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Impact of Obesity on Perioperative Morbidity and Mortality Following Pancreaticoduodenectomy

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ABSTRACT

Background**:** Obesity has been implicated as a risk factor for perioperative and postoperative complications. The aim of this study was determine the impact of obesity on morbidity and mortality in patients undergoing pancreaticoduodenectomy (PD).

Study Design: Between January 2000 and July 2007, 262 patients underwent PD at Thomas Jefferson University Hospital (TJUH), of whom 240 had complete data, including body mass index (BMI) for analysis. Data on BMI, preoperative parameters, operative details, and post-operative course were collected. Patients were categorized as obese (BMI $\geq$30 kg/m2), overweight (25$\leq$BMI<30), or normal weight (BMI<25). Complications were graded according to previous published scales. Other endpoints included length of postoperative hospital stay, blood loss, and operative duration. Analyses were performed using univariate and multivariable models.

Results: There were 103 (42.9%) normal weight, 71 (29.6%) overweight and 66 (27.5%) obese patients. There were 5 perioperative deaths (2.1%) with no differences across BMI categories. A significant difference in median operative duration and blood loss between obese and normal weight patients was identified (439vs. 362.5minutes, p= 0.0004; 650 vs. 500 ml, p=0.0139). Furthermore, median length of stay was marginally significantly longer for by BMI (9.5 vs. 8 days, p=0.095). While there were no significant differences in superficial wound infections,

obese patients did have an increased rate of serious complications compared to normal weight patients (24.2% vs. 13.6%, respectively; p=0.10).

Conclusions: Obese patients undergoing PD have a significantly increased blood loss and longer operative time, but do not have a significantly increased length of postoperative hospital stay or rate of serious complications. These findings should be considered when assessing patients for operation and when counseling patients regarding operative risk, but do not preclude obese individuals from undergoing definitive pancreatic surgery.

INTRODUCTION

Pancreaticoduodenectomy is the surgical standard for several disease states. Although largely performed for periampullary malignancies, it is often performed for a variety of benign pathologies as well.[1] Despite advances in the technique of pancreaticoduodenectomy over the years, it remains a procedure that carries significant morbidity, even when performed at high volume centers.[2] Accordingly, numerous studies have been performed that evaluate preoperative risk factors for perioperative and postoperative morbidity and mortality in these patients. Advanced age, as well as certain co-morbid conditions (i.e. diabetes and coronary artery disease) and serologic factors (i.e. elevated blood urea nitrogen and low serum albumin) have been demonstrated to be independent risk factors for the incidence of postoperative complications following pancreaticoduodenectomy.[3-5] However, few studies to date have evaluated the impact of obesity on postoperative complications following pancreaticoduodenectomy.[2]

The National Institutes of Health (NIH) defines obesity as a body mass index (BMI) of ≥30 kg/m2. Normal weight individuals are considered to have a BMI of <25 kg/m2, while

overweight is defined as having a BMI ≥25 and <30 kg/m2. At epidemic proportions in our society today, obesity affects approximately 30 percent of adults in the USA. By the year 2015, that value is projected to reach 40 percent.[6] Obesity is linked to many illnesses such as diabetes, osteoarthritis, hypertension and others. It has also been shown to be a risk factor for the development of several malignancies, including pancreatic cancer.[7] Obesity has also been implicated as a risk factor for the development of postoperative complications following a variety of operations.[8-11] The purpose of this study is to evaluate the impact of obesity on the occurrence of perioperative and postoperative morbidity and mortality in patients undergoing pancreaticoduodenectomy at a high volume tertiary care hospital.

METHODS

Aim

This is a retrospective analysis of an Institutional Review Board approved prospectively maintained database for all patients undergoing pancreatic surgery at the Thomas Jefferson University Hospital (TJUH). All cases included in this study were resected at our institution between January 2000 and July 2007. During this time period, 262 pancreaticoduodenectomies were performed. Of these cases, 240 had data on BMI at the time of surgery and were selected for analysis. Twenty patients were excluded due to incomplete data collection, and two cases performed for penetrating abdominal trauma were also excluded from analysis.

Preoperative Data

The prospective database used in this study was populated from patient charts, an electronic medical record and anesthesia records. Demographic and preoperative clinical data utilized for this study included age, sex, height, weight, serum albumin level, the presence or

absence of a preoperative biliary stent, and the American Society of Anesthesiologists (ASA) score. Body mass index was calculated using the following formula: $BMI = weight(kg)/height(m)^2$. For this analysis, patients were divided into three groups based on BMI: normal weight (BMI <25), overweight ($25 \leq BMI < 30$), or obese (≥ 30). This BMI classification system is endorsed by the World Health Organization and the National Institutes of Health, and is the most widely accepted means of stratifying individuals based on weight.

Surgical Technique

A total of thirteen surgeons performed Whipple operations during this time period; however, the majority of cases (217) were performed by four surgeons. Surgical technique was based largely on surgeon preference. The two main techniques used were the pancreaticoduodenectomy (PD) with antrectomy (classic type), and the pylorus preserving pancreaticoduodenectomy (PPPD). Over this time period, there were a total of 129 (54%) pylorus preserving and 103 (43%) classic type PD. Eight patients (3%) underwent other types of pancreatic resections, mainly completion or total pancreatectomies. Over the study period, there was a transition from classic Whipple operations to pylorus-preserving PD. Furthermore, the volume of operations performed increased substantially over the last 2 years of the study period. Sixty-six patients were enrolled in a randomized clinical trial which began in July 2006 at TJUH and randomized patients to a duct-to-mucosa or invagination method of pancreaticojejunostomy (NCT00359320). Postoperative care was again by surgeon preference. However, in October 2005, we initiated a critical pathway for patients undergoing PD—the results of this have been described previously.[12] For this study, 76 patients were treated before the pathway and 164 were treated after its implementation.

Endpoints

Perioperative data collected for analysis included intraoperative blood loss, length of operation and specimen pathology. Postoperative clinical endpoints included length of postoperative hospital stay and complications. Postoperative complications were categorized based on a modified version of the surgical complication classification system of Clavien *et al* (Table 1).[13,14] This system has been established as a means of objectively classifying postoperative complications. Grade 1 and 2 complications were considered minor, whereas grades 3-5 were considered severe. While some patients did experience more than one complication, only the highest grade complication was included in the comparative analysis across BMI groups. Delayed gastric emptying (DGE) was determined by whether the patient had a nasogastric tube for more than 10 days after surgery, could not proceed to a regular diet within 10 days, and had vomiting for more than 3 consecutive days after the fifth postoperative day. Pancreatic fistula was defined using the definition of the International Study Group.

Statistical Analyses

Patients with normal weight preoperatively (BMI < 25) were defined as the control group for this analysis. BMI was categorized according to usual convention, <25, 25-29.9, and $\geq 30 k/m^2$. Complications were categorized according to severity, as 0, 1-2 and 3-5. A number of pre- and post- operative continuous variables had skewed, non-normal distributions. Comparisons between BMI categories for these variables were made using the Kruskal-Wallis test, and if significant, followed by pairwise Bonferroni-corrected Wilcoxon tests. Pre- peri- and post-operative categorical variables were analyzed using univariate logistic regression (for dichotomous variables) or proportional odds modeling (for polytomous variables). Post-hoc

Bonferroni-corrected pairwise Wald chi-square tests were completed if univariate results were significant. Pairwise test results for univariate analyses are reported in the text only.

The proportional odds model, a form of logistic regression that establishes separate starting points (intercepts) with single odds ratios estimated for each level of outcome across covariates, was used to build multivariable models of association with endpoints estimated blood loss (EBL), operative duration, and length of stay. EBL was categorized as <400, 400-600, 601-900, or >900ml for these analyses,, surgical duration was categorized according to quartiles observed in the population, namely ≤329 minutes, >329-399, >399-472, or >472 minutes, length of stay was categorized as ≤ 6, 7-9, 10-14, and 15 or more days, and ASA was categorized as 1-2 and 3-4. Each of these models initially included the following: sex, BMI, ASA, albumin, type of resection, age, and presence of complications. For each outcome, multivariable modeling proceeded in a backwards stepwise manner, retaining those effects where $p<0.05$. In the case of multi-level covariates, if an individual level of the covariate was significant at $p<0.05$, the variable was also retained.

RESULTS

Preoperative Variables

Of the 240 patients, 103 (42.9%) were normal weight, 71 (29.6%) were overweight, and 66 (27.5%) were obese. There were no significant differences between the BMI groups with regard to age, sex, ASA class, or preoperative albumin (Table 2). The American Society of Anesthesiologists (ASA) class was used as an indication of co-morbid illness for this study. For the subgroups based on BMI, 66% of normal weight, 60.9% of overweight and 72.3% of obese individuals were ASA class III. Most of the remaining patients were ASA class II (Table 2).

Although there was an increased number of ASA class III obese patients, this did not reach statistical significance. There was a statistically higher prevalence of preoperative biliary stents in the obese and overweight groups compared to normal weight group ($p = 0.0003$, and $P = 0.02$, respectively)

Pathology

All surgical specimens were analyzed by a pathologist skilled in evaluating pancreatic pathology. Most operations (74%) were performed for cancer and nearly half were for pancreatic cancer (n=117; 49%). Other malignant diagnoses included ampullary and duodenal adenocarcinomas, cholangiocarcinoma, duodenal GIST (n=2), neuroendocrine tumors, and metastatic lesions (n=2). The most common benign lesions for which PD was performed was intraductal papillary mucinous neoplasm (IPMN, n=23). Resections were also performed for mucinous or serous cystadenoma, autoimmune pancreatitis, and adenoma (Table 3).

Intraoperative Estimated Blood Loss

There were significant differences in blood loss in the 3 groups of patients. The median EBL for normal weight patients was 500 ml vs. 650 ml in both overweight and obese patients, respectively. On univariate analysis (Table 4), blood loss was globally associated with BMI ($p=0.02$). Using the Bonferroni-corrected alpha of 0.025, overweight values were marginally and obese values significantly increased compared to normal weight ($p=0.06$, $p=0.04$, respectively). By multivariable analysis, obesity proved to be an independent risk factor for increased intraoperative blood loss (OR 2.00, $p=0.02$), however being overweight did not quite reach statistical significance (OR=1.74, $p=0.05$). Interestingly, multivariable analysis identified male

sex as an independent risk factor for increased intraoperative blood loss (OR 3.88, p<0.0001) (Table 5).

Duration of Surgery

The lengths of the procedures were analyzed utilizing the BMI categories described above. Normal weight patients had the lowest median operative time (363 minutes). In comparison, overweight and obese patients had increased operative duration in the univariate model, with a medians of 413 and 439 minutes (Bonferroni-adjusted p = 0.0736 and p=0.0008, respectively) (Table 4). Again, the multivariable model supported obesity, but not overweight as a significant risk factor for increased surgery duration (OR=2.39, p=0.005) (Table 5). As was seen for intraoperative blood loss, male sex was identified as an independent risk factor for increased duration of surgery (OR=2.55, p=0.0002).

Length of Stay

Postoperative length of hospital stay was chosen as an endpoint, as it serves as a measure of resource utilization. In this analysis, normal weight individuals had a median postoperative length of stay of 8 days. Overweight individuals did not have a significantly different median LOS in comparison to normal weight patients (Table 4). Obese individuals did stay longer postoperatively compared with normal weight patients but this was not significant (9.5 days, p=0.06). Based on the multivariable analysis, obesity proved to be an independent risk factor for increased length of stay (OR=1.9, p=0.04) (Table 5). Also seen on the multivariable analysis is that the type of resection is an independent risk factor for the increased length of stay (OR = 15.2, p<0.001) (Table 5). This is partially reflected by a doubling of the occurrence of delayed gastric emptying (7% vs. 3%) in patients undergoing classic PD.

Postoperative Complications

A total of 120 (50%) patients experienced one or more complications postoperatively. There were 29 (12.1%) grade I, 50 (20.8%) grade II, 25 (10.4%) grade III, 11 (4.6%) grade IV and 5 (2.1%) grade V complications (Table 6). On univariate analysis, there was no significant difference in the complication rate by BMI, although the individual comparison between obese and normal individuals was marginally significant (56.3% vs. 42.7%, p = 0.08) (Table 4). The prevalence of serious complications (grades 3-5) across BMI groups was: normal weight (13.6%), overweight (15.5%), and obese (24.2%). On univariate analysis, this increase in serious complications between normal weight and obese patients was not statistically significant (p=0.13), neither was this trend statistically significant in the multivariable analysis. The mortality rates were similar across the groups. The complication rate was higher amongst patients undergoing classic PD compared to PPPD (54% vs. 49%); however, this was not statistically significant. Additionally, after October 2005, when the volume of PD significantly increased, the complication rate also decreased from 56% to 49%. Again this was not a significant change. It does partially reflect the change from predominantly classic PD and PPPD and the increase in volume at our institution as well as the implementation of a critical pathway.

In regards to specific complications, the risk of local wound infections was not statistically significantly different across BMI categories (6%, 4%, and 5%). Additionally, the occurrence of pancreatic fistula was similar in all BMI categories (4%, 6%, and 6%, respectively). There was no difference in pancreatic fistula rate in classic PD versus PPPD. However, there was a higher rate of intra-abdominal collections requiring either an interventional or open drainage procedure for obese patients, as compared to normal weight patients (7% vs. 14%, respectively, p=0.05).

DISCUSSION

Our series implicates obesity (defined as BMI $\geq$30) as an independent predictor for several perioperative and postoperative complications following pancreaticoduodenectomy (PD). These include increased operative blood loss, increased operative duration and increased length of postoperative hospital stay. Furthermore, obesity appears to be a risk factor for an increased overall complication rate. More specifically, it serves as a risk factor for intra-abdominal collections requiring a drainage procedure.

Intraoperative Blood Loss and Duration of Surgery

Our series demonstrates a significantly increased intraoperative blood loss in obese patients compared to normal weight individuals. While this finding has not been previously described in patients undergoing PD, it has been noted for a variety of other surgical procedures. In a recent series, increased blood loss was noted for obese patients undergoing open gastrectomy.[15] Other studies have reached similar conclusions in patients undergoing laparoscopic hysterectomy and transhiatal esophagectomy.[16,17] An increase in the occurrence of perioperative complications in patients with increased blood loss is supported by many studies in the literature. For example, in a study of over 500 laparoscopic nephrectomies, Turna *et al* demonstrated that increased blood loss was an independent and significant predictor of postoperative complications.[18] Additionally, other studies have also demonstrated increased complication rates in those undergoing spine surgeries when blood loss was greater.[19] Interestingly, in a study of 367 patients undergoing PD, House *et al* found that there was not a significant difference in blood loss for patients with BMI $\geq$ 30 kg/m2 compared to those with BMI <30 kg/m^2.

There is also a common association between perioperative blood transfusion and increased complications, with transfusion usually being a surrogate for increased blood loss in the operating room. The impact of blood transfusion on patients undergoing cardiac surgery has been clearly established as an independent risk factor for postoperative morbidity and mortality, as well as increased length of postoperative hospital stay and increased incidence of low-output heart failure.[20-22] In patients undergoing liver resection, perioperative blood transfusion is a prognostic factor for postoperative complications in general.[22] In a study of 100 patients undergoing hepatobiliary resections for cancer, the complication rate was 94% in those receiving transfusion vs. 52% for those who were not transfused.[23]

Additionally, we report a significantly longer operative duration for obese patients. While intuitive, this conclusion has not been described for patients undergoing PD. This finding has been reported for patients undergoing gynecologic, and general surgical/oncologic procedures however.[15,16,24] The clinical significance of this finding is less well studied, but in one study of 136 patients undergoing liver surgery, the complication rate was 10% for operations of 2 hours or less and 44% for operations greater than 3.5 hours.[22] In a study of abdominal wound dehiscence after laparotomy using the Veteran's Health Administration NSQIP database, Webster *et al* found that operative time greater than 2.5 hours was a significant contributing factor for dehiscence (albeit not nearly as important as many other factors).[25] Obviously patients undergoing PD will have operative times greater than two and a half hours, but increased operative time is associated with increased complications.

Length of Postoperative Hospital Stay

In this analysis, obese patients stayed in the hospital significantly longer than normal weight patients. This endpoint was not evaluated in a recent series by House *et al* examining preoperative predictors (including obesity) of postoperative complications in patients undergoing PD.[2] Several studies involving non-pancreatic surgery have evaluated this endpoint but failed to show that obesity correlates with increased length of stay.[15-17,24,26,27]

Although not deemed a postoperative complication directly, increased postoperative length of stay frequently reflects the occurrence of a postoperative complication, and may serve as a surrogate for postoperative morbidity. Our multivariable analysis shows that postoperative complications do correlate with increased length of stay. This conclusion was supported by the recent study of House *et al.*[2] Since our analysis did show an increased risk of serious complications in obese compared to normal weight patients, it seems intuitive that obese patients would have an increased length of stay. The fact that the above mentioned studies failed to show an increased length of stay in obese patients may therefore be explained by the fact that these studies did not show an increased rate of complications in obese patients.[15,16,24,26,27]

Previous work from our institution has demonstrated that the implementation of a critical pathway resulted in a decreased length of stay and a significant decrease in hospital costs.[12] In this study, the median length of stay decreased from 13 days to 7 days with a decrease in hospital charges by approximately $120,000.[12] Interestingly, when we re-examined the length of stay data for patients operated on after the initiation of the clinical pathway, the median length of stay was 6, 7, and 7 days respectively for normal weight, overweight, and obese patients. Therefore, it seems that when patients are maintained on a strict clinical pathway, large differences in postoperative length of stay may not be seen for obese and overweight patients.

Postoperative Complications

Despite refinements in surgical technique over the past several decades, pancreaticoduodenectomy remains a procedure with a high complication rate. When PD is performed at high volume centers mortality rates have dropped significantly over the years, but other complications such as pancreatic fistula still occur frequently.[1] Contemporary series' report overall complication rates ranging from 27 to 47 percent.[1,28] Interestingly, Grobmeyer *et al* recently reported a series, employing a complication grading system adapted from Clavien *et al* similar to that used in this analysis, with an overall complication rate of 47%.[14,28] This is consistent with the 50% overall complication rate from our series. Several studies have looked specifically at preoperative variables that may serve as risk factors for complications following pancreaticoduodenectomy. Preoperative serologic factors such as an albumin level < 3.5 and a BUN level > 18 have been implicated as risk factors for mortality following PD.[3] In our study, preoperative albumin levels were collected on all patients and utilized as an indicator of preoperative nutritional status. The mean preoperative albumin level was 4.21 for normal weight, 4.15 for overweight, and 4.19 for obese patients. There were no significant differences across these groups (Table 2). One observation we noted was that the incidence of preoperative biliary stents was higher in patients with increased BMI; however, our analysis showed that this did not impact on the occurrence of perioperative or postoperative complications.

With regard to specific complications, we found that the prevalence of postoperative local wound infections was not significantly different across all BMI groups . This is in contrast to the conclusions of a recent series of patients undergoing pancreaticoduodenectomy.[2] Several studies in the literature have also concluded that obesity is an independent risk factor for local wound infection for patients undergoing both cardiac and non-cardiac surgery.[8,10,11,29,30]

However, several other studies have failed to establish an increased incidence of wound infections in obese general surgical patients as seen in our series.[15,17,24] In our practice we insure that appropriate prophylactic antibiotics are administered at high dose within 1 hour of the skin incision, the wound edges are protected with moistened laparotomy sponges, and the antibiotics are redosed 4 hours into the operation. No postoperative antibiotics are administered for wound prophylaxis.

Our data did demonstrate an increased rate of intraabominal collections (either abscess or fistula) requiring a drainage procedure in obese patients compared to normal weight patients, 14% vs. 7%, respectively . This conclusion has been documented previously, in Japanese patients where patients with a BMI $\geq$ 27 had an increased risk of intra-abdominal infections after gastrectomy.[31]

CONCLUSION

PD remains the resectional procedure of choice for many patients with malignant and benign neoplasms of the pancreas and periampullary region. In most cases, this procedure is not an "elective" procedure, and efforts to lose weight prior to surgery may be impractical, unrealistic and unlikely to be successful. While obese patients may incur a modestly increased perioperative and postoperative risk compared to normal weight patients, this risk should not preclude patients from undergoing definitive surgery. In general, pancreaticoduodenectomy can be performed safely and with a low postoperative mortality rate on patients across all BMI categories.

REFERENCES

1. Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg. 1997;226:248-257; discussion 257-260.
2. House MG, Fong Y, Arnaoutakis DJ, et al. Preoperative Predictors for Complications after Pancreaticoduodenectomy: Impact of BMI and Body Fat Distribution. J Gastrointest Surg. 2008;12:270-278.
3. Winter JM, Cameron JL, Yeo CJ, et al. Biochemical markers predict morbidity and mortality after pancreaticoduodenectomy. J Am Coll Surg. 2007;204:1029-1036; discussion 1037-1028.
4. Muscari F, Suc B, Kirzin S, et al. Risk factors for mortality and intra-abdominal complications after pancreatoduodenectomy: multivariate analysis in 300 patients. Surgery. 2006;139:591-598.
5. Lin JW, Cameron JL, Yeo CJ, Riall TS, Lillemoe KD. Risk factors and outcomes in postpancreaticoduodenectomy pancreaticocutaneous fistula. J Gastrointest Surg. 2004;8:951-959.
6. Veerman JL, Barendregt JJ, van Beeck EF, Seidell JC, Mackenbach JP. Stemming the obesity epidemic: a tantalizing prospect. Obesity (Silver Spring). 2007;15:2365-2370.
7. Patel AV, Rodriguez C, Bernstein L, Chao A, Thun MJ, Calle EE. Obesity, recreational physical activity, and risk of pancreatic cancer in a large U.S. Cohort. Cancer Epidemiol Biomarkers Prev. 2005;14:459-466.
8. Villavicencio MA, Sundt TM, 3rd, Daly RC, et al. Cardiac surgery in patients with body mass index of 50 or greater. Ann Thorac Surg. 2007;83:1403-1411.

9. Benoist S, Panis Y, Alves A, Valleur P. Impact of obesity on surgical outcomes after colorectal resection. Am J Surg. 2000;179:275-281.

10. Thomas EJ, Goldman L, Mangione CM, et al. Body mass index as a correlate of postoperative complications and resource utilization. Am J Med. 1997;102:277-283.

11. Choban PS, Flancbaum L. The impact of obesity on surgical outcomes: a review. J Am Coll Surg. 1997;185:593-603.

12. Kennedy EP, Rosato EL, Sauter PK, et al. Initiation of a critical pathway for pancreaticoduodenectomy at an academic institution--the first step in multidisciplinary team building. J Am Coll Surg. 2007;204:917-923; discussion 923-914.

13. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205-213.

14. Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. Surgery. 1992;111:518-526.

15. Yamada H, Kojima K, Inokuchi M, Kawano T, Sugihara K. Effect of Obesity on Technical Feasibility and Postoperative Outcomes of Laparoscopy-Assisted Distal Gastrectomy-Comparison with Open Distal Gastrectomy. J Gastrointest Surg. 2007.

16. Heinberg EM, Crawford BL, 3rd, Weitzen SH, Bonilla DJ. Total laparoscopic hysterectomy in obese versus nonobese patients. Obstet Gynecol. 2004;103:674-680.

17. Scipione CN, Chang AC, Pickens A, Lau CL, Orringer MB. Transhiatal esophagectomy in the profoundly obese: implications and experience. Ann Thorac Surg. 2007;84:376-382; discussion 383.

18. Turna B, Frota R, Kamoi K, et al. Risk factor analysis of postoperative complications in laparoscopic partial nephrectomy. J Urol. 2008;179:1289-1294; discussion 1294-1285.

19. Guest JD, Vanni S, Silbert L. Mild hypothermia, blood loss and complications in elective spinal surgery. Spine J. 2004;4:130-137.

20. Surgenor SD, DeFoe GR, Fillinger MP, et al. Intraoperative red blood cell transfusion during coronary artery bypass graft surgery increases the risk of postoperative low-output heart failure. Circulation. 2006;114:I43-48.

21. Scott BH, Seifert FC, Grimson R. Blood transfusion is associated with increased resource utilisation, morbidity and mortality in cardiac surgery. Ann Card Anaesth. 2008;11:15-19.

22. Mutsaerts E, Zoetmulder F, Hart A, van Coevorden F. Perioperative morbidity in hepatic surgery. Hepatogastroenterology. 2007;54:458-462.

23. Nagino M, Kamiya J, Arai T, Nishio H, Ebata T, Nimura Y. One hundred consecutive hepatobiliary resections for biliary hilar malignancy: preoperative blood donation, blood loss, transfusion, and outcome. Surgery. 2005;137:148-155.

24. Hawn MT, Bian J, Leeth RR, et al. Impact of obesity on resource utilization for general surgical procedures. Ann Surg. 2005;241:821-826; discussion 826-828.

25. Webster C, Neumayer L, Smout R, et al. Prognostic models of abdominal wound dehiscence after laparotomy. J Surg Res. 2003;109:130-137.

26. Klasen J, Junger A, Hartmann B, et al. Increased body mass index and peri-operative risk in patients undergoing non-cardiac surgery. Obes Surg. 2004;14:275-281.

27. Kessler S, Kafer W. Overweight and obesity: two predictors for worse early outcome in total hip replacement? Obesity (Silver Spring). 2007;15:2840-2845.

28. Grobmyer SR, Pieracci FM, Allen PJ, Brennan MF, Jaques DP. Defining morbidity after pancreaticoduodenectomy: use of a prospective complication grading system. J Am Coll Surg. 2007;204:356-364.

29. Pessaux P, Msika S, Atalla D, Hay JM, Flamant Y. Risk factors for postoperative infectious complications in noncolorectal abdominal surgery: a multivariate analysis based on a prospective multicenter study of 4718 patients. Arch Surg. 2003;138:314-324.

30. Dindo D, Muller MK, Weber M, Clavien PA. Obesity in general elective surgery. Lancet. 2003;361:2032-2035.

31. Kodera Y, Ito S, Yamamura Y, et al. Obesity and outcome of distal gastrectomy with D2 lymphadenectomy for carcinoma. Hepatogastroenterology. 2004;51:1225-1228.

Tables

Table 1. Modified Classification of Surgical Complications*

Grade	Definition
Grade I	Any deviation from normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, or radiological intervention
	Allowed therapeutic regimens are: drugs such as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included here.
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IV	Life-threatening complication (including CNS complications) requiring ICU management
Grade V	Death of patient

* adapted from Classification of Surgical Complications published by Clavien *et al*[13,14]

Table 2. Preoperative Demographic Characteristics

	Total		BMI < 25		25 ≤ BMI < 30		BMI ≥ 30		p value
	n	(%)	n	(%)	n	(%)	n	(%)	
Number of Patients	240	(100.0)	103	(42.9)	71	(26.9)	66	(27.5)	--
Age (median, IQR)	66	(55.0, 73.0)	65	(54.0, 75.0)	66	(56.0, 76.0)	63.5	(53.0, 72.0)	0.45*
Sex									
Male	117	(48.8)	49	(47.6)	38	(53.5)	30	(45.5)	0.61⊥
Female	123	(51.3)	54	(52.4)	33	(46.5)	36	(54.5)	
Preoperative Biliary Stent	132	(55.0)	70	(67.3)	36	(50.7)	26	(39.4)	0.001⊥
ASA Class§									
I	2	(0.8)	1	(1.0)	0	(0.0)	1	(1.5)	0.31±
II	70	(29.5)	32	(31.1)	24	(34.8)	14	(21.5)	
III	157	(66.2)	68	(66.0)	42	(60.9)	47	(72.3)	
IV	8	(3.4)	2	(1.9)	3	(4.4)	3	(4.6)	
Preoperative Albumin (g/dL)(median, IQR)§§	4.3	(3.8, 4.6)	4.3	(3.8, 4.6)	4.3	(3.9, 4.6)	4.3	(3.9, 4.6)	0.96*

§25≤BMI<30, n = 69, BMI ≥ 30, n= 65; §§ BMI< 25, n= 99, 25≤BMI<30, n = 68, BMI ≥ 30, n= 60

⊥ p-value from univariate logistic regression

± p-value from univariate polymotous regression

* p-value from Kruskal-Wallis test

Table 3. Surgical Pathology

DIAGNOSIS	NUMBER (%)
Pancreatic adenocarcinoma	117 (49%)
Ampullary adenocarcinoma	34 (14%)
IPMN	23 (10%)
Neuroendocrine	11 (5%)
Cystadenoma	10 (4%)
Pancreatitis (chronic or autoimmune)	10 (4%)
Duodenal adenocarcinoma	9 (4%)
Cholangiocarcinoma	6 (3%)
Dysplasia/PANIN/ lesions	5 (2%)
Adenoma	5 (%)
Other Malignant	6 (%)
Other Benign	4 (%)

Table 4. Perioperative and Postoperative Endpoints

	BMI < 25		**25 ≤ BMI < 30**		**BMI ≥ 30**		**p value**
	n	**(%)**	**N**	**(%)**	**n**	**(%)**	
Cancer	83	(80.6)	51	(71.8)	44	(66.7)	0.12$^{\perp}$
Estimated Blood Loss (median, IQR)	500	(350.0, 800.0)	650	(450.0, 1000.0)	650	(450.0, 1100.0)	0.02*
Surgery Duration§ (median, IQR)	363	(320.0, 424.0)	413	(324.0, 482.0)	439	(353.0, 496.0)	0.001*
Postoperative Length of Stay in Days (median, IQR)	8	(6.0, 12.0)	8	(6.0, 14.0)	9.5	(7.0, 15.0)	0.10 *
Any Complications	44	(42.7)	40	(56.3)	36	(54.6)	0.15$^{\perp}$
Complications							0.13$^{\pm}$
No Complications	59	(57.3)	31	(43.7)	30	(45.5)	
Mild Complications (Grade 1-2)	30	(29.1)	29	(40.9)	20	(30.3)	
Severe Complication (Grade 3-5)	14	(13.6)	11	(15.5)	16	(24.2)	

§ BMI< 25, n= 100, 25≤BMI<30, n = 69, BMI ≥ 30, n= 65

$\perp$ p-value from univariate logistic regression

$\pm$ p-value from univariate polymotous regression

* p-value from Kruskal-Wallis test

Table 5. Multivariable Analysis by polytomous regression

	OR	95% CI	p value
Intraoperative Blood Loss			
BMI			0.04
<25	1.00		
25-29.9	1.74	(0.99, 3.06)	0.05
>30	2.00	(1.12, 3.57)	0.02
Sex			<0.0001
Female	1.00		
Male	3.88	(2.38, 6.33)	
Complications			0.05
No	1.00		
Yes	1.61	(1.00, 2.61)	
ASA			0.04
1-2	1.00		
3-4	1.72	(1.02, 2.92)	
Operative Duration			
BMI			0.01
<25	1.00		
25-29.9	1.72	(0.96, 3.08)	0.07
>30	2.39	(1.30, 4.39)	0.005
Sex			0.0002
Female	1.00		
Male	2.55	(1.55, 4.21)	
Resection			<0.001
PPPD			
Classic	4.40	(2.59, 7.46)	<0.001
Other	3.73	(0.61, 22.98)	0.16
Preoperative Albumin	0.06	(0.37, 0.86)	0.009
Length of Stay			
BMI			0.12
<25	1.00		
25-29.9	1.24	(0.68, 2.27)	0.48
>30	1.90	(1.03, 3.50)	0.04
Resection			<0.001
PPPD	1.00		
Classic	15.21	(8.48, 27.30)	<0.001
Other	4.09	(0.63, 26.82)	0.1417
Complications			<0.001
No	1.00		
Yes	6.58	(3.83, 11.30)	
Age	1.03	(1.00, 1.05)	0.02

Table 6. Total Postoperative Complications

Variable	Value	
Total Complications	120	50.0%
Complications by Grade		
I	29	12.1%
II	50	20.8%
III	25	10.4%
IV	11	4.6%
V	5	2.1%
Complications by BMI		
BMI < 25	44	42.7%
25≥ BMI<30	40	56.3%
BMI ≥ 30	36	54.5%