

Retrospective Cohort Study

Impact of body mass index on complications following pancreatotomy: Ten-year experience at National Cancer Center in China

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Abstract

AIM: To examine the impact of body mass index (BMI) on outcomes following pancreatic resection in the Chinese population.

METHODS: A retrospective cohort study using prospectively collected data was conducted at the Cancer Hospital of the Chinese Academy of Medical Sciences, China National Cancer Center. Individuals who underwent pancreatic resection between January 2004 and December 2013 were identified and included in the study. Persons were classified as having a normal weight if their BMI was $< 24 \text{ kg/m}^2$ and overweight/obese if their BMI was $\geq 24 \text{ kg/m}^2$ as defined by the International Life Sciences Institute Focal Point in China. A χ^2 test (for categorical variables) or a t test (for continuous variables) was used to examine the differences in patients' characteristics between normal weight and overweight/obese groups. Multiple logistic regression models were used to assess the associations

of postoperative complications, operative difficulty, length of hospital stay, and cost with BMI, adjusting for age, sex, and type of surgery procedures.

RESULTS: A total of 362 consecutive patients with data available for BMI calculation underwent pancreatic resection for benign or malignant disease from January 1, 2004 to December 31, 2013. Of the 362 patients, 156 were overweight or obese and 206 were of normal weight. One or more postoperative complications occurred in 35.4% of the patients following pancreatic resection. Among patients who were overweight or obese, 42.9% experienced one or more complications, significantly higher than normal weight (29.6%) individuals ($P = 0.0086$). Compared with individuals who had normal weight, those with a BMI ≥ 24.0 kg/m² had higher delayed gastric emptying (19.9% vs 5.8%, $P < 0.0001$) and bile leak (7.7% vs 1.9%, $P = 0.0068$). There were no significant differences seen in pancreatic fistula, gastrointestinal hemorrhage, reoperation, readmission, or other complications. BMI did not show a significant association with intraoperative blood loss, operative time, length of hospital stay, or cost.

CONCLUSION: Higher BMI increases the risk for postoperative complications after pancreatectomy in the Chinese population. The findings require replication in future studies with larger sample sizes.

Key words: Body mass index; China; Pancreatectomy; Pancreatic cancer; Postoperative complications

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Core tip: The influence of body mass index on post-surgical complications after pancreatectomy remains controversial. Moreover, a majority of these studies were conducted in Western countries. This study was conducted to examine the associations between body mass index and complications after pancreatectomy in a cohort of Chinese patients.

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INTRODUCTION

Over the past 20 years, overweight and obesity rates have increased dramatically in China^[1-3]. The national survey showed that the prevalence of overweight and obesity in Chinese adults was 39.6% in 2009^[1]. Body mass index (BMI), an indirect measure of adiposity,

has been linked to an increased risk of chronic pancreatitis and pancreatic cancer^[4-8]. For both conditions, pancreatectomy is imperative.

The influence of BMI on post-surgical complications after pancreatectomy remains controversial. Several studies have reported a positive association between BMI and risk of postoperative complications^[9-15], including increased length of hospital stay^[9-12], blood loss^[13,14], and surgical site infection^[15]; whereas others found no association^[16-18]. Moreover, a majority of these studies were conducted in Western countries. Because body fat distribution, genetic predisposition to obesity, and background lifestyle factors are different between Caucasians and Asians^[19], it is possible that the associations between BMI and postoperative complications following pancreatectomy may differ by ethnic group. Thus, a retrospective study of Chinese patients was conducted to examine the associations between BMI and complications after pancreatectomy.

MATERIALS AND METHODS

Patient selection and data collection

Patients who underwent pancreatic resection at the Cancer Hospital of the Chinese Academy of Medical Sciences, China National Cancer Center between January 2004 and December 2013 were identified and included in the study. The prospective database tracks data on patient anthropometrics, demographics, clinical history, past medical history, smoking and alcohol consumption, occupational exposure, medical conditions and medication use, diet, family and social history, physical findings, diagnostic tests, therapeutic interventions, complications, pathologic data, and outcomes, including perioperative mortality and long-term survival. Adult height and weight measurements were used to calculate BMI. All data were backed up by source documents and the accuracy of the data entered into the database was periodically reviewed. All study procedures were approved by the Institutional Review Board at the Cancer Hospital of the Chinese Academy of Medical Sciences.

Outcome measures

Postoperative outcomes included occurrence of pancreatic fistula, delayed gastric emptying, gastrointestinal hemorrhage, reoperation, readmission, surgical site infection or other complications, mortality, operative time, intraoperative blood loss, and length of hospital stay. Pancreatic fistula was reported if it met the criteria for the International Study Group of Pancreatic Fistula grade B or C^[20]. Delayed gastric emptying was defined as the failure to maintain oral intake by postoperative day 14. Bile leak was defined as bilious drainage from peripancreatic, intraoperatively placed drains or radiographically proven fluid collection requiring percutaneous drainage and demonstrating elevated bilirubin levels. Gastrointestinal hemorrhage

was defined as any blood loss that could only be attributed to the gastrointestinal tract, including hematemesis, hematochezia, or melena requiring blood product transfusion or reoperation. Mortality was defined as death during the resection hospitalization or within 30 d of discharge after resection. Other complications were defined as any of the following: wound infection was defined as culture-positive purulent drainage from the postoperative wound and requiring open packing; cholangitis was defined as fever, leukocytosis, and culture-positive bilious drainage from operative or percutaneous drains; urinary tract infection was defined as culture-positive urine with urinalysis-proven pyuria and bacteriuria; pneumonia was defined as fever, leukocytosis, culture-positive sputum with polymorphonuclear leukocytes on Gram stain, and chest radiograph demonstrating focal infiltrates; central line infection was defined as culture-positive line segment from an erythematous or purulent insertion site; pulmonary embolus was defined as radiographically proven pulmonary perfusion abnormality in the setting of hypoxemia or respiratory distress and requiring anticoagulation therapy; deep venous thrombosis was defined as characteristic venous obstruction of an involved extremity as demonstrated on Doppler ultrasound; arrhythmia was defined as characteristic electrocardiographic abnormality with or without symptoms and requiring pharmacologic or electrical intervention; cerebrovascular accident was defined as characteristic neurologic findings on physical examination with radiographically proven lesion. Operative time and blood loss were retrieved from anesthesiology records. Length of stay was calculated from date of surgery until time of discharge or transfer from the acute care setting.

Statistical analysis

BMI was calculated as weight (kg) divided by the square of height (m), using self-reported values. Normal weight was defined as BMI < 24 kg/m² and overweight/obese was defined as BMI ≥ 24 kg/m² based on the definitions by the International Life Sciences Institute Focal Point in China^[21]. χ^2 tests (for categorical variables) or *t* tests (for continuous variables) were used to examine the differences in patients' characteristics between normal weight and overweight/obese groups.

Multiple logistic regression models were used to assess the associations of postoperative complications, operative difficulty, length of hospital stay, and cost with BMI, adjusting for age, sex, and type of surgery procedures. Additional adjustment for smoking, alcohol consumption, and family history did not result in material changes in the observed associations, and these variables were not included in the final models reported here. All tests were considered significant with

a two-sided $\alpha < 0.05$. All analyses were performed using SAS Software version 9.3 (SAS Institute Inc., Cary, NC, United States).

RESULTS

Demographics and comorbidities

A total of 362 patients who underwent pancreatic resection, performed by the authors (Zhao DB, Tian YT, and Wang CF) between January 2004 and December 2013, were identified and included in the study (Table 1). The procedures included pancreaticoduodenectomy (*n* = 195), distal pancreatectomy (*n* = 142), and middle-segment pancreatectomy (*n* = 25). Among these patients, 206 were normal weight, and 156 were overweight/obese. The mean BMI was 21.075 kg/m² for the normal weight group, and 26.993 kg/m² for the overweight/obese group. The mean patient age of the overweight/obese group was higher than the normal weight group (*P* = 0.0111). Comorbidity burden was greater in overweight/obese patients, as 68.6% had one or more comorbidities compared with 36.9% in the normal weight group (*P* < 0.0001). Compared with patients with normal weight, those with a BMI ≥ 24.0 kg/m² were more likely to have a family history of cancer (*P* < 0.0001). No significant differences in sex, smoking, alcohol consumption, or surgical procedures were observed between the two groups.

BMI and postoperative complications

One or more postoperative complications occurred in 35.4% of the patients following surgery (Table 2). Of overweight/obese patients, 42.9% suffered complications of any type, compared to only 29.6% of normal weight patients (*P* = 0.0086). Overweight/obese patients had a significantly higher delayed gastric emptying compared with normal weight patients (*P* < 0.0001). In addition, the presence of bile leak in overweight/obese patients was significantly higher than in the normal weight group (*P* = 0.0068). However, no significant differences were seen in pancreatic fistula, mortality, reoperation, readmission, gastrointestinal hemorrhage, or other complications.

BMI and operative variables/length of hospital stay

BMI did not show a significant association with intraoperative blood loss, or operative time (Table 3). Mean intraoperative blood loss varied from 450 mL to 520 mL depending on BMI, and mean operative time was 229 min in normal weight patients compared to 235 min in those who were overweight or obese. In addition, an increased mean length of hospital stay of 24.22 d was seen in patients with a BMI of 24 kg/m² or more compared to those with normal weight (21.85 d), but this was not statistically significant. There was no significant difference in the cost of hospitalization between the two groups.

Table 1 Demographic, comorbidity, and operation type in patients grouped according to body mass index

Variable	BMI < 24 kg/m ² (n = 206)	BMI ≥ 24 kg/m ² (n = 156)	Total (n = 362)	P value
Mean age (yr)	59.32	63.14	60.97	0.0111
Sex				
Male	95	84	179	
Female	111	72	183	
Male/female ratio	0.9	1.2	1.0	0.1452
Mean BMI (kg/m ²)	21.075	26.993	23.625	< 0.0001
Smoking				0.3641
Never	135	95	230	
Ever	71	61	132	
Smoking amount (packs/yr)	51	57	53	0.3166
Mean smoking time (yr)	23.25	26.94	25.00	0.3558
Alcohol, n				0.6835
Never	166	123	289	
Ever	40	33	73	
Comorbidity, n				
Any comorbidity	76	107	183	< 0.0001
Diabetes	38	43	81	0.0610
Coronary artery disease	9	40	49	< 0.0001
Hypertension	43	41	84	0.8930
COPD	6	6	12	0.6232
HBV	12	5	17	0.2198
HCV	5	2	7	0.4201
Previous history of cancer, n	1	2	3	0.4253
Previous abdominal surgery, n	21	16	37	0.9514
Family history of cancer, n	11	38	49	< 0.0001
Operation type, n				
Pancreaticoduodenectomy	116	79	195	0.2839
Distal pancreatectomy	75	67	142	0.2069
Middle-segment pancreatectomy	15	10	25	0.7461

COPD: Chronic obstructive pulmonary disease; HBV: Hepatitis B virus; HCV: Hepatitis C virus; BMI: Body mass index.

Table 2 Postoperative complications in patients grouped according to body mass index n (%)

Complication	BMI < 24 kg/m ² (n = 206)	BMI ≥ 24 kg/m ² (n = 156)	Total (n = 362)	OR	95%CI	P value
Patients with any complication	61 (29.6)	67 (42.9)	128 (35.4)	1.128	1.087-1.376	0.0086
Pancreatic fistula	34 (16.5)	30 (19.2)	64 (17.7)	0.825	0.430-1.582	0.4340
Delayed gastric emptying	12 (5.8)	31 (19.9)	43 (11.9)	1.279	1.072-1.487	< 0.0001
Bile leak	4 (1.9)	12 (7.7)	16 (4.4)	1.332	1.193-1.725	0.0068
Reoperation	4 (1.9)	2 (1.3)	6 (1.7)	1.513	0.267-8.570	0.6627
Readmission	1 (0.5)	1 (0.6)	2 (0.6)	0.382	0.291-0.532	0.3897
Gastrointestinal hemorrhage	6 (2.9)	4 (2.6)	10 (2.8)	1.271	0.344-4.697	0.8782
Wound infection	8 (3.9)	8 (5.1)	16 (4.4)	0.513	0.193-1.367	0.2229
Cholangitis	3 (1.5)	2 (1.3)	5 (1.4)	1.162	0.253-3.921	0.8881
Urinary tract infection	8 (3.9)	10 (6.4)	18 (5.0)	0.469	0.212-1.219	0.2229
Pneumonia	2 (1.0)	3 (1.9)	5 (1.4)	1.143	0.893-2.134	0.4421
Intra-abdominal abscess	6 (2.9)	3 (1.9)	9 (2.5)	0.450	0.112-5.321	0.5493
Bacteremia	3 (1.5)	6 (3.8)	9 (2.5)	0.631	0.461-5.235	0.1481
Central line infection	7 (3.4)	6 (3.8)	13 (3.6)	0.778	0.353-2.341	0.8205
Pulmonary embolus	0 (0.0)	0 (0.0)	0 (0.0)	NA	NA	NA
Deep venous thrombosis	1 (0.5)	1 (0.6)	2 (0.6)	0.124	0.064-7.320	0.8432
Arrhythmia	7 (3.4)	7 (4.5)	14 (3.9)	0.491	0.212-1.625	0.5467
Cerebrovascular accident	1 (0.5)	0 (0.0)	1 (0.3)	NA	NA	0.3919
Mortality	3 (1.5)	2 (1.3)	5 (1.4)	1.259	0.203-7.815	0.9288

NA: Not applicable; BMI: Body mass index.

DISCUSSION

Pancreatectomy is recognized as a highly invasive surgery. Despite recent advances in surgical technique, devices, and perioperative care, pancreatectomy

is associated with a mortality of approximately 5% and a morbidity of 35%-60%^[22-24]. Several studies suggested that the mortality after pancreatic surgery in most high-volume centers should be < 3%^[25-27]. The present study was performed in a tertiary care

Table 3 Association between operative difficulty, length of hospital stay, and cost with body mass index

Variable	BMI < 24 kg/m ² (<i>n</i> = 206)	BMI ≥ 24 kg/m ² (<i>n</i> = 156)	Total (<i>n</i> = 362)	OR	95%CI	<i>P</i> value
Mean operative time (min)	229.59	235.03	231.91	0.942	0.651-1.362	0.6050
Mean intraoperative blood loss (mL)	450	520.41	481.16	0.926	0.617-1.389	0.4433
Blood transfusion, <i>n</i>	103	79	182	0.703	0.413-1.197	0.9311
Mean hospital stay (d)	21.85	24.22	22.87	0.968	0.670-1.398	0.1167
Mean cost (in RMB)	78519.62	76160.05	77527.28	1.493	0.760-2.931	0.8532

RMB: Renminbi.

and academic institution having the aforementioned prerequisites and resulted in a mortality rate (1.4%) that was in accordance with experienced centers. During the past six years, the annual caseload has increased to more than 40 resections, which might be partially responsible for the improved outcome. Moreover, operative time and blood administration were comparable to other series because of the high volume. Our study is consistent with others that have found comparable mortality in the control and overweight/obese group^[16-18]. Analysis of the cause of mortality in our study revealed that pancreatic fistula with subsequent hemorrhage was responsible for 100% (5/5) of the deaths.

Several studies have consistently reported a greater risk for postoperative complications in the obese population as compared to lean subjects^[9-15]. However, many recent reports seem to challenge this long-held opinion^[16-18]. Morbidity after pancreatectomy in the present study was 35.4%, and the most frequent causes for morbidity were pancreatic fistulas resulting from pancreatic anastomotic insufficiency, bile leak resulting from biliary anastomotic insufficiency, surgical site infection, and delayed gastric emptying. Among patients who were overweight or obese, 42.9% experienced one or more complications, and this is significantly higher than normal weight individuals (29.6%). The results of the present study add to the growing debate over whether BMI increases complications after pancreatectomy.

Sledzianowski *et al.*^[28] identified obesity as an additional risk factor for leakage after distal pancreatectomy, and the study by Noun *et al.*^[12] highlights the increased risk after pancreaticoduodenectomy. The results of the present study are consistent with these studies that found higher bile leakage in the overweight/obese group. Pancreatic fistula is the factor most strongly linked with death in the majority of case series and remains the leading cause of morbidity after pancreatectomy. Noun *et al.*^[12] reported a significant association between BMI and pancreatic fistula after pancreatectomy. In this study, however, BMI did not show a significant association with pancreatic fistula. One potential explanation for this conflicting result is that there were only 92 cases included in their study.

In this study, an increased risk of delayed gastric

emptying was observed in the overweight/obese group. In contrast, two earlier studies from American medical centers suggested that BMI was not significantly associated with delayed gastric emptying after pancreaticoduodenectomy^[29,30]. One potential explanation for these conflicting results is that the association between BMI and delayed gastric emptying following pancreatectomy may differ by ethnic group. Additionally, the study by Sfarti *et al.*^[31] revealed that higher BMI correlated with delayed gastric emptying in type 1 diabetic patients, which might responsible for the phenomenon.

The influence of obesity on the operative difficulty of several abdominal procedures has previously been reported and has translated into increased blood loss and longer operating times than in normal-weight individuals^[32,33]. In the present study, however, intraoperative difficulty was not significantly altered by intraoperative variables (blood transfusion, blood loss, and operative time) in the overweight/obese group. No one can ignore the fact that performing pancreatectomy in obese patients is more challenging and hazardous. There was no significant difference in the length of hospital stay between the two groups, which is consistent with many other studies^[16,18].

There are several limitations of the current study. The retrospective nature of this study can be associated with selection bias as well as increased risk of differential misclassification bias. In addition, all patients were analyzed from a single institution, so the findings may not be generalizable to other settings. The limited sample size makes it difficult to adequately adjust for all potential confounding factors. There was an insufficient number of patients to perform subcategory analysis by BMI. Additionally, the relatively small sample size made it impossible to evaluate anything other than the overall complication rate on multivariable analyses. Although the majority of patients were tracked in a prospective database, a proportion required retrospective chart analysis.

In conclusion, the data show that pancreatectomy can be performed safely in overweight/obese patients, although with somewhat higher postoperative complications, bile leak, and delayed gastric emptying rate. However, the positive results in this study need to be replicated in studies with larger sample sizes with

greater power.

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COMMENTS

Background

The impact of body mass index (BMI) on complications following pancreatectomy remains controversial, and most pivotal studies have been conducted in Western countries. For the Chinese population, however, the results are scarce.

Research frontiers

The aim of this study was to examine the impact of BMI on outcomes following pancreatic resection in a Chinese population.

Innovations and breakthroughs

Higher BMI increases the risk for postoperative complications after pancreatectomy in the Chinese population.

Applications

The data from this study show that pancreatectomy can be performed safely in overweight/obese patients, although with somewhat higher postoperative complications, bile leak, and delayed gastric emptying rate.

Terminology

BMI is an indirect measure of adiposity, calculated as weight (kg) divided by the square of height (m).

Peer-review

This is an interesting study regarding the impact of BMI on complications following pancreatectomy. In this study, the authors examined the impact of BMI on outcomes following pancreatic resection in a Chinese population.

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