



Original Research

Impact of obesity on short and long term results following a pancreatico-duodenectomy



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HIGHLIGHTS

- Obesity is an independent factor for post-operative pancreatic fistula.
- Obesity does not affect oncological outcomes following Pancreatico-duodenectomy.
- Obesity is associated with greater operative time and higher intra-operative blood loss.

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ABSTRACT

Background: The impact of obesity on short and long term outcomes following a pancreatico-duodenectomy (PD) is still unclear and needs further clarification.

Methods: Demographic, operative and outcomes data in 524 patients undergoing PD were analysed.

Results: Ninety-seven patients (18.5%) had BMI greater than or equal to 30 kg/m² (group A) and 427 patients (81.5%) had BMI less than 30 kg/m² (group B). Group A had a significantly greater operative duration, (375 vs 360 min, $p = 0.024$) and a higher intra-operative blood loss, (660 vs 500 ml, $p = 0.005$). Post-operative pancreatic fistula (POPF) were more common in Group A (28.9% vs 16.2%, $p = 0.006$), this difference was also observed when considering only major POPF (Grade B and C) (16.5% vs 8.0%, $p = 0.020$). Intra-abdominal collections were higher in Group A, 28.9% compared to 19.0% in Group B ($p = 0.037$). On multivariate analysis BMI (OR 2.006; 95% CI 1.147–4.985, $p = 0.040$), small pancreatic duct (OR 2.755; 95% CI 1.589–2.968, $p = 0.026$) and soft pancreas (OR 2.289; 95% CI 1.126–3.665, $p = 0.040$) were found to be independent factors for POPF. The median survival for adenocarcinomas was 20 months in Group A and 22 months in Group B, ($p = 0.109$).

Conclusion: Patients with BMI ≥ 30 are at an increased risk of developing pancreatic fistula following PD. Obesity does not appear to have an impact on long term outcomes in patients undergoing a PD for adenocarcinomas.

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1. Introduction

Over the last 25 years, the prevalence of obesity has increased dramatically. More than 400 million adults worldwide are considered to be obese (body mass index (BMI) ≥ 30) and nearly 1.6 billion are overweight (BMI between 25 and 30) [1]. Obesity is a risk factor for adverse surgical outcomes of patients undergoing

abdominal surgery [2–4], and consequently a high BMI has a negative impact on the course of medical conditions such as acute pancreatitis [5,6].

Pancreatico-duodenectomy (PD) is a complex abdominal surgical procedure with an operative mortality of up to 5% and morbidity ranging from 23 to 60% [7,8]. A leading cause of this morbidity is post-operative pancreatic fistula (POPF), sepsis and haemorrhage [9,10]. A substantial risk factor for POPF after PD is the status of the pancreatic remnant with soft pancreatic remnant and small size duct being associated with a higher risk of anastomotic leakage [11,12].

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The impact of obesity on surgical complication after PD is still unclear. Some studies have shown that pancreatic resections in overweight/obese patients are associated with an increased risk of post-operative complications [13–18]. Other studies have reported that high BMI is not associated with an increase of post-operative morbidity [19,20]. However, these studies showed inconsistent results and conflicting conclusions with small sample sizes, different pancreatic resection procedures and heterogeneity in analysis. This data is further confounded by the definition of obesity. Most studies considered a BMI of 25 as obese where as others used 30 as a cut-off, however, obesity is defined as a BMI ≥ 30 [1]. Furthermore, long term oncologic outcomes of PD in patients with a high BMI are not widely reported and there is a significant discrepancy in the few available reports [15,21].

Given the limited and controversial existing data, the objective of the current study was to examine the impact of obesity on outcomes, including survival, in patients undergoing PD for adenocarcinomas. Obesity is increasing throughout the world and understanding its impact on diseases is important.

2. Method

2.1. Study design and setting

An analysis of a prospectively collected database of all PD resections undertaken from January 2007 to December 2015 in a single tertiary Hepatobiliary and Pancreatic surgical unit in the UK.

2.2. Study population

Patients who underwent PD resection for both benign and malignant disease (conventional Whipple's procedure or pylorus preserving procedure) during the study period were included. All individuals were offered surgery following a consensus decision by the Hepatobiliary Multidisciplinary Team (MDT) meeting. Indications for resection of benign or malignant pancreatic and periampullary lesions with curative intent included exocrine pancreatic adenocarcinoma, ampullary adenocarcinoma, intraductal papillary mucinous neoplasm (IPMN), neuroendocrine tumour, cholangiocarcinoma, and other lesions such as pancreatic cysts and chronic pancreatitis. Patients were divided into two groups according to BMI: Group A consisting of patients with a BMI ≥ 30 , and Group B consisting of patients with a BMI < 30 . Our decision to use 30 kg/m² as a cut-off was based on the definition of obesity [1]. In addition, our study is evaluating the population of patients in the United Kingdom, where the mean BMI is 27.0 kg/m² for men and 27.3 kg/m² for women [22].

2.3. Data collection and study definitions

Data was obtained from our prospectively collected database and included: Demographics, past medical history, score of the American Society of Anaesthesiology (ASA), previous history of acute/recurrent pancreatitis, presence of jaundice on presentation and any documented history of weight loss in the last six months.

Operative details included vascular resection, blood loss volume (minimal blood loss was defined as at least 100 mL [mls]), whether blood transfusion was required and duration of surgery. The pancreatic parenchymal consistency was graded as soft or firm to hard based on intra-operative assessment by the operating surgeon. All the patients received prophylactic Octreotide prior to pancreas transection and stopped 5 days after surgery, unless a persistent high volume fistula was observed. After surgery, patients were routinely monitored in a High Dependency Unit (HDU), with input from the Critical Care team. Two abdominal drains were

regularly tested for amylase levels on post-operative course. If the amylase levels were normal, the drains were removed and if levels were elevated more than three times the serum levels, the drains were kept and further drain fluid amylase tests were performed.

Post-operative complications were stratified according to Clavien-Dindo grades, [23]. Pancreatic fistula was defined according to the International Study Group for Pancreatic Surgery (ISGPS) for postoperative pancreatic fistula (POPF) [9], Delayed Gastric Emptying (DGE) [24], and Post-Pancreatectomy Haemorrhage (PPH) [10]. Major complications included grade III and IV according to Clavien-Dindo classification. Major pancreatic fistula included Grade B or C fistulas.

Peri-operative mortality was defined as either in-hospital mortality (all deaths whatever the length of hospital stay) or death within 30 days of surgery in cases of an earlier discharge. The length of the hospital stay was also recorded.

Pathological data (histology) of the resected surgical specimen, including the tumour size, lymph node ratio, microscopic tumour infiltration, lympho-vascular invasion, peri-neural invasion and tumour differentiation were also analysed. The seventh edition of the American Joint Committee on Cancer (AJCC) classification for malignant neoplasms was used [25].

All patients diagnosed with adenocarcinomas were followed up for five-years. These included all pancreatic ductal adenocarcinomas (PDAC), ampullary adenocarcinomas, duodenal adenocarcinomas and common bile duct (CBD) cholangiocarcinomas. Follow-up data for these patients entailed a clinical assessment with blood chemistry parameters every six months. A CT thorax and abdomen was scheduled annually.

2.4. Study outcomes

- The primary study outcome was assessing the post-operative pancreatic fistula rate in obese patients following PD resection for benign and malignant disease.
- Secondary outcome was assessing the long-term outcomes in obese patients who underwent PD for adenocarcinomas.

2.5. Statistical analysis

Statistical analyses was performed using SPSS version 22.0 (SPSS Inc. Chicago, IL, USA). Median values and inter-quartile ranges were considered for continuous variables. The non-parametric Mann-Whitney test was used to compare continuous variables. Chi-square or Fisher's exact test was applied for analysis of categorical variables.

Multiple logistic regression models were used to identify independent factors predictive of post-operative pancreatic fistula. The model contained both categorical and continuous predictor variables, and these were added in a stepwise regression analysis. Significance levels were set at $p < 0.05$ to enter and $p > 0.1$ for removal. Long-term survival was analysed using Kaplan Meier. Two-tailed p value of less than 0.05 was considered to be significant.

3. Results

3.1. Demographics and operative details

Five hundred and twenty-four consecutive patients were identified of which 97 patients (18.5%) had a BMI greater than or equal to 30 kg/m² (group A) and 427 patients (81.5%) had a BMI of less than 30 kg/m² (group B).

The two groups were comparable for age, gender, weight loss,

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