ORIGINAL ARTICLE

The Impact of Obesity on Surgical Outcome after Pancreaticoduodenectomy

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ABSTRACT

Context The effect of obesity on surgical outcome is becoming an increasingly relevant issue given the growing rate of obesity worldwide.

Objective To investigate the specific impact of obesity on pancreaticoduodenectomy.

Design A retrospective comparative study of a prospectively maintained database was carried out to investigate the specific impact of obesity on the technical aspects and postoperative outcome of pancreaticoduodenectomy.

Patients Between 1999 and 2006, 92 consecutive patients underwent pancreaticoduodenectomy using a standardized technique. The study population was subdivided according to the presence or absence of obesity.

Results Nineteen (20.7%) patients were obese and 73 (79.3%) patients were non-obese. The two groups were comparable in terms of demographics, American Society of Anesthesiology (ASA) score as well as nature and type of pancreatico-digestive anastomosis. The rate of clinically relevant pancreatic fistula (36.8% *vs*. 15.1%; P=0.050) and hospital stay (23.1±13.9 *vs*. 17.0±8.0 days; P=0.015) were significantly increased in obese *vs*. non-obese patients, respectively. Pancreatic fistula was responsible for one-half of the deaths (2/4) and two ruptured pseudoaneurysms. The incidence of the other procedure-related and general postoperative complications were not significantly different between the two groups. Intrapancreatic fat was increased in 10 obese patients (52.6%) and correlated positively both with BMI (P=0.001) and with the occurrence of pancreatic fistula (P=0.003).

Conclusion Obese patients are at increased risk for developing pancreatic fistula after pancreaticoduodenectomy. Special surgical caution as well as vigilant postoperative monitoring are therefore recommended in obese patients.

INTRODUCTION

Obesity, whose incidence is growing at epidemic rates in the general population, has been considered a risk factor for surgical outcomes of patients undergoing abdominal surgery [1, 2, 3]. The presence of excessive fat tissue inside and outside the viscera has often increased operative times and blood losses while impairing surgical quality. Also, many authors have consistently reported a greater risk for leakage and postoperative complications in the obese population as compared to lean subjects [2, 3, 4, 5]. However, recent reports seem to challenge this long-held opinion [6, 7].

Pancreaticoduodenectomy (PD) is still considered a complex high-risk surgical procedure. Although its operative mortality is

now decreased to less than 5% in high-volume institutions, its morbidity rates remain unchanged, ranging from 23 to more than 40% [8, 9]. A leading cause of this morbidity is represented by disruption of the pancreatic anastomosis, with subsequent pancreatic fistula, sepsis and hemorrhage [10, 11]. A substantial risk factor for pancreatic fistula after PD is the status of the pancreatic remnant. It has been verified that a soft pancreatic remnant without ductal dilatation is associated with a high risk of leakage [12, 13].

Performing PD in the obese patient is more challenging and hazardous. The presence of obesity impairs the surgical procedure as a result of massive fat deposition inside and outside the pancreas.

The purpose of the present study was to compare the results of PD in obese and non-obese patients and to investigate the specific impact of obesity on the technical aspects and postoperative outcome of this procedure.

PATIENTS AND METHODS

Between 1999 and 2006, among 116 consecutive patients who had had pancreaticoduodenal resection in the Department of Digestive Surgery at Hôtel-Dieu de France, 92 were included in the present study. Patients who underwent total pancreatectomy and patients who underwent PD for chronic pancreatitis were excluded. All procedures were carried out by the senior author (RN). A retrospective review of a prospectively maintained database was performed. The study population was divided into two groups ("Obese" and "Non-Obese") according to the presence or the absence of a body mass index (BMI) value equal to or higher than 30 kg/m^2.

Conventional PD was performed in all patients [14]. A pancreaticojejunostomy or pancreaticogastrostomy were performed end-to-side using a single layer of Prolene$^®$ 5/0 either with the pancreatic stump cut surface (stump anastomosis) in patients with a small duct (less than 3 mm) or included the pancreatic ductal wall (ductal anastomosis) in patients with a dilated duct. Pancreatic duct

stent and fibrin glue were not used. Hepaticojejunal anastomosis was performed end-to-side without stenting followed by a standard end-to-side gastrojejunostomy. In all patients, a silicone rubber closed-suction drain was placed in front of and behind the pancreatic anastomosis and the abdomen was closed with continuous sutures. Vagotomy, tubal gastrostomy or feeding jejunostomy were not performed on any patient. The majority of patients received erythromycin lactobionate as a prophylaxis for delayed gastric emptying and octreotide prophylaxis as a prophylaxis for pancreatic fistula.

After surgery, the patients were monitored in the intensive care unit and were returned to the wards at the discretion of the intensivist. Abdominal drainage fluids were stented for amylase and lipase levels when a pancreatic fistula was suspected. A routine abdominal CT scan was carried out at day 7 or on any patient with a suspected infected collection. All fluid collections were drained percutaneously with amylase dosage and bacteriologic cultures.

The main endpoints assessed were in-hospital mortality and morbidity rates, intraoperative data, incidence, nature and number of postoperative complications, and the length of hospital stay. Pancreatic fistula was defined as any measurable drainage (from an operatively placed drain or a subsequently placed percutaneous drain) having an amylase content greater than 3 times the upper limit of the reference serum amylase level requiring specific management (grade B and C fistulas according to the International Study Group on pancreatic fistula [15]). Surgical pathology specimens from the pancreatic neck of the obese group were studied further for the amount of intrapancreatic fat, and were graded from absent to massive on a 4-point pancreatic fat scale: 0-absent, 1-normal, 2-high, 3-massive.

ETHICS

The study was approved by the Ethics and Research Committee of the Hôtel-Dieu de France Hospital, Beirut, Lebanon. Oral informed consent was obtained from each

Table 1. Demographic and clinical characteristics.

	Obese (No. 19)	Non-Obese (No. 73)	P value
Age, years: mean±SD (range)	61.7±13.0 (36-76)	63.2±12.5 (23-82)	0.657
Gender:			0.602
- Male	13 (68.4%)	44 (60.3%)	
- Female	6 (31.6%)	29 (39.7%)	
ASA score:			0.799
- I	9 (47.4%)	38 (52.1%)	
- II or more	10 (52.6%)	35 (47.9%)	
BMI, kg/m^2: mean±SD (range)	31.8±2.2 (30-38)	24.2±2.6 (17-28)	<0.001

patient and the study protocol conforms to the ethical guidelines of the Declaration of Helsinki.

STATISTICS

All data and statistical procedures were carried out using the SPSS version 14.0 for Windows statistical package (SPSS Inc., Chicago, IL, USA). Results are reported as mean±SD and range or as frequencies, as appropriate. Statistical analysis was conducted by using the Fisher's exact and the linear-by-linear association tests for qualitative variables, the ANOVA for the comparison of means, and the Spearman rank for testing correlations. Two-tailed P values less than 0.05 were considered to be significant.

RESULTS

Population Characteristics

The study population included 92 patients with a mean age of 62.9±12.5 years (range:

23-82 years). There were 57 (62.0%) men and 35 (38.0%) women. Forty-seven (51%) patients were classified as American Society of Anesthesiology (ASA) score I. The Obese Group included 19 (20.7%) patients and the Non-Obese Group included 73 (79.3%) patients. The BMI was 31.8±2.2 kg/m^2 (range: 30-38 kg/m^2) *vs.* 24.2±2.6 kg/m^2 (range: 17-28 kg/m^2) in the Obese and Non-Obese groups, respectively (P<0.001). As shown in Table 1, the two groups were comparable in terms of demographics and ASA score.

Intraoperative Course

Pancreatico-gastrostomy was performed in 53 (57.6%) patients and pancreatico-jejunostomy in 39 (42.4%) patients. A pancreatico-digestive anastomosis was performed with the pancreatic stump cut surface in 71 (77.2%) and included the pancreatic ductal wall in 21 (22.8%). The intraoperative parameters of the two groups are listed in Table 2. The two groups were comparable according to the

Table 2. Intraoperative parameters.

	Obese (No. 19)	Non-Obese (No. 73)	P value
Nature of anastomosis:			0.312
- Pancreatico-gastrostomy	13 (68.4%)	40 (54.8%)	
- Pancreatico-jejunostomy	6 (31.6%)	33 (45.2%)	
Type of anastomosis:			0.761
- Ductal	5 (26.3%)	16 (21.9%)	
- Stump	14 (73.7%)	57 (78.1%)	
Transfusion	7 (36.8%)	25 (34.2%)	1.000
Units of transfusion: mean±SD (range)	1.47±1.47 (1-4)	1.20±1.38 (1-7)	0.459
Vein resection	1 (5.3%)	6 (8.2%)	1.000
Operative time, hours: mean±SD (range)	6.7±1.0 (5.0-7.5)	6.4±0.9 (4.5-7.5)	0.280

Table 3. Postoperative factors and complications.

	Obese (No. 19)	Non-Obese (No. 73)	P value
Pancreatic fistula: grade B or greater	7 (36.8%)	11 (15.1%)	0.050
Delayed gastric emptying	2 (10.5%)	13 (17.8%)	0.728
Intra-abdominal abscess	2 (10.5%)	6 (8.2%)	0.667
Wound infection	3 (15.8%)	8 (11.0%)	0.691
Hemorrhage	2 (10.5%)	5 (6.8%)	0.631
Pneumonia	1 (5.3%)	5 (6.8%)	1.000
Re-operation	1 (5.3%)	2 (2.7%)	0.505
Morbidity	7 (36.8%)	26 (35.6%)	1.000
Mortality	2 (10.5%)	2 (2.7%)	0.188
Postoperative hospital stay, days: mean±SD (range)	23.1±13.9 (9-67)	17.0±8.0 (6-61)	0.015

nature and type of pancreatico-digestive anastomosis. Sixty patients (65.2%) did not require a blood transfusion during surgery while the remaining 32 (34.8%) received blood transfusions with a mean of 1.26±1.38 units of red blood cells. Seven (7.6%) patients underwent resection of portions of either the portal vein or the superior mesenteric vein. Although the operating time was longer in the Obese Group (6.7±1.0 h) than in the Non-Obese Group (6.4±0.9 h), the difference did not reach the statistical significance (P=0.280).

Postoperative Course

There were 4 postoperative deaths, 2 in each group for an in-hospital mortality rate of 4.3%. The cause of death was sepsis in the setting of pancreatic fistula in two patients of the Obese Group, a myocardial infarction and a death resulting from a catastrophic scenario following percutaneous biliary drainage in the Non-Obese Group.

Thirty three (35.9%) patients developed a postoperative complication (Table 3). The overall rate of clinically relevant pancreatic fistula was 36.8% in the Obese Group and 15.1% in the Non-Obese Group (P=0.050). Analysis of the incidence of pancreatic fistula revealed that it was not significantly influenced by the nature (pancreatico-gastrostomy *vs.* pancreaticojejunostomy) and the type (ductal *vs.* stump) of pancreatic anastomosis in all patients and within each of the two groups (Table 4). The incidence of the other postoperative complications was not significantly different between the two groups (Table 3). Seven (7.6%) patients presented postoperative hemorrhage (2 in the Obese group and 5 in the Non-Obese group). Three were re-operated on, including hemostasis of a bleeding artery of the pancreatic capsule in one obese patient, and completion pancreatectomy in two non-obese patients (one for early pancreatic anastomotic bleeding and one for a bleeding pseudoaneurysm of the

Table 4. Frequency of pancreatic fistula according to the nature and type of pancreatic anastomosis.

	All patients (No. 92)	Obese (No. 19)	Non-Obese (No. 73)	P value
Nature of anastomosis:				
- Pancreatico-gastric	12/53 (22.6%)	5/13 (38.5%)	7/40 (17.5%)	0.140
- Pancreatico-jejunal	6/39 (15.4%)	2/6 (33.3%)	4/33 (12.1%)	0.224
	P=0.436	P=1.000	P=0.744	
Type of anastomosis:				
- Ductal	2/21 (9.5%)	1/5 (20.0%)	1/16 (6.3%)	0.429
- Stump	16/71 (22.5%)	6/14 (42.9%)	10/57 (17.5%)	0.070
	P=0.228	P=0.603	P=0.437	
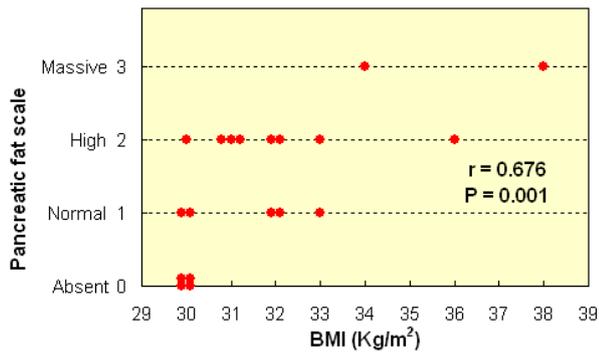
Figure 1. Correlation between BMI and intrapancreatic fat graded from absent to massive on a four-point scale (Spearman rank correlation test).

gastroduodenal arterial stump in the setting of pancreatic fistula). Two patients necessitated embolization of the hepatic artery, the first (obese) for a bleeding pseudoaneurysm of the gastroduodenal arterial stump in the setting of pancreatic fistula which resulted in biliary ischemia, and the second (non-obese), who is included in the 4 in-hospital deaths, for uncontrollable hemobilia from a percutaneous transhepatic biliary drain which resulted in acute liver necrosis and death. The remaining 2 non-obese patients responded to conservative management. All the re-operations were performed for bleeding. The mean length of hospital stay was significantly longer (P=0.015) in the Obese Group (23.1±13.9 days; range: 9-67 days) as compared with the Non-Obese Group (17.0±8.0 days; range: 6-61 days).

The final pathologic diagnoses of the resected specimens revealed periampullary adenocarcinoma in 13 (68.4%) patients of the Obese Group and in 52 (71.2%) patients of the Non-Obese Group (P=0.785). Surgical pathology specimens from the pancreatic neck of the Obese group showed that the amount of intrapancreatic fat was increased in 10 patients (52.6%; pancreatic fat scale equal to 2 or 3) and correlated positively both with BMI (P=0.001; Figure 1) and with the occurrence of pancreatic fistula (P=0.003; Figure 2).

DISCUSSION

Johns Hopkins Hospital, as well as other high-volume centers worldwide, have reported a substantial decrease in hospital mortality for PD, about 5% or lower [8, 9, 16, 17]. In addition to careful patient selection, improved surgical technique and improvements in perioperative care, the high-volume of PD made have contributed to this drop. The current series was performed in a tertiary care and academic institution having the aforementioned prerequisites and resulted in an operative mortality rate which is in accordance with experienced centers. During the last 5 years, the annual caseload has increased to more than 15 resections which might have contributed in part to the improved outcome. Furthermore, because of the high volume, intraoperative mishaps were not encountered, and operative time and blood administration were comparable to other series.

Despite a substantial drop in mortality after PD, the morbidity rates remained unchanged ranging from 23 to more than 40% and were led by the occurrence of a pancreatic fistula [8, 9, 16, 17, 18, 19]. It has repeatedly been demonstrated that both soft pancreatic remnant texture and small duct size are major risk factors for pancreatic fistula [12, 13]. Although, obesity was recently identified as an additional risk factor for leakage after distal pancreatectomy, the current study highlights the increased risk after PD [20]. Our results demonstrated that the presence of obesity more than doubled the risk of
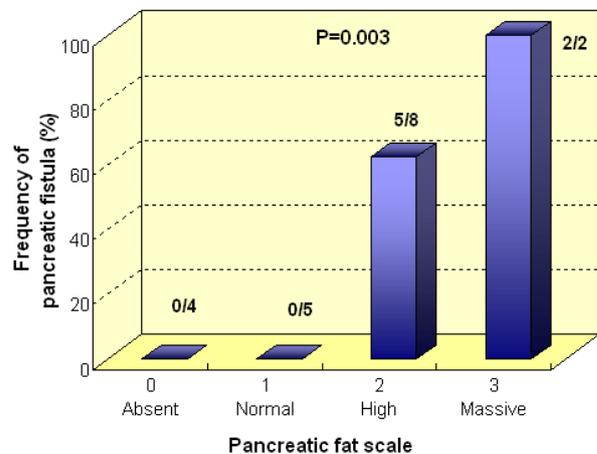

Figure 2. Correlation between the occurrence of pancreatic fistula and intrapancreatic fat graded from absent to massive on a four-point scale (linear-by-linear association test).

pancreatic fistula after PD despite a standardized technique which was performed by the same surgeon.

Obesity seems to affect both the texture of the pancreatic remnant and the quality of pancreatic anastomosis construction. It is well known that, in almost every individual, there is a variable amount of intrapancreatic fat which varies from 3 to 20%, according to the nutritional state [21]. Our results demonstrated that the amount of intrapancreatic fat was increased in 50% of our obese patients and that this increase correlated positively with BMI. As illustrated in Figure 3, fat infiltration of the pancreatic remnant makes it prone to laceration during suturing or tying. In addition, the presence of a bulky pancreatic remnant with obscure demarcation in a deep operating field would affect technical precision in anastomosis construction which are essential factors for the prevention of pancreatic fistula.

The impact of obesity on the technical difficulty of many abdominal procedures has previously been reported and has translated into longer operating times and increased blood losses than in lean subjects [5, 22]. In this study, we have noted that, in the obese patients, some stages of the procedure were more laborious, particularly transection of the mesentery of the first jejunal loop, complete excision of the retroportal pancreatic process as well as complete dissection of the right side of the superior mesenteric artery and of
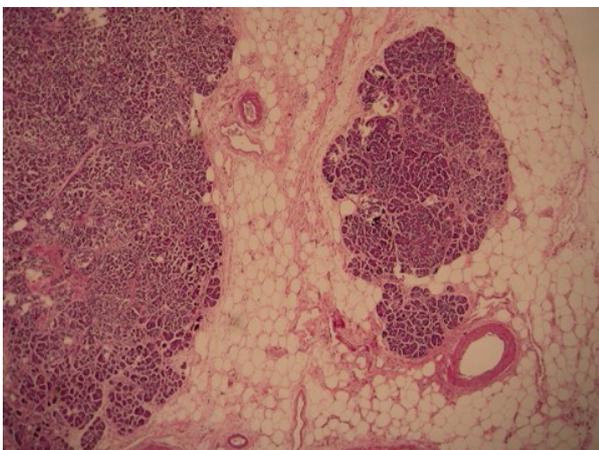
Figure 3. Typical histological specimen of the pancreatic neck cut surface showing massive intrapancreatic fat deposition (H&E, x4).

the portal vein. However, intraoperative difficulty has not significantly altered intraoperative parameters (blood transfusions and operating time) in the obese group. This is probably related to the fact that except for one mesentericoportal venous reconstruction, all were performed in the non-obese group. No one can ignore the fact that blood transfusions and operating time are increased in patients undergoing PD with venous reconstruction [23, 24].

Pancreatic fistula is the factor most strongly linked with death in the majority of case series and remains the leading cause of morbidity after PD [9, 25]. Analysis of the cause of mortality in the current series revealed that pancreatic fistula was responsible of one-half (2/4) of the deaths. In addition, pancreatic fistula resulted in two life-threatening bleeding pseudoaneurysms which are known to result from sepsis in the pancreatic bed [26, 27, 28]. According to our results, the pancreatic surgeon, while performing PD in an obese patient, must be prepared for an increased risk of anastomotic leak and for subsequent, often lethal, hemorrhage. Like others, we advocate trying to avoid vascular injuries during lymphadenectomy, meticulous anastomosis, wrapping of the dissected vessels and adequate abdominal drainage [27]. We also anticipate the problems related to interrupting the hepatic arterial flow after PD where its consequences may be disastrous as we observed in two of our patients [28, 29]. We therefore recommend a gastroduodenal arterial stump of at least 1 cm in length in order to enable safe microcoil embolization in the case of bleeding from the arterial stump. Postoperatively, percutaneous placement of a covered stent in the hepatic artery can arrest pseudoaneurysm bleeding while preserving common hepatic artery patency [30, 31].

The effects of obesity on surgical outcome after major abdominal surgery are becoming an increasingly relevant issue given the growing rate of obesity worldwide. In the current series, 19 out of 92 patients (21%) undergoing PD were obese (i.e., a BMI equal to or greater than 30 kg/m^2). Obesity is known

to affect surgical outcome through both procedure-related and general complications. In the present study, in addition to the increased risk of pancreatic fistula which lengthened the hospital stay in obese patients, one unexpected result was the same trend for general complications when compared to non-obese patients. Because the majority of obese patients were mildly obese (17 out of 19 patients had a BMI ranging from 30.0 to 34.9 kg/m^2), associated comorbidity conditions such as cardiovascular disease, pulmonary dysfunction and diabetes were infrequent as reflected by the comparable ASA scores. Like others, we believe that obesity alone is not a risk factor for postoperative general complications [7, 32]. Rather, their likelihood seems more related to ASA score. In addition, we believe that mild obesity without associated comorbidities is relatively protective for patients undergoing PD for malignancy owing to relatively preserved nutritional and immunological status.

CONCLUSION

The current single-institution retrospective study showed that obese patients are at increased risk for developing pancreatic fistula after PD. Special surgical caution as well as vigilant postoperative monitoring are therefore recommended when performing PD in obese patients.

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