The impact of race/ethnicity on pancreaticoduodenectomy outcomes for pancreatic cancer

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Abstract

Purpose: To investigate the impact of race/ethnicity on surgical outcomes following pancreaticoduodenectomy for pancreatic cancer.

Methods: A retrospective review of patients undergoing pancreaticoduodenectomy for adenocarcinoma in the National Surgical Quality Improvement Program (NSQIP) database from 2014 to 2019. Patient and tumor characteristics and 30-day postoperative outcomes were compared. Multivariable logistic and linear regression models were conducted to investigate the relationship between race/ethnicity and surgical outcomes.

Results: Six thousand five hundred and sixty-two patients were included (84.5% White, 7.9% Black, 3% Hispanic, 4.6% Asian). Larger proportions of Blacks had preoperative American Society of Anesthesiologists class 3 or 4. There were no significant differences in tumor characteristics or operative techniques. A smaller proportion of Asians and Hispanics received neoadjuvant chemotherapy and/or radiation than Blacks and Whites. Relative to White, the Black race was independently associated with postoperative sepsis and reoperation. Both Black and Hispanic race/ethnicity were associated with prolonged intubation and delayed gastric emptying, and minorities races/ethnicities were associated with longer length of hospital stay. Relative to White, Hispanic, and Asian race/ethnicity were independently associated with a lower likelihood of neoadjuvant therapy (NAT) receipt.

Conclusion: In ACS-NSQIP participating hospitals, non-White race/ethnicity was independently associated with adverse outcomes after pancreatic cancer resection. A possible disparity in NAT receipt may exist in Asian and Hispanic patients undergoing surgical resection.

Keywords
ACSN SQIP, outcomes, pancreatic cancer, pancreaticoduodenectomy, racial disparity

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INTRODUCTION

Pancreatic cancer is the third most common cause of cancer-related deaths in the United States (US) with an estimated 57,600 new cases and about 47,000 related deaths in 2020. The majority of newly diagnosed patients present at a locally advanced or metastatic stage (30% and 52%, respectively). Due to the usual late-stage presentation, only about 20% are surgically resectable and the overall 5-year survival rate is less than 10%.

Patients’ race has been shown to have an impact on their access to surgical treatment in addition to operative outcomes in several procedures including esophagectomy, carotid endarterectomy, cardiac valve replacement, pulmonary lobectomy, and urologic malignancy surgeries. Racial/ethnic disparities have been previously described in pancreatic cancer care. Studies have reported that Black and Hispanic patients have lower rates of surgical resection, are less likely to receive chemotherapy or radiation therapy, and are more likely to be treated at low-volume hospitals than White patients. Studies have also shown that Blacks with pancreatic cancer present at a later cancer stage, are less likely to be offered surgery, and have worse postoperative outcomes than Whites. Others have shown comparable short-term postoperative outcomes between White and Black patients.

For resectable pancreatic cancer, systemic treatment with adjuvant chemotherapy has been the standard of care due to the high rates of recurrence after surgery with poor prognosis. Nevertheless; up to 50% of eligible patients never receive adjuvant therapy mostly due to postoperative complications and delayed recovery. In recent years, randomized controlled trials (RCTs) demonstrating survival benefits and/or improved R0 resection rates with neoadjuvant therapy (NAT) compared to upfront surgery have led to changes in guidelines which now recommend NAT for patients with borderline resectable disease. However, the use of NAT remains controversial for resectable diseases and no consensus has been reached on a standard of care approach due to conflicting data and concerns of selection biases in published studies. Whether or not this lack of clear criteria for NAT has contributed to racial/ethnic disparities in the rates of NAT receipt in patients with nonmetastatic disease has yet to be elucidated.

Data evaluating the impact of race/ethnicity on pancreatic cancer mostly come from studies with limited emphasis on oncologic treatments. Furthermore, large comparative studies of the clinical outcomes in ethnic minorities other than Blacks are lacking as those patients are often excluded or grouped together due to smaller sample sizes. Hispanics are estimated to comprise approximately 28% of the US population by 2060; therefore, there is an increasing need for studies evaluating the contemporary practice of pancreatic cancer treatment in a racially/ethnically representative patient sample at the national level.

This study aimed to utilize a large multicenter national data set to investigate the relationship between race/ethnicity and surgical outcomes following pancreaticoduodenectomy, and the impact of race/ethnicity on the receipt of NAT, in White, Black, Hispanic, and Asian patients with pancreatic cancer.

METHODS

Database and patient population

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database was queried for patients with pancreatic cancer who underwent pancreateoduodenectomy between January 2014 and December 2019. ACS NSQIP contains over 150 variables captured from deidentified surgical cases performed in participating hospitals. These variables include preoperative characteristics, intraoperative events, and postoperative outcomes within 30 days of the operation. Additionally, we used the procedure targeted participant use data files for pancreatectomy which provides additional 44 relevant variables with data regarding preoperative cancer staging, operative approach and technique, neoadjuvant chemotherapy and radiation, and others.

The Current Procedural Terminology (CPT) codes were used to identify patients who underwent a Whipple procedure with pylorus-sparing (CPT 48153) or without (CPT 48150 and 48152). Only patients with the International Classification of Diseases, Clinical Modification diagnosis codes for malignant pancreatic tumors (ICD-9-CM 157 and ICD-10-CM C25) and underwent open procedures were included. Patients who underwent a Whipple procedure for other pancreatic pathologies including Intraductal papillary mucinous neoplasm, cholangiocarcinoma, and neuroendocrine tumors were excluded. Patients with the American Society of Anesthesiologists Physical Status Classification (ASA class) 5 and cases performed in emergent settings were excluded. Given the deidentified nature of the data, this study did not require approval by an institutional review board.

Preoperative patient demographics, clinical characteristics, and study outcomes

The following preoperative variables were studied: demographic and anthropomorphic information (age, sex, race/ethnicity, body mass index [BMI]), ASA class, comorbid conditions (diabetes, hypertension [on medications], severe chronic obstructive pulmonary disease [COPD], congestive heart failure [CHF] within 30 days before surgery, and end-stage renal disease [ESRD] requiring dialysis), weight loss greater than 10% within 6 months, smoking within 1 year before surgery, and laboratory results for serum creatinine and albumin. The NSQIP 5-factor modified frailty index was calculated for each patient based on diabetes mellitus, hypertension, congestive heart failure, chronic obstructive pulmonary disease and functional dependence. Tumor characteristics included the most recent American Joint Committee on Cancer (AJCC) tumor, node and metastasis (TNM) pathological stage, pancreatic gland texture, and the size of the...
pancreatic duct. Receipt of neoadjuvant chemotherapy and radiation within 90 days of surgery was evaluated. Operative data studied were preoperative biliary stent placement, surgical technique (pylorus-preserving or classic Whipple), vascular reconstruction (arterial, venous, or both), drain placement, and operative time.

Primary outcomes of the study were the 30-day surgical complications including: bleeding requiring transfusion, surgical site infections, delayed gastric emptying, \( ^{25} \) clinically significant pancreatic fistula (grades B and C), \( ^{25} \) pneumonia, pulmonary embolism, prolonged intubation (>48 h), unplanned re-intubation, urinary tract infection, acute renal failure, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, deep venous thrombosis (DVT), stroke, sepsis, extended length of hospital stay (LOS; LOS > 6 days and LOS > 30 days), reoperation, readmission, and death. Secondary outcomes included the rates of neoadjuvant chemotherapy and radiation therapy receipt.

Patients of the following racial/ethnic groups were compared: White, Black, Hispanic, and Asian. Race/ethnicity data in the ACS NSQIP are obtained from admission questionnaires which include inquiries regarding both race and ethnicity. Race variable is reported as one of the following possibilities: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, Unknown/Not Reported, and White. Hispanic ethnicity is reported as a separate variable. In accordance with the Centers for Disease Control and Prevention reported incidence of pancreatic cancer for the following groups: White, Black, Asian, and Hispanic, we chose to use a variable combining both race and ethnicity to match the CDC reporting categories. \(^{3} \) In our analysis, White and Black patients of Hispanic ethnicity were considered Hispanic. White and Black refer to non-Hispanic White and non-Hispanic Black, respectively. Patients with races reported as others or not reported and American Indian patients were excluded due to the small sample size.

### 2.3 Statistical analyses

Continuous variables were presented as the mean ± standard deviation and compared between racial/ethnic groups using one-way ANOVA, whereas categorical variables were compared using Pearson’s Chi-square or Fisher’s exact test. To evaluate factors independently associated with selected adverse surgical outcomes, binary logistic regression and multiple linear regression analyses with a backward selection procedure (using the Akaike information criterion) were constructed with the following covariates: patient’s demographics (age, sex, race/ethnicity, BMI), comorbidities (diabetes, hypertension, COPD, CHF, ESRD), history of weight loss >10%, smoking, tumor characteristics (AJCC pathological staging, pancreatic gland texture, size of the pancreatic duct), preoperative serum albumin and creatinine, preoperative biliary stent placement, and surgical technique (pylorus-preserving or classic Whipple). Another binary logistic regression model was used to evaluate factors independently associated with the receipt of NAT. Covariates included in the model were age, sex, race/ethnicity, BMI, smoking, and comorbidities in addition to the following variables as surrogates of criteria usually considered for NAT patient selection: pathological stage, size of the pancreatic duct, preoperative biliary stent placement, and the need for vascular reconstruction (tumor stage and respectability surrogates); the 5-factor modified frailty index (patient performance and functional status)\(^ {15} \); and weight loss >10%, and preoperative serum albumin (clinical suspicion of advanced disease and nutritional status). SAS V9.4 (SAS Institute) was used for all analyses and statistical significance was determined if \( p < 0.05 \).

### 3 RESULTS

#### 3.1 Preoperative patient characteristics, NAT, and cancer staging

A total of 6562 patients were included in the study (84.5% White, 7.9% Black, 3% Hispanic, 4.6% Asian). Preoperative patient demographics, comorbidities, serum creatinine and albumin, and functional status are presented in Table 1. The mean age was 66.9 ± 9.8 years, 52.4% were males, and 80.6% had ASA Class 3 or 4. Black patients had a higher frailty index and ASA class than others while Asians had lower rates of smoking, COPD, and hypertension.

There were no significant differences between race/ethnicity groups in pathological staging or presence of preoperative obstructive jaundice (Table 2). 39.4% had neoadjuvant chemotherapy and 16.8% received neoadjuvant radiation therapy. The rates of NAT receipt differed significantly between groups. A higher proportion of Whites and Blacks received chemotherapy (40.3% and 41.4%, respectively) than Hispanics and Asians (30.4% and 31.2%, respectively) and, similarly, Blacks had the highest rate of radiation therapy (19.1%) followed by Whites (17.1%) with lower rates in Hispanics (12.4%) and Asians (11.1%), \( p < 0.01 \) (Table 2).

#### 3.2 Pancreatic characteristics, and operative technique and time

Preoperative biliary stent, pancreatic characteristics, and operative technique are presented in Table 3. There were no significant differences between race/ethnicity groups in rates of preoperative biliary stent placement, pancreatic duct size, or gland texture. Operative technique was also similar between groups with no significant differences in the type of Whipple procedure, vascular construction, or placement of drains. The mean operative time was 376 ± 137 min without statistical differences between groups (Table 3).

#### 3.3 Thirty-day perioperative outcomes

Thirty-day perioperative complications are presented in Table 4. Bleeding requiring blood transfusion, delayed gastric emptying and
Sepsis were the three most common complications and occurred in 21.6%, 14.4%, and 7.8% respectively. Black patients had higher rates of sepsis and delayed gastric emptying while Hispanics had a higher rate of prolonged intubation (5.6%). Pancreatic fistula occurred in 3.7% of Blacks and Asians and less frequently in others.

Mean LOS was 9.5 ± 6.2 days and differed between the race/ethnicity groups, with White patients having a significantly shorter LOS and a smaller proportion with extended LOS (Table 4). Discharge destination, 30-day readmission, and mortality rates were similar between groups. Readmission was required in 15% and death occurred in 1.8%. Thirty-day reoperation occurred in 4.3% of all patients and was more frequent in Black patients (6.9%).

3.4 Factors independently associated with NAT receipt and adverse surgical outcomes

Relative to White, Hispanic, and Asian race/ethnicity were independently associated with a decreased likelihood for patients to receive NAT within 90-days before surgery (Hispanic AOR: 0.63, 95% CI: 0.41–0.95, p = 0.03; Asian AOR: 0.53, 95% CI: 0.38–0.75, p < 0.001). The pathological stage and other variables were also independently associated with NAT receipt (Supporting Information: Table 1).

Factors independently associated with adverse surgical outcomes are summarized in Table 5. Relative to White, only Black race/ethnicity was independently associated with postoperative sepsis (AOR: 1.48, 95% CI: 1.04–2.11, p = 0.03) and reoperation (AOR: 1.82, CI: 1.16–2.85, p = 0.008). Both Black and race/ethnicity were associated with prolonged intubation (Black: [AOR: 2.91, 95% CI: 1.58–5.35, p < 0.001], Hispanic: [AOR: 2.84, 95% CI: 1.1–7.34, p = 0.031]) and delayed gastric emptying (Black: [AOR: 1.53, 95% CI: 1.14–2.06, p = 0.004], Hispanic: [AOR: 1.63, 95% CI: 1.02–2.61, p = 0.041]). Finally, Black, Hispanic, and Asian race/ethnicity were all independently associated with longer LOS, relative to White. Race/ethnicity was not significantly associated with bleeding, pancreatic fistula, or mortality. Factors that were associated with these adverse outcomes are presented in Supporting Information: Table 2.
**TABLE 2** Pathological stage, preoperative obstructive jaundice, and neoadjuvant therapy receipt by race/ethnicity in patients who had pancreaticoduodenectomy for pancreatic adenocarcinoma in the American College of Surgeons National Surgical Quality Improvement Program database from January 2014 through December 2019.

|                          | Total N = 6562 | White N = 5544 | Black N = 522 | Hispanic N = 197 | Asian N = 299 | P value |
|--------------------------|----------------|----------------|---------------|------------------|---------------|---------|
| **Pathological stage**   |                |                |               |                  |               |         |
| Stage 0                  | 9 (0.14)       | 8 (0.15)       | 1 (0.2)       | 0 (0)            | 0 (0.0)       | 0.64    |
| Stage I                  | 1072 (16.8)    | 888 (16.44)    | 93 (18.6)     | 32 (16.4)        | 59 (20.3)     |         |
| Stage II                 | 4909 (76.9)    | 4176 (77.3)    | 373 (74.5)    | 150 (76.9)       | 210 (72.2)    |         |
| Stage III                | 397 (6.2)      | 328 (6.1)      | 34 (6.8)      | 13 (6.7)         | 2 (7.56)      |         |
| **Preoperative obstructive jaundice** | 3510 (53.8)    | 2964 (53.8)    | 261 (50.5)    | 117 (60.3)       | 168 (56.2)    | 0.10    |
| **Upfront surgery**      | 3857 (59.1)    | 3228 (58.4)    | 295 (56.9)    | 134 (69.1)       | 200 (67.1)    | <0.01   |
| Neoadjuvant therapy<sup>a</sup> | 2679 (40.9)    | 2298 (41.6)    | 223 (43.1)    | 60 (30.9)        | 98 (32.9)     |         |
| Neoadjuvant chemotherapy  | 2591 (39.7)    | 2224 (40.3)    | 215 (41.4)    | 59 (30.4)        | 93 (31.2)     | <0.01   |
| Neoadjuvant radiation     | 1095 (16.8)    | 940 (17.1)     | 98 (19.1)     | 24 (12.4)        | 33 (11.1)     | <0.01   |

<sup>a</sup>Neoadjuvant therapy within 90 days before surgery.

**TABLE 3** Preoperative biliary stent, pancreatic characteristics and operative technique and time by race/ethnicity in patients who had pancreaticoduodenectomy for pancreatic adenocarcinoma in the American College of Surgeons National Surgical Quality Improvement Program database from January 2014 through December 2019.

|                          | Total N = 6562 | White N = 5544 | Black N = 522 | Hispanic N = 197 | Asian N = 299 | P value |
|--------------------------|----------------|----------------|---------------|------------------|---------------|---------|
| **Preoperative biliary stent** | 2021 (31.4)    | 1698 (31.4)    | 153 (31)      | 71 (37)          | 99 (34.4)     | 0.30    |
| **Pancreatic duct size:** |                |                |               |                  |               |         |
| 3–6 mm                   | 3321 (60.7)    | 2789 (60.4)    | 276 (62.4)    | 91 (59.1)        | 165 (63.5)    |         |
| <3 mm                    | 1195 (21.8)    | 1011 (21.9)    | 93 (21)       | 40 (26)          | 51 (19.6)     |         |
| >6 mm                    | 959 (17.5)     | 819 (17.7)     | 73 (16.5)     | 23 (14.9)        | 44 (16.2)     | 0.73    |
| **Pancreatic gland texture** |                |                |               |                  |               |         |
| Hard                     | 3151 (59.2)    | 2671 (59.4)    | 252 (59.9)    | 80 (53.7)        | 148 (58.3)    |         |
| Intermediate             | 821 (15.4)     | 693 (15.4)     | 51 (12.1)     | 33 (22.2)        | 44 (17.3)     |         |
| Soft                     | 1351 (25.4)    | 1135 (25.2)    | 118 (28)      | 36 (25.2)        | 62 (24.4)     | 0.12    |
| **Surgical technique:**  |                |                |               |                  |               |         |
| Standard Whipple         | 3910 (59.6)    | 3303 (59.6)    | 304 (58.2)    | 127 (64.5)       | 176 (58.9)    |         |
| Without PJ               | 84 (1.3)       | 69 (1.2)       | 5 (1)         | 5 (2.5)          | 5 (1.7)       |         |
| Pylorus preserving       | 2568 (39.1)    | 2172 (39.2)    | 213 (40.8)    | 65 (33)          | 118 (39.5)    | 0.37    |
| **Vascular construction** |                |                |               |                  |               |         |
| None                     | 4892 (75.1)    | 4132 (75)      | 401 (77.4)    | 152 (78)         | 207 (69.5)    |         |
| Arterial                 | 102 (1.6)      | 83 (1.5)       | 9 (1.7)       | 3 (1.5)          | 7 (2.4)       |         |
| Venous                   | 1317 (20.2)    | 1116 (20.3)    | 96 (18.5)     | 33 (16.9)        | 72 (24.2)     | 0.41    |
| Both                     | 207 (3.2)      | 176 (3.2)      | 12 (2.3)      | 7 (3.6)          | 12 (4)        |         |
| **Pancreatic drains**    | 5761 (87.9)    | 4879 (88.1)    | 442 (85)      | 174 (88.3)       | 266 (89.3)    | 0.18    |
| Total operative time (min) | 376 ± 137     | 376 ± 136     | 379 ± 141     | 375 ± 145        | 367 ± 133     | 0.48    |

Note: Comparison of operative characteristics among surgical groups.

Abbreviation: PJ, pancreaticojejunostomy.
DISCUSSION

In this analysis of over 6000 patients in the ACS NSQIP 2014–2019 data, we found a significant association of race/ethnicity with 30-day adverse surgical outcomes after open pancreaticoduodenectomy for pancreatic adenocarcinoma in Black, Hispanic, and Asian patients, compared to White. Furthermore, our study demonstrates that Asian and Hispanic patients received less NAT independent of cancer stage and other preoperative clinical factors.

The disproportionately higher incidence of pancreatic cancer in Black patients and worse outcomes compared to White patients is well documented in the literature, even after controlling for modifiable risk factors such as diet, alcohol, and tobacco use. In our study, Black patients had higher rates of comorbidities at baseline, perhaps contributing to overall worse perioperative outcomes as shown in our univariate analyses; however, our logistic regression results demonstrate an independent association of Black race with several 30-day adverse outcomes. Conversely, published data support a less aggressive pancreatic tumor pathology and a better prognosis in Asians when compared to White or Black patients.

Racial/ethnic disparities among pancreatic cancer patients between 1992 and 2011 were examined by Nipp et al. who found worse survival in Black and Hispanic patients compared to their White counterparts, despite adjusting for demographic characteristics. Additionally, and in agreement with our finding of a lower rate of NAT receipt in Asian and Hispanic patients, the authors suggested non-White patients had a lower likelihood of undergoing chemoradiation. Others have also reported a disparity in the proportion of minority patients who undergo surgical resection for pancreatic adenocarcinoma. Importantly, with the changing race/ethnicity demographics in the US, our findings add to the current

TABLE 4

| Thirty-day perioperative complications, mortality, reoperation, length of stay, discharge destination, and readmission by race/ethnicity in patients who had pancreaticoduodenectomy for pancreatic adenocarcinoma in the American College of Surgeons National Surgical Quality Improvement Program database from January 2014 through December 2019. |
|-----------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                            | Total N = 6562 | White N = 5544 | Black N = 522  | Hispanic N = 197 | Asian N = 299  | P value        |
| Bleeding requiring transfusion | 1414 (21.6)   | 1158 (20.9)   | 132 (25.3)    | 45 (22.8)      | 79 (26.4)     | 0.02           |
| Delayed gastric emptying    | 938 (14.4)    | 769 (14)      | 96 (18.5)     | 32 (16.6)      | 41 (13.8)     | 0.03           |
| Sepsis                      | 512 (7.8)     | 408 (7.4)     | 60 (11.5)     | 18 (9.1)       | 26 (8.7)      | <0.01          |
| Pancreatic fistula grade B or C | 143 (2.2)    | 110 (2)       | 19 (3.7)      | 3 (1.5)        | 11 (3.7)      | 0.02           |
| Prolonged intubation >48 h  | 155 (2.4)     | 144 (2.1)     | 20 (3.8)      | 11 (5.6)       | 10 (3.4)      | <0.01          |
| Pneumonia                   | 158 (2.4)     | 133 (2.4)     | 13 (2.5)      | 3 (1.5)        | 9 (3)         | 0.77           |
| DVT/thrombophlebitis        | 181 (2.8)     | 154 (2.8)     | 14 (2.7)      | 8 (4.1)        | 5 (1.7)       | 0.46           |
| Pulmonary embolism          | 56 (0.9)      | 49 (0.9)      | 4 (0.8)       | 3 (1.5)        | 0 (0)         | 0.29           |
| Unplanned intubation        | 185 (2.8)     | 152 (2.7)     | 16 (3.1)      | 8 (4.1)        | 9 (3)         | 0.71           |
| Urinary tract infection     | 172 (2.6)     | 141 (2.5)     | 16 (3.1)      | 4 (2)          | 11 (3.7)      | 0.55           |
| Cardiac arrest              | 62 (0.9)      | 55 (1)        | 5 (1)         | 1 (0.5)        | 1 (0.3)       | 0.63           |
| Myocardial infarction       | 59 (0.9)      | 49 (0.9)      | 5 (1)         | 1 (0.5)        | 4 (1.3)       | 0.80           |
| CVA with neurological deficit | 18 (0.3)     | 16 (0.3)      | 0 (0)         | 2 (1)          | 0 (0)         | 0.10           |
| Acute renal failure         | 54 (0.8)      | 42 (0.8)      | 8 (1.5)       | 2 (1.0)        | 2 (0.7)       | 0.29           |
| Mortality                   | 116 (1.8)     | 101 (1.8)     | 7 (1.3)       | 5 (2.5)        | 3 (1)         | 0.51           |
| Reoperation                 | 285 (4.3)     | 228 (4.1)     | 36 (6.9)      | 7 (3.6)        | 14 (4.7)      | 0.03           |
| Length of stay (Days):      | 9.5 ± 6.2     | 9.4 ± 5.9     | 10.2 ± 7.3    | 10.6 ± 9       | 10.6 ± 7.0    | <0.01          |
| >6 Days                     | 4477 (68.2)   | 3750 (67.6)   | 359 (68.8)    | 141 (71.6)     | 227 (76)      | 0.02           |
| >30 Days                    | 121 (1.8)     | 86 (1.6)      | 14 (2.7)      | 12 (6.1)       | 9 (3)         | <0.01          |
| Discharge destination:      |                |                |                |                |                |                |
| Home                        | 5631 (86.3)   | 4754 (86.1)   | 448 (86.7)    | 169 (87.1)     | 260 (88.1)    | 0.95           |
| Other facility              | 815 (12.5)    | 697 (12.6)    | 64 (12.4)     | 22 (11.3)      | 32 (10.9)     |                |
| Readmission                 | 966 (14.7)    | 815 (14.7)    | 77 (14.8)     | 28 (14.2)      | 46 (15.4)     | 0.98           |

Note: Continuous variables are presented as mean ± standard deviation and categorical variables as number (percentage).
Abbreviations: CVA, cerebrovascular accident; DVT, deep venous thrombosis; SSI, surgical site infection.

4 | DISCUSSION

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The disproportionately higher incidence of pancreatic cancer in Black patients and worse outcomes compared to White patients is well documented in the literature, even after controlling for modifiable risk factors such as diet, alcohol, and tobacco use. In our study, Black patients had higher rates of comorbidities at baseline, perhaps contributing to overall worse perioperative outcomes as shown in our univariate analyses; however, our logistic regression results demonstrate an independent association of Black race with several 30-day adverse outcomes. Conversely, published data support a less aggressive pancreatic tumor pathology and a better prognosis in Asians when compared to White or Black patients.

Racial/ethnic disparities among pancreatic cancer patients between 1992 and 2011 were examined by Nipp et al. who found worse survival in Black and Hispanic patients compared to their White counterparts, despite adjusting for demographic characteristics. Additionally, and in agreement with our finding of a lower rate of NAT receipt in Asian and Hispanic patients, the authors suggested non-White patients had a lower likelihood of undergoing chemoradiation. Others have also reported a disparity in the proportion of minority patients who undergo surgical resection for pancreatic adenocarcinoma. Importantly, with the changing race/ethnicity demographics in the US, our findings add to the current
literature describing increased postoperative complications among minorities in a contemporary analysis from a national-level database which includes a diverse population of White, Black, Hispanic, and Asian patients. We found an increased risk of sepsis and reoperations in Blacks, prolonged intubation, and delayed gastric emptying in both Blacks and Hispanics and a significant association with longer hospital stay in Black, Hispanic and Asian patients. Similar outcome discrepancies among non-White patients have been studied in various other cancer populations, including urologic, breast, lung, and esophageal cancers.

Postoperative morbidity after pancreaticoduodenectomy may have a significant implication on overall cancer treatment outcomes. Surgical resection alone is associated with a high recurrence rate with a poor prognosis, and thus, adjuvant therapy has been the standard

| Table 5 | Factors independently associated with 30-day adverse surgical outcomes in patients who had pancreaticoduodenectomy for pancreatic adenocarcinoma in the American College of Surgeons National Surgical Quality Improvement Program database from January 2014 through December 2019. | Adverse surgical outcome | Adjusted odds ratio | 95% confidence interval | P value |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|----------------------|------------------------|
| Sepsis: |                                                                                                                                                                                                  |                         |                      |                        |
| Black race/ethnicity (relative to White) | 1.48 | 1.04–2.11 | 0.030 |
| Body mass index | 1.02 | 1.01–1.04 | 0.015 |
| Preoperative biliary stent | 1.89 | 1.43–2.51 | <0.001 |
| Pancreatic duct size <3 mm (relative to 3–6 mm) | 1.32 | 1.02–1.70 | 0.035 |
| Preoperative creatinine | 1.35 | 1.12–1.64 | 0.001 |
| Prolonged intubation:* | | | |
| Race/ethnicity (relative to White): Black | 2.91 | 1.58–5.35 | <0.001 |
| Hispanic | 2.84 | 1.1–7.34 | 0.031 |
| Preoperative albumin | 0.67 | 0.46–0.98 | 0.037 |
| Age | 1.04 | 1.02–1.07 | 0.001 |
| Body mass index | 1.06 | 1.02–1.10 | 0.003 |
| Smoking | 1.98 | 11.13–3.45 | 0.016 |
| Delayed gastric emptying: | | | |
| Race/ethnicity (relative to White): Black | 1.53 | 1.14–2.06 | 0.004 |
| Hispanic | 1.63 | 1.02–2.61 | 0.041 |
| Male sex | 1.56 | 1.31–1.86 | <0.001 |
| Pylorus preserving (relative to classic Whipple) | 1.24 | 1.04–1.47 | 0.014 |
| Length of stay:* | | | |
| Race/ethnicity (relative to White): Black | 0.94 | 0.27–1.6 | 0.005 |
| Hispanic | 1.68 | 0.63–2.75 | 0.001 |
| Asian | 1.37 | 0.54–2.19 | 0.001 |
| Preoperative albumin | −0.86 | −1.07 to −0.54 | <0.001 |
| Age | 0.05 | 0.03–0.07 | <0.001 |
| Soft pancreatic gland texture (relative to hard) | 1.24 | 0.81–1.67 | <0.001 |
| Male sex | 0.43 | 0.08–0.79 | 0.016 |
| Body mass index | 0.04 | 0.01–0.07 | 0.009 |
| Pancreatic duct size <3 mm (relative to 3–6 mm) | 0.63 | 0.18–1.08 | 0.005 |
| Reoperation: | | | |
| Black race/ethnicity (relative to White) | 1.82 | 1.16–2.85 | 0.008 |
| Smoking | 1.58 | 1.12–2.24 | 0.010 |

*Intubation was considered prolonged if it extended beyond 48 h.

*Multiple linear regression was used for the analysis of factors associated with length of stay, difference (CI).
of care due to its associated survival benefits. However, a major concern is the high proportion of patients who either never receive adjuvant therapy or have a significant delay in treatment initiation due to adverse surgical outcomes. Merkow et al. have demonstrated a significant increase in the risk of both adjuvant therapy omission and more than 70 days delay not only in patients with the most serious complications (e.g., prolonged ventilation, reintubation, pneumonia, renal failure, sepsis) but also in those with less severe events such as urinary tract infection and wound dehiscence. Consistent results have been reported in RCTs and other population studies showing that only 50%–60% of patients who undergo surgical resection ultimately receive adjuvant therapy. A neoadjuvant approach for systemic treatment has been studied in comparison with upfront surgery and promising data have recently been reported from RCTs. Potential benefits of NAT in nonmetastatic disease include increased rates of RO resection, micrometastatic disease control, downstaging, and guaranteed early systemic treatment delivery to all patients without the physiological compromise associated with major surgery. Consequently, the use of NAT in a subset of patients with resectable and/or borderline resectable disease has been recommended by different guidelines. However, a standard of care consensus for patient selection is still lacking. Importantly, NAT may be associated with preoperative attrition in patients with aggressive disease. Delaying surgery may deny a subset of patients the chance of curative resection. Nevertheless, allowing some time to uncover early metastatic disease or underlying patient frailty and higher risk of serious adverse surgical outcomes can be considered an advantage in allowing NAT to triage patients for surgery.

An important finding in our study is the possible disparity in NAT receipt in Asians and Hispanics undergoing surgical resection, but not in Blacks. A possible explanation may come from a recent study that included all stages of pancreatic cancer using the National Cancer Database. Heller et al. found that Black patients were much more likely to be treated at academic or tertiary care centers compared to Whites. Such centers are more likely to implement a multidisciplinary treatment approach. To our knowledge, evidence for other specific minorities’ access to tertiary hospitals for pancreatic cancer treatment is lacking. However, Molina and colleagues found a disparity in surgical resection rates in non-White patients grouped together which is consistent with some previous reports. Interestingly, this disparity disappeared in patients who received NAT possibly due to the multimodal treatment approach in centers offering NAT for borderline resectable disease. In light of the above, it is important to point out that our results should not be interpreted as a finding of undertreatment or overtreatment of different racial/ethnic groups; rather, we provide a contemporary evaluation of the current state of utilization of NAT in different races/ethnicities after adjusting for several patient and tumor characteristics. Other factors such as the type of surgical facility, teaching status, or geographic location likely play a role in patient selection. Additionally, the association of race/ethnicity with NAT receipt rates applies only to patients who had a surgical resection, as NAT may be associated with a potential loss of eligibility for surgery in a subset of NAT recipients. The potential impact of this disparity on survival outcomes is beyond the scope of our study. It is important to point out, however, that putting together the known implications of postoperative complications on adjuvant therapy initiation and our findings of independent associations between race/ethnicity and both higher rates of adverse surgical outcomes and lower NAT receipt may suggest a potentially increased risk in minority groups in regard to the overall likelihood of receiving systemic anticancer therapy (both NAT and adjuvant therapy). There is, therefore, an opportunity for improvements in pancreatic cancer outcomes if such factors are confirmed in future studies, especially with the recent advancements in NAT regimens which are currently being evaluated in RCTs. In debating the pros and cons of NAT utilization in resectable and borderline resectable pancreatic cancer, we advocate that policy-makers and cancer societies take into consideration the impact of postoperative morbidity on adjuvant therapy, especially in high-risk groups. Standard of care recommendations largely rely on evidence from high-quality studies but pancreatic cancer RCTs are often unable to enroll a large and diverse patient sample enough to appropriately account for potential differences in factors that can influence treatment sequencing and completion in an intention-to-treat analytical approach. Several RCTs have been terminated for slow accrual or outdated treatment regimens and most of the recent and ongoing trials are conducted outside the US without the ability to include a diverse sample. Therefore, findings of well-designed population studies should be considered in areas that have been shown to be influenced by population factors such as race/ethnicity and access to care.

Pancreatic cancer outcomes are arguably confounded by the lack of effective cancer screening. Given the malignancy often presents with vague symptoms, it can be hypothesized that those with limited access to healthcare may be slower to seek out work-up, ultimately resulting in delayed recognition of the disease. Patients with access to routine primary care may be quicker to note changes, prompting more timely diagnosis and treatment. Additional nonmodifiable risk factors, including genotypic make-up, chronic pancreatitis, non-O blood type, and predisposition to diabetes, may also play a role in outcome discrepancies in patients with pancreatic cancer. Furthermore, structural racism is a powerful entity that must not be overlooked in the discussion of healthcare inequities. Gee et al define structural racism as “the macro-level systems, social forces, institutions, ideologies, and processes that interact with one another to generate and reinforce inequities among racial and ethnic groups.” Structural racism is a deeply-rooted confounder, interwoven into multiple aspects of healthcare delivery and oftentimes difficult to both identify and correct, as it “does not require the actions or intent of individuals” to perpetuate.

Some of the predictors of adverse outcomes in our logistic regression model point to the dire need for further research and opportunities for improvement in pancreatic adenocarcinoma care. Preoperative patients’ nutrition presented by serum albumin levels was independently associated with multiple adverse outcomes emphasizing the importance of perioperative nutritional optimization.
Pylorus preservation was associated with higher rates of post-operative delayed gastric emptying, compared to classic Whipple, a finding that agrees with results from a recent meta-analysis of RCTs.\(^4\)\(^{31}\) We also found that short pancreatic duct and soft gland texture were independent risk factors for the development of pancreatic fistula (data shown in Supporting Information: Table 2), similar to reports from previous retrospective studies.\(^4\)\(^{2}\)\(^3\) Younger age, male gender, and having a preoperative biliary stent were associated with higher rates of NAT receipt. Of note, stage II/III compared to stage I was associated with lower likelihood of NAT receipt on multivariate analysis likely related to a downstaging effect (Supporting Information: Table 1). Because our univariate analysis showed no significant differences in the proportions of patients with different pathological stages between race/ethnic groups, it is reasonable to think that pathological stage in the groups with higher NAT receipt rates, White and Black, may have been more influenced by downstaging. Nevertheless, both race/ethnicity and pathological stage (among the other available oncological data) were among the independent variables entered in the logistic regression model for surgical outcomes and NAT receipt analyses.

Our study has several limitations. First, due to its retrospective nature, endpoint investigation was limited to previously collected data. This inhibited further inquiry into individual facility performance, institution-specific protocol, or additional data points such as patient-specific criteria used for NAT versus upfront surgery approach, CA 19-9 levels, access and rates of adjuvant therapy, and long-term outcomes. Second, our analyses did not account for other possible confounding factors such as socioeconomic status, type of surgical facility, and geographic location as those data are unavailable in the ACS NSQIP database. Third, our study only included patients who have received a surgical resection; therefore, we did not evaluate disparities in surgical treatment or access to curative resection. We did not study the possible disparities in care in the subset of patients with the seemingly resectable disease who may be deemed ineligible upon surgical exploration. Fourth, The most recent AJCC guidelines were used to determine the pathological stage prognostic group (0–IV) using the TNM staging data provided by the ACS-NSQIP. However, we did not adjust the TNM data for changes implemented starting in 2018 based on the 8th edition of the AJCC cancer staging manual. This is due to the unavailability of the raw data for the TNM staging (namely, tumor size and extension and number of metastatic regional lymph nodes). Nevertheless, the findings of our multivariate analyses that included pathological stage as a covariate, among others, are unlikely to be influenced by the potential differences in staging criteria between 2018–2019 and previous years as those differences would have a similar impact on all race/ethnic groups. Lastly, the ACS NSQIP database, while providing comprehensive surgical outcomes data from hundreds of care centers across the country, does not necessarily reflect data generalizable to the entirety of the US population. We elected to use the ACS NSQIP, however, because it is the largest available national-level clinical database with detailed information on surgical outcomes that are risk-adjusted (to account for differences in risk factors between patients) and case-mix-adjusted (to account for differences between hospitals). These qualities made the ACS-NSQIP particularly suitable to answer our study questions.

5 CONCLUSION

In ACS-NSQIP participating hospitals, non-White race/ethnicity was independently associated with adverse surgical outcomes after pancreatic cancer resection. A possible disparity in NAT receipt may exist in Asian and Hispanic patients undergoing surgical resection. Both findings emphasize the importance of large-scale prospective studies assessing disparity in pancreatic cancer care and the need for a standard of care consensus for NAT.

AUTHOR CONTRIBUTIONS

Drs. Alwatari, Mosquera, Khoraki, Wall, Sevdalis, Stover, Trevino, and Kaplan were responsible for study design, and data acquisition. Mr. Rustom was responsible for data acquisition and statistical analysis. All authors contributed to drafting the manuscript, revising it critically, and provided approval of the final manuscript version.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

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