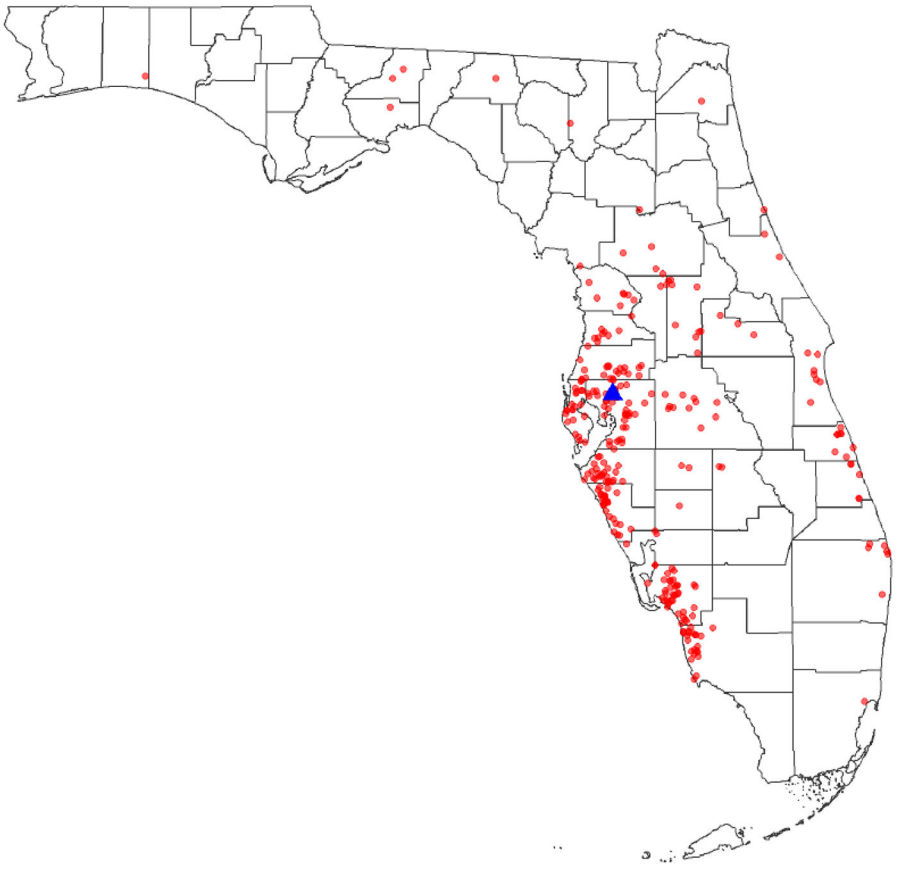

Figure 1.

(A) Flowchart of PDAC patients entering the MCC standardized clinical pathway by socioeconomic deprivation (B) Density map of Hillsborough and Pinellas counties, FL showing SED decile (1–10) scores at the census block group level with the least disadvantaged block groups in blue and the most disadvantaged block groups in red. (C) Zip code level map of Hillsborough and Pinellas counties, FL, showing the geographic distribution of patients (red dots) from the treating facility (blue triangle). (D) County-level map of Florida, showing the geographic distribution of patients (red dots) from the treating facility (blue triangle).

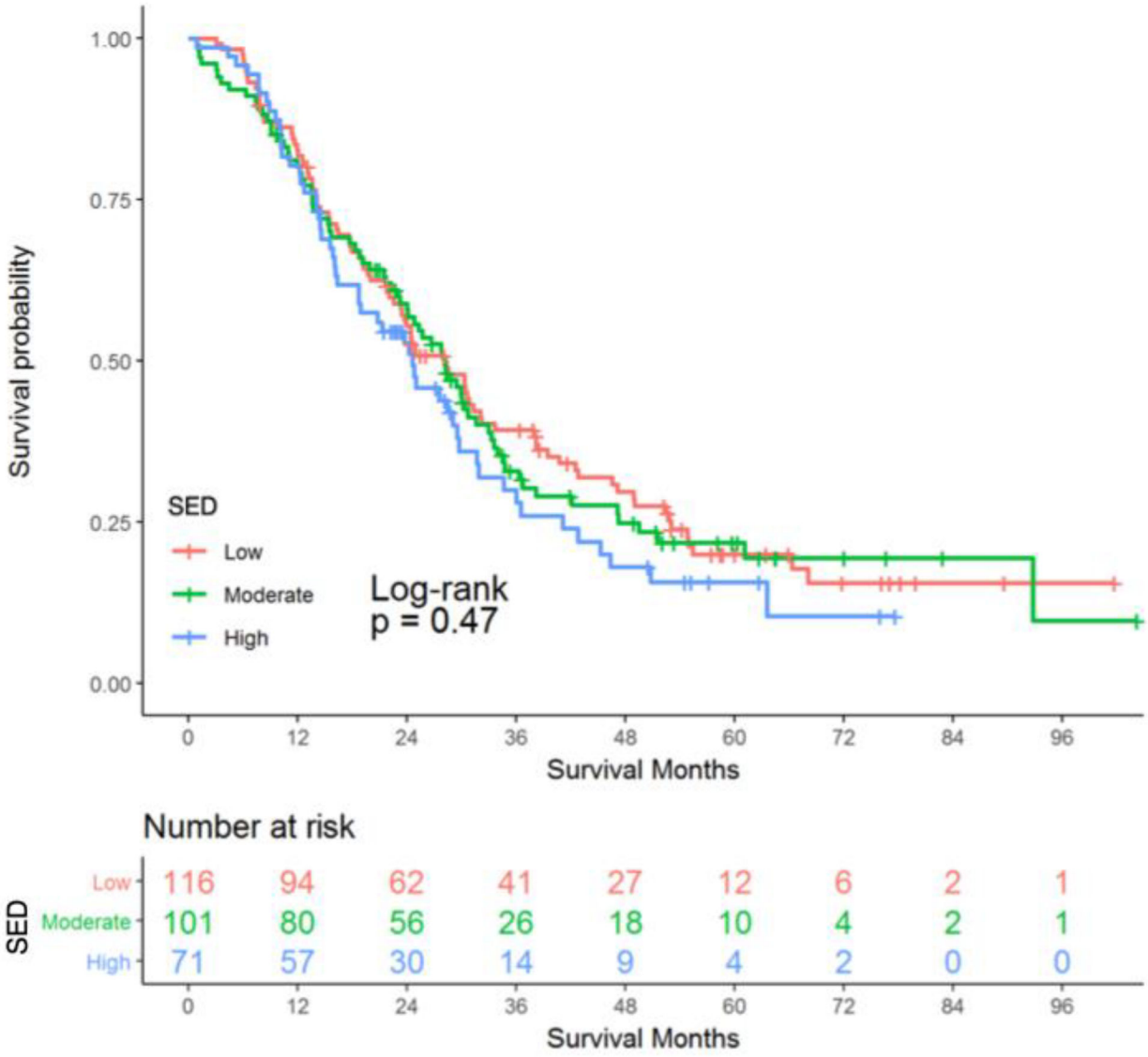

Figure 2.

Kaplan-Meier Curve of the Probability of Overall Survival for Resected Pancreatic Adenocarcinoma Patients

Table 1:

Baseline Characteristics of Patients with Resected PDAC at Moffitt Cancer Center Between 2008 and 2015 by SED

	Low SED (n=117)	Moderate SED (n=101)	High SED (n=71)	Overall p	T rend p
Age	68.0 [64.0; 76.0]	68.0 [61.0; 75.0]	68.0 [61.0; 72.5]	0.465	0.220
Age (binary)				0.639	0.361
<70	66 (56.4%)	59 (58.4%)	45 (63.4%)		
≥70	51 (43.6%)	42 (41.6%)	26 (36.6%)		
Sex				0.203	0.124
Female	54 (46.2%)	46 (45.5%)	24 (33.8%)		
Male	63 (53.8%)	55 (54.5%)	47 (66.2%)		
Race				0.748	0.184
White	110 (94.0%)	91 (90.1%)	63 (88.7%)		
Black	4 (3.42%)	5 (4.95%)	4 (5.63%)		
Other / unknown	3 (2.56%)	5 (4.95%)	4 (5.63%)		
Insurance				0.237	0.083
Private	41 (35.0%)	25 (24.8%)	19 (26.8%)		
Government with private supplement	46 (39.3%)	48 (47.5%)	26 (36.6%)		
Government	30 (25.6%)	28 (27.7%)	26 (36.6%)		
Distance from Moffitt (miles)	56.5 [24.4; 128]	48.9 [20.1; 97.3]	54.8 [33.2; 104]	0.062	0.460
Distance from Moffitt (binary)				0.195	0.412
< 85 miles	71 (60.7%)	73 (72.3%)	46 (64.8%)		
≥ 85 miles	46 (39.3%)	28 (27.7%)	25 (35.2%)		
Charlson comorbidity index				0.355	0.339
≤3	31 (26.5%)	23 (22.8%)	13 (18.3%)		
4–5	60 (51.3%)	47 (46.5%)	42 (59.2%)		
≥6	26 (22.2%)	31 (30.7%)	16 (22.5%)		
BMI	26.0 [23.7; 28.8]	25.8 [23.5; 29.6]	27.1 [23.1; 31.8]	0.399	0.281
Diabetes mellitus				0.193	0.102
No	91 (77.8%)	69 (68.3%)	48 (67.6%)		
Yes	26 (22.2%)	32 (31.7%)	23 (32.4%)		
Preoperative biliary stent				0.433	0.335
No	55 (47.0%)	39 (38.6%)	29 (40.8%)		
Yes	62 (53.0%)	62 (61.4%)	42 (59.2%)		
Preoperative resectability				0.550	0.649
Resectable	80 (68.4%)	62 (61.4%)	47 (66.2%)		
Borderline resectable	37 (31.6%)	39 (38.6%)	24 (33.8%)		
Neoadjuvant therapy				0.456	0.632
No	80 (68.4%)	61 (60.4%)	47 (66.2%)		
Yes	37 (31.6%)	40 (39.6%)	24 (33.8%)		

	Low SED (n=117)	Moderate SED (n=101)	High SED (n=71)	Overall p	T rend p
ASA class				0.144	0.197
2	57 (48.7%)	36 (35.6%)	29 (40.8%)		
3	60 (51.3%)	65 (64.4%)	42 (59.2%)		
Surgery				0.590	0.336
Whipple/total pancreatectomy	90 (76.9%)	79 (78.2%)	59 (83.1%)		
Distal pancreatectomy/splenectomy	27 (23.1%)	22 (21.8%)	12 (16.9%)		
Vascular Reconstruction				0.226	0.130
No	105 (89.7%)	90 (89.1%)	58 (81.7%)		
Venous	12 (10.3%)	11 (10.9%)	13 (18.3%)		
Estimated blood loss	300 [200;525]	300 [200;500]	300 [150;500]	0.551	0.830
Operative Time (hours)	6.33 [4.67;8.00]	6.92 [5.03;8.47]	7.32 [5.46;9.24]	0.074	**0.022**
Pathologic tumor stage				0.202	0.106
CR or in situ	11 (9.40%)	9 (8.91%)	1 (1.41%)		
T1	9 (7.69%)	6 (5.94%)	9 (12.7%)		
T2	59 (50.4%)	47 (46.5%)	31 (43.7%)		
T3	38 (32.5%)	39 (38.6%)	30 (42.3%)		
Positive lymph nodes				0.252	0.111
N0 (0)	51 (43.6%)	48 (47.5%)	24 (33.8%)		
N1 (1–3)	47 (40.2%)	37 (36.6%)	28 (39.4%)		
N2 (4+)	19 (16.2%)	16 (15.8%)	19 (26.8%)		
Margin Status				0.066	0.304
R0	100 (85.5%)	96 (95.0%)	63 (88.7%)		
R1	17 (14.5%)	5 (4.95%)	8 (11.3%)		
Lymphovascular invasion				0.191	0.229
No	29 (25.0%)	36 (36.4%)	22 (31.9%)		
Yes	87 (75.0%)	63 (63.6%)	47 (68.1%)		
Perineural invasion				0.143	0.208
No	15 (12.9%)	23 (23.2%)	13 (18.8%)		
Yes	101 (87.1%)	76 (76.8%)	56 (81.2%)		
Clavien complication (grade 3/4)				0.412	0.920
No	102 (87.2%)	83 (82.2%)	63 (88.7%)		
Yes	15 (12.8%)	18 (17.8%)	8 (11.3%)		
Pancreatic fistula (grade B/C)				0.891	0.639
None	101 (86.3%)	88 (87.1%)	63 (88.7%)		
Yes	16 (13.7%)	13 (12.9%)	8 (11.3%)		
Length of stay	10.0 [8.00; 13.0]	11.0 [9.00; 14.0]	10.0 [8.00; 15.0]	0.361	0.230
Readmission by 90 days				0.082	0.406
No	98 (83.8%)	78 (77.2%)	64 (90.1%)		
Yes	19 (16.2%)	23 (22.8%)	7 (9.86%)		

	Low SED (n=117)	Moderate SED (n=101)	High SED (n=71)	Overall p	T rend p
Initiated adjuvant therapy				0.504	0.958
No, failed to initiate	19 (16.7%)	22 (22.0%)	11 (15.9%)		
Yes, initiated	95 (83.3%)	78 (78.0%)	58 (84.1%)		
Completed adjuvant therapy				0.636	0.983
No, failed to complete	37 (32.7%)	38 (38.0%)	22 (31.9%)		
Yes, completed	76 (67.3%)	62 (62.0%)	47 (68.1%)		
Overall survival					
Alive	29 (24.8)	27 (26.7)	18 (25.4)	0.946	0.705
Dead	88 (75.2)	74 (73.3)	53 (74.6)		

Table 2:

Relative Odds of Clavien Grade 3/4 Complication: Univariable and Multivariable Logistic Regression Models, Odds Ratios (95% CI)

	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
SED (reference: Low SED)			0.416			0.657
Moderate SED	1.48 (0.70, 3.14)	0.306		1.13 (0.48, 2.72)	0.777	
High SED	0.86 (0.33, 2.11)	0.753		0.70 (0.23, 1.97)	0.511	

The multivariable model was adjusted for age, sex, race, insurance status, distance from MCC, Charlson comorbidity index, diabetes mellitus, BMI, presence of a preoperative biliary stent, receipt of neoadjuvant therapy, ASA class, type of resection, venous reconstruction, estimated blood loss, operative time, pathologic tumor stage, pathological nodal stage, and margin status.

Table 3:

Relative Odds of Initiation of Adjuvant Therapy: Univariable and Multivariable Logistic Regression Models, Odds Ratios (95% CI)

	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
SED (reference: Low SED)			0.506			0.286
Moderate SED	0.71 (0.36, 1.40)	0.324		0.55 (0.22, 1.32)	0.184	
High SED	1.06 (0.48, 2.44)	0.898		1.12 (0.39, 3.31)	0.837	
Age	**0.92 (0.89, 0.96)**	**<0.001**		**0.88 (0.83, 0.94)**	**<0.001**	
Male sex (reference: female)	0.58 (0.30, 1.09)	0.096		**0.35 (0.15, 0.77)**	**0.011**	
Race (reference: White)			0.403			0.416
Black	2.89 (0.55, 53.16)	0.314		1.34 (0.18, 27.69)	0.803	
Other / unknown	2.64 (0.50, 48.89)	0.357		5.39 (0.61, 136.18)	0.194	
Insurance (reference: private)			0.031			0.167
Government with private supplement	0.48 (0.19, 1.10)	0.094		0.97 (0.30, 2.98)	0.962	
Government	**0.31 (0.12, 0.72)**	**0.009**		0.46 (0.13, 1.44)	0.193	
Distance from Moffitt (miles)	1.00 (0.99, 1.00)	0.502		1.00 (0.99, 1.01)	0.715	
Charlson comorbidity index	**0.77 (0.63, 0.95)**	**0.015**		1.36 (0.94, 2.01)	0.113	
Diabetes mellitus (reference: no)	0.61 (0.33, 1.17)	0.127		0.66 (0.28, 1.54)	0.330	
BMI	0.99 (0.94, 1.05)	0.720		0.98 (0.92, 1.05)	0.559	
Preoperative biliary stent (reference: none)	1.00 (0.54, 1.82)	0.988		1.21 (0.47, 3.00)	0.681	
Neoadjuvant Therapy (reference: none)	1.02 (0.55, 1.95)	0.951		0.91 (0.34, 2.47)	0.843	
ASA class 3 (reference: ASA 2)	**0.34 (0.16, 0.67)**	**0.003**		0.58 (0.22, 1.45)	0.252	
Distal pancreatectomy +/− splenectomy (reference: Whipple/total pancreatectomy)	1.32 (0.63, 3.05)	0.488		1.27 (0.34, 4.86)	0.728	
Venous reconstruction (reference: none)	0.92 (0.40, 2.41)	0.859		1.68 (0.50, 6.45)	0.423	
Estimated blood loss	**1.00 (1.00, 1.00)**	**0.021**		1.00 (0.99, 1.00)	0.060	
Operative time	0.90 (0.80, 1.02)	0.100		0.87 (0.72, 1.04)	0.131	
Pathologic tumor stage (reference: CR/in situ)			0.602			0.691
T1	2.80 (0.48, 22.14)	0.268		2.02 (0.21, 28.58)	0.565	
T2	1.23 (0.33, 3.76)	0.729		1.06 (0.22, 4.54)	0.939	
T3	1.02 (0.27, 3.14)	0.977		0.68 (0.13, 3.08)	0.622	
Pathologic nodal stage (reference: N0)			0.262			0.157

	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
N1	1.78 (0.90, 3.63)	0.102		2.71 (0.99, 7.70)	0.055	
N2	1.19 (0.54, 2.79)	0.669		1.78 (0.53, 6.30)	0.361	
R1 Margin status (reference: R0)	1.09 (0.43, 3.37)	0.868		0.39 (0.11, 1.53)	0.159	
Lymphovascular invasion (reference: none)	1.15 (0.59, 2.16)	0.682		0.85 (0.27, 2.62)	0.784	
Perineural invasion (reference: none)	1.00 (0.43, 2.14)	0.997		0.99 (0.30, 3.14)	0.986	
Clavien grade 3/4 complication (reference: none)	**0.31 (0.15, 0.66)**	**0.002**		**0.22 (0.08, 0.57)**	**0.002**	

Table 4:

Relative Odds of Completion of Adjuvant Therapy: Univariable and Multivariable Logistic Regression Models, Odds Ratios (95% CI)

	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
SED (reference: Low SED)			0.637			0.462
Moderate SED	0.79 (0.45, 1.40)	0.423		0.64 (0.32, 1.29)	0.215	
High SED	1.04 (0.55, 1.99)	0.904		0.82 (0.37, 1.86)	0.634	
Age	**0.94 (0.91, 0.97)**	**<0.001**		**0.93 (0.88, 0.97)**	**0.002**	
Male sex (reference: female)	0.79 (0.48, 1.30)	0.360		0.68 (0.37, 1.25)	0.220	
Race (reference: White)			0.146			0.088
Black	1.89 (0.56, 8.59)	0.343		1.03 (0.25, 5.38)	0.968	
Other / unknown	6.24 (1.19, 114.92)	0.082		**14.14 (1.92, 310.59)**	**0.028**	
Insurance (reference: private)			0.112			0.982
Government with private supplement	0.56 (0.30, 1.04)	0.071		0.99 (0.42, 2.32)	0.987	
Government	0.52 (0.26, 1.00)	0.052		0.93 (0.37, 2.34)	0.882	
Distance from Moffitt (miles)	1.00 (0.99, 1.00)	0.189		1.00 (0.99, 1.00)	0.091	
Charlson comorbidity index	**0.80 (0.67, 0.95)**	**0.012**		1.03 (0.76, 1.40)	0.848	
Diabetes mellitus (reference: no)	0.69 (0.41, 1.19)	0.179		0.78 (0.38, 1.60)	0.497	
BMI	1.02 (0.98, 1.07)	0.346		1.06 (0.99, 1.12)	0.076	
Preoperative biliary stent (reference: none)	1.64 (0.99, 2.70)	0.051		1.84 (0.88, 3.86)	0.104	
Neoadjuvant Therapy (reference: none)	0.88 (0.53, 1.47)	0.609		0.75 (0.35, 1.60)	0.451	
ASA class 3 (reference: ASA 2)	**0.47 (0.28, 0.79)**	**0.005**		0.89 (0.44, 1.82)	0.747	
Distal pancreatectomy +/− splenectomy (reference: Whipple/total pancreatectomy)	0.78 (0.43, 1.42)	0.405		0.52 (0.18, 1.45)	0.213	
Venous reconstruction (reference: none)	**0.42 (0.20, 0.84)**	**0.015**		0.64 (0.25, 1.66)	0.354	
Estimated blood loss	**1.00 (1.00, 1.00)**	**0.015**		1.00 (0.99, 1.00)	0.103	
Operative time	0.94 (0.85, 1.04)	0.213		0.88 (0.75, 1.02)	0.082	
Pathologic tumor stage (reference: CR/in situ)			0.275			0.443
T1	1.70 (0.38, 7.98)	0.485		0.79 (0.13, 4.81)	0.792	
T2	0.60 (0.19, 1.67)	0.354		0.51 (0.12, 1.88)	0.324	
T3	0.64 (0.19, 1.82)	0.423		0.36 (0.08, 1.42)	0.154	
Pathologic nodal stage (reference: N0)			0.574			0.191

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	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
N1	1.34 (0.78, 2.32)	0.300		2.11 (0.95, 4.76)	0.069	
N2	1.21 (0.61, 2.45)	0.586		1.69 (0.63, 4.69)	0.306	
R1 Margin status (reference: R0)	0.84 (0.39, 1.92)	0.673		0.36 (0.13, 1.03)	0.056	
Lymphovascular invasion (reference: none)	0.94 (0.55, 1.60)	0.826		0.48 (0.18, 1.21)	0.126	
Perineural invasion (reference: none)	1.24 (0.65, 2.33)	0.505		2.20 (0.87, 5.64)	0.096	
Clavien grade 3/4 complication (reference: none)	**0.49 (0.25, 0.97)**	**0.038**		**0.33 (0.14, 0.77)**	**0.011**	

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Table 5:

Relative Hazard of Death: Univariable and Multivariable Cox Proportional Hazards Regression Model, Hazard Ratios (95% CI)

	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
SED (reference: Low SED)			0.471			0.953
Moderate SED	1.05 (0.77, 1.43)	0.772		1.02 (0.72, 1.46)	0.897	
High SED	1.24 (0.88, 1.74)	0.228		1.07 (0.72, 1.58)	0.757	
Age	**1.02 (1.00, 1.03)**	**0.016**		0.99 (0.97, 1.01)	0.408	
Male sex (reference: female)	1.25 (0.95, 1.65)	0.108		1.21 (0.88, 1.68)	0.248	
Race (reference: White)			0.497			0.749
Black	0.75 (0.37, 1.52)	0.422		0.84 (0.37, 1.88)	0.664	
Other / unknown	0.69 (0.31, 1.56)	0.373		0.76 (0.32, 1.80)	0.529	
Insurance (reference: private)			0.153			0.096
Government with private supplement	0.91 (0.65, 1.26)	0.556		0.67 (0.43, 1.03)	0.066	
Government	1.24 (0.88, 1.76)	0.221		0.94 (0.60, 1.47)	0.787	
Distance from Moffitt (miles)	1.00 (0.99, 1.00)	0.526		1.00 (0.99, 1.00)	0.123	
Charlson comorbidity index	**1.17 (1.07, 1.28)**	**0.001**		1.02 (0.86, 1.21)	0.835	
Diabetes mellitus (reference: no)	1.08 (0.80, 1.46)	0.631		1.12 (0.75, 1.66)	0.585	
BMI	1.01 (0.99, 1.02)	0.278		1.00 (0.97, 1.03)	0.835	
Preoperative biliary stent (reference: none)	1.19 (0.90, 1.56)	0.216		1.19 (0.79, 1.79)	0.411	
Neoadjuvant Therapy (reference: none)	**0.59 (0.44, 0.79)**	**0.001**		**0.54 (0.36, 0.80)**	**0.002**	
ASA class 3 (reference: ASA 2)	**1.37 (1.04, 1.81)**	**0.024**		1.36 (0.95, 1.93)	0.092	
Distal pancreatectomy +/− splenectomy (reference: Whipple/total pancreatectomy)	0.93 (0.66, 1.31)	0.677		1.52 (0.86, 2.69)	0.150	
Venous reconstruction (reference: none)	1.16 (0.77, 1.74)	0.474		0.99 (0.58, 1.68)	0.967	
Estimated blood loss	1.00 (1.00, 1.00)	0.150		1.00 (1.00, 1.00)	0.602	
Operative time	**1.06 (1.00, 1.12)**	**0.035**		**1.12 (1.03, 1.21)**	**0.006**	
Pathologic tumor stage (reference: CR/in situ)			**<0.001**			**0.004**
T1	1.77 (0.76, 4.15)	0.189		1.23 (0.45, 3.38)	0.689	
T2	**3.49 (1.76, 6.92)**	**<0.001**		**2.86 (1.26, 6.49)**	**0.012**	
T3	**4.19 (2.10, 8.35)**	**<0.001**		**3.42 (1.52, 7.73)**	**0.003**	
Pathologic nodal stage (reference: N0)			**<0.001**			**0.001**

	Univariable	P value	Overall P value	Multivariable	P value	Overall P value
N1	**2.14 (1.57, 2.91)**	**<0.001**		**2.34 (1.51, 3.63)**	**0.001**	
N2	**2.56 (1.77, 3.69)**	**<0.001**		**2.36 (1.41, 3.96)**	**0.001**	
R1 Margin status (reference: R0)	1.37 (0.88, 2.11)	0.161		1.07 (0.62, 1.84)	0.802	
Lymphovascular invasion (reference: none)	**2.22 (1.60, 3.08)**	**<0.001**		1.01 (0.61, 1.68)	0.967	
Perineural invasion (reference: none)	**1.85 (1.25, 2.74)**	**0.002**		1.17 (0.72, 1.91)	0.531	
Clavien grade 3/4 complication (reference: none)	**1.51 (1.04, 2.20)**	**0.032**		1.27 (0.77, 2.07)	0.350	
Length of stay (days)	**1.04 (1.01, 1.06)**	**0.001**		**1.03 (1.00, 1.06)**	**0.041**	
Readmission by 90 days	0.95 (0.66, 1.37)	0.796		0.64 (0.41, 1.01)	0.053	
Initiation of adjuvant therapy	**0.47 (0.34, 0.65)**	**<0.001**		0.71 (0.41, 1.23)	0.220	
Completion of adjuvant therapy	**0.42 (0.32, 0.56)**	**<0.001**		**0.38 (0.25, 0.58)**	**<0.001**	