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Tobacco smoking associated with increased anastomotic disruption following pancreaticoduodenectomy



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ABSTRACT

Background: The effect of cigarette smoking on postoperative morbidity following pancreaticoduodenectomy (PD) for cancer is unclear. We hypothesize that smoking is associated with higher morbidity following PD.

Methods: A retrospective review of patients undergoing PD for cancer from 2010 to 2016 at a single institution was performed. Patients who had never smoked were compared to current or past-smokers with at least 1 pack-year history. Univariate and multivariable analyses were performed.

Results: Two hundred fifty-two patients met inclusion criteria. On univariate analysis, there was a significant difference between smokers and never-smokers in age at diagnosis (65.5 versus 68.6 y, $P = 0.013$) and fistula rate (28.5% versus 16.2%, $P = 0.024$). Male sex was significantly associated with fistula rate compared with female sex (15.5% versus 7.1%, $P = 0.023$). Comparing males and females separately, smoking correlated with higher fistula development only in the male cohort (22.5% versus 5.8%, $P = 0.016$ in men and 7.3% versus 9.1%, $P = 1.00$ in women). On multivariable analysis, current and past smoking was independently predictive of developing a fistula: odds ratio of 2.038 ($P = 0.030$). For current and past-smokers, male sex was an independent risk factor for developing a fistula: odds ratio 2.817 ($P = 0.022$). There were no other significant differences between groups in rates of postoperative complications.

Conclusions: Smoking status is independently predictive of postoperative pancreatic fistula following PD for cancer. Among smokers, male sex is an independent risk factor for fistula. Further studies are needed to determine if smoking cessation before surgery decreases this risk, and if so, the optimal duration of cessation.

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Introduction

Pancreatic cancer is the fourth leading cause of cancer-related deaths in the United States, with one of the lowest 5-y survival rates at only 8%.¹ Pancreaticoduodenectomy (PD) remains the mainstay of treatment for cancer of the pancreatic head, and while operative mortality has decreased throughout the years, morbidity remains high (38%-44%).²⁻⁴ Numerous investigators have demonstrated significant correlations between patient-specific characteristics and increased risk of complications after PD.⁵⁻¹⁵ However, many of these risk factors, such as obesity, are difficult to modify in a short period of time, and some, such as having congestive heart failure, are impossible to modify.

Several studies have demonstrated that tobacco smokers have an increased risk for the development of pancreatic ductal adenocarcinoma (PDAC),¹⁶ making it likely that many patients who present for consideration of PD for PDAC will be smokers. Active smoking is a potential risk factor for postoperative morbidity that patients can change in a short period of time, making it critical for us to better understand the relationship between smoking and outcomes for patients undergoing PD. Most surgeons encourage smoking cessation before operative intervention for many reasons. Yet, available evidence regarding the effects of smoking on complication rates following PD is unclear. Furthermore, present studies have not specifically focused on analyzing smoking as a primary risk factor for complications.

The aim of this study is to investigate the relationship between current and past smoking with postoperative morbidity including postoperative pancreatic fistula (POPF) in patients undergoing resection for pancreatic cancer. We hypothesize that smoking will be independently associated with increased overall morbidity, and specifically increased POPF rates, following PD for PDAC and other related cancers.

Methods

Study design

We conducted a retrospective chart review of patients with PDAC treated with PD for curative intent at the University of Oklahoma Medical Center from January 1, 2010 to December 31, 2016. Patients with periampullary carcinoma and distal cholangiocarcinoma who underwent PD were also included. Patients without adequate clinic and hospital records were excluded. Patients were divided into groups based on smoking status: never-smokers *versus* those with at least 1 pack-year smoking history or current smokers with at least 1 pack-year smoking history. The study design was in accordance with STROBE guidelines.¹⁷ Approval from the University of Oklahoma Health Sciences Center Institutional Review Board with a waiver of informed consent was obtained.

Preoperative and intraoperative variables

Data were gathered from inpatient and outpatient electronic medical records. Demographic data included age at primary

diagnosis, sex, preoperative albumin, body mass index (BMI) at the time of surgery, major medical comorbidities, past surgical history, neoadjuvant chemotherapy and radiation therapy, and smoking status, including current *versus* past smoking, overall duration in pack-years, and time elapsed since cessation if applicable. Operative data were gathered from dictated operative notes, anesthesia records, and blood bank records. Pathologic data were collected from pathology reports and included margin status, tumor, nodes, metastases classification, and presence or absence of both lymphovascular and perineural invasion.

Operative technique

All pancreaticoduodenectomies were performed by two senior staff surgeons. All surgeries were performed open, with antecolic duodenojejunostomies or gastrojejunostomies. Pancreaticojejunostomy anastomoses were typically performed in a two-layer duct-to-mucosa fashion if the pancreatic duct was able to be identified intraoperatively and was estimated to be of adequate size (>3 mm). If ducts were estimated to be ≤3 mm or unable to be identified, an invaginated pancreaticojejunostomy was typically performed. However, the decision of which anastomotic technique to use was ultimately left to the operating surgeon's discretion. Both surgeons left two 19-French round Blake drains: one positioned behind the pancreaticojejunostomy and one behind the hepaticojejunostomy. Drains were left in place until output was ≤30 mL per day or at the discretion of the attending surgeon. Drain fluid was routinely analyzed for amylase content on postoperative day 3. Pancreatic parenchymal texture was not regularly documented in operative reports but was captured in this study when available. Similarly, pancreatic duct size was not routinely documented but was obtained when available from operative reports, official imaging reports, and endoscopic retrograde cholangiopancreatography procedure notes.

Postoperative outcome

Information regarding postoperative complications and morbidity was gathered from a review of daily progress notes, discharge summaries, clinic follow-up notes, inpatient and outpatient laboratory data, imaging reports, pathology and microbiology samples, and blood bank records. POPF grade was defined using the International Study Group of Pancreatic Fistula (ISGPF)¹⁸ classification scheme and calculated with the International Study Group of Pancreatic Surgery online calculator for leak found on the Pancreas Club website. Delayed gastric emptying was also defined and stratified using ISGPF criteria.¹⁹ Length of stay was measured in days from the date of surgery to the date of hospital discharge. Readmission was defined as admittance after initial discharge within 30 d of the primary operative intervention for sequelae directly relating to the operation. Death data were collected using the United States Social Security Death Index, as well as hospital death notes and death certificates found in clinic records.

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