Laparoscopic Pancreaticoduodenectomy Should Not Be Routine for Resection of Periampullary Tumors

Safi Dokmak, MD, Fadhel Samir Ftériche, MD, Béatrice Aussilhou, MD, Yacine Bensafta, MD, Philippe Lévy, MD, Philippe Ruszniewski, MD, Jacques Belghiti, MD, Alain Sauvanet, MD

BACKGROUND: Laparoscopic pancreaticoduodenectomy (LPD) is a difficult procedure that has become increasingly popular. Nevertheless, comparative data on outcomes remain limited. Our aim was to compare the outcomes of LPD and open pancreaticoduodenectomy (OPD).

STUDY DESIGN: Between April 2011 and April 2014, 46 LPD were performed and compared with 46 OPD, which theoretically can be done by the laparoscopic approach. Patients were also matched for demographic data, associated comorbidities, and underlying disease. Patient demographics and perioperative and postoperative outcomes were studied from our single center prospective database.

RESULTS: Lower BMI (23 vs 27 kg/m^2, $p < 0.001$) and a soft pancreas (57% vs 47%, $p = 0.38$) were observed in patients with LPD, but there were no differences in associated comorbidities or underlying disease. Surgery lasted longer in the LPD group (342 vs 264 minutes, $p < 0.001$). One death occurred in the LPD group (2.1% vs 0%, $p = 0.28$) and severe morbidity was higher (28% vs 20%, $p = 0.32$) in LPD due to grade C pancreatic fistula (PF) (24% vs 6%, $p = 0.007$), bleeding (24% vs 7%, $p = 0.02$), and revision surgery (24% vs 11%, $p = 0.09$). Pathologic examination for malignant diseases did not identify any differences between the LPD and OPD as far as size (2.51 vs 2.82 cm, $p = 0.27$), number of harvested (20 vs 23, $p = 0.62$) or invaded (2.4 vs 2, $p = 0.22$) lymph nodes, or R0 resection (80% vs 80%; $p = 1$). Hospital stays were similar (25 vs 23 days, $p = 0.59$). There was no difference in outcomes between approaches in patients at a lower risk of PF.

CONCLUSIONS: This study found that LPD is associated with higher morbidity, mainly due to more severe PF. Laparoscopic pancreaticoduodenectomy should be considered only in the subgroup of patients with a low risk of PF. (J Am Coll Surg 2015;220:831−838. © 2015 by the American College of Surgeons)

Pancreaticoduodenectomy (PD) remains the only curative treatment for many malignant and benign pancreatic and periampullary diseases. At present, this technique is associated with a low and acceptable mortality rate (3% to 5%), but a high rate of morbidity (40% to 50%), mainly due to pancreatic fistula (PF) and delayed gastric emptying.[1-5]

Disclosure Information: Nothing to disclose.

Presented at the Congress of French Surgical Association, Paris, France, October 2014.

Received October 22, 2014; Revised December 12, 2014; Accepted December 15, 2014.

From the Departments of HPB Surgery and Liver Transplantation (Dokmak, Ftériche, Aussilhou, Bensafta, Belghiti, Sauvanet) and Gastroenterology (Lévy, Ruszniewski,) Beaujon Hospital, Clichy, France.

Correspondence address: Safi Dokmak, MD, Beaujon Hospital, 100 Bd du Général Leclerc, 92110 Clichy, France. email: safi.dokmak@bjn.aphp.fr

Technically, randomized studies have failed to shown any major difference between the different types of pancreatic anastomoses,[6-8] the gastrojejunal route for digestive reconstruction,[9,10] or the extent of lymphadenectomy.[11,12] The most important technical breakthroughs in the last 20 years were probably the development of mesopancreatic dissection[13,14] and the feasibility of this procedure by laparoscopic approach.

Although laparoscopic pancreaticoduodenectomy (LPD) was first described in 1994,[15] application of this technique has progressed slowly[16] until recently in highly specialized centers.[17-24] This procedure is very challenging even for experienced surgeons because extensive dissection is necessary along the mesenterico-portal vein, the superior mesenteric artery (SMA), and the celiac trunk branches, while 3 difficult laparoscopic anastomoses must be performed.

Published by Elsevier Inc.

http://dx.doi.org/10.1016/j.jamcollsurg.2014.12.052
ISSN 1072-7515/15

Abbreviations and Acronyms

GDA = gastro-duodenal artery
IPMN = intraductal papillary mucinous neoplasms
LN = lymph node
LPD = laparoscopic pancreaticoduodenectomy
OPD = open pancreaticoduodenectomy
PF = pancreatic fistula
SMA = superior mesenteric artery

Although there are no randomized studies, the results of retrospective studies are encouraging, and even comparative studies have shown that LPD is better than OPD[20,21] for blood loss and transfusions,[20] length of hospital stay,[20,21] and harvested lymph nodes (LN).[20] But recently, although a comparative study reported less blood loss with LPD, the number of harvested LN and the rate of R0 resection were poorer.[25] Due to the limited number of comparative studies, it is still difficult to assess the value of LPD. As a tertiary hepato-pancreato-biliary (HPB) center, we began our experience in laparoscopic pancreatic resection in January 2008 and have been performing LPD since April 2011. This study reports the results of 46 cases of LPD performed by the same surgical team, compared with open pancreaticoduodenectomy (OPD).

METHODS

Study design

From April 2011 to April 2014, 357 consecutive patients underwent PD in our department, including 46 LPD and 311 OPD. Data were extracted from our prospective database. Indications for LPD were mainly in patients with small periampullary lesions without vascular invasion, neoadjuvant therapy, chronic/acute pancreatitis, who did not require multiple frozen sections such as for intraductal papillary mucinous neoplasms (IPMN), or require the division of a median arcuate ligament.

The 46 patients who underwent LPD were compared with 46 matched patients who underwent OPD. To avoid a selection bias and improve the comparison, patients in the OPD group who were theoretically not suitable for LPD (vascular resection, neoadjuvant radiochemotherapy, chronic or acute pancreatitis, suspected diffuse IPMN, and PD with division of a median arcuate ligament) were excluded from the analysis. Patients were matched according to demographic data (age, sex), associated comorbidities, and underlying disease.

Comparison of groups

Surgical data, overall and major morbidity (Clavien-Dindo III+IV) based on pancreas-specific complications and the Clavien-Dindo classification,[26] and the pathology of resected specimens were compared. The number of Clavien III–IV complications was recorded by patient and not by the total number of all complications in each patient. Tumor size was recorded only for tumors with a measurable mass (IPMN were excluded). Prognostic factors for clinically significant (grades B and C) PF were also analyzed. A subgroup analysis was performed for pancreatic adenocarcinoma. The first 20 LPD were compared with the last 26 LPD to study any learning curve effect. Mortality was defined as mortality within 90 days after surgery. The International Study Group of Pancreatic Fistula definition was used to define PF.[27]

Surgical technique

Open laparoscopy was performed and trocar placement is shown in Figure 1. Hemostasis and lymphostasis were obtained by ligation, clips, or Harmonic scissors (Ethicon Endo-Surgery). After exploration of the liver and peritoneum, the right gastrocolic ligament was divided and the pancreatic head was freed from the right mesocolon. The inferior rim of the pancreatic neck was freed, the mesenterico-portal vein was identified and the right gastrocolic venous trunk was ligated to avoid tearing and bleeding during mobilization of the mesocolon. After performing a Kocher maneuver, the third portion of the duodenum was completely freed from the mesocolon and the ligament of Treitz was divided behind the SMA from the right. A cholecystectomy was performed, the upper bile duct was divided, and a lymphadenectomy was performed on the right border of the hepatic pedicle. The distal antrum or the first duodenum was sectioned. The superior pancreatic border was freed and, after division of the right gastric artery, lymphadenectomy was completed along the hepatic artery and left border of the pedicle. The pancreatic neck was divided by stapler or Harmonic scissors, and the gastroduodenal artery (GDA) was then divided after ligation with clips (Hem-o-lok) or more recently, by endovascular stapler (35 mm, Ethicon Endo-surgery). The proximal jejunal loop and its mesentery were sectioned and pulled from the left to the right of the mesenteric axis. The retroperitoneal pancreatic tissue was sectioned after posterior dissection of the superior mesenteric vein and identification of the right border of the SMA. Once resection was complete, the specimen was placed in a plastic bag and placed in the left hypochondrium. The jejunal loop was passed through the mesocolon and reconstruction was achieved laparoscopically by 1-layer pancreaticojejunal anastomosis with interrupted 3/0 polyglactin (Vicryl) sutures (Ethicon), and end-to-side biliary anastomosis was performed 15 to 20 cm distal to the pancreatic

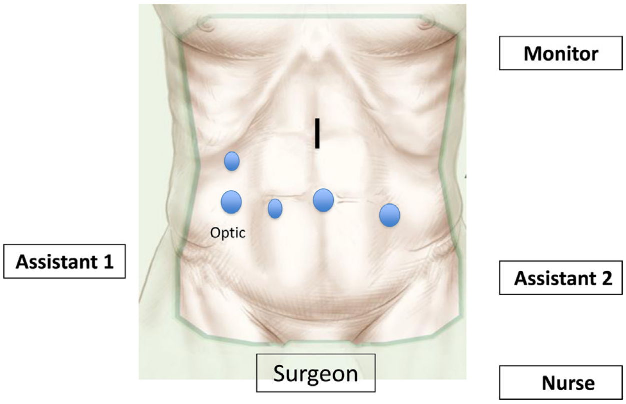

Figure 1. Trocar placement is indicated. Five trocars were usually used for this procedure. A very small midline incision (4 cm) is used in some patients for specimen removal and gastroenteric anastomosis.

anastomosis with interrupted 4/0 or 5/0 polyglactin (Vicryl) sutures. The gastrojejunal anastomosis was performed laparoscopically by stapler or manually through a 4-cm midline incision where the specimen was removed. A tubular drain was left behind the pancreatic anastomosis and was pulled out through the 10-mm right orifice. Patients were discharged after all medical or surgical complications had been completely managed.

Statistical analysis

Values are expressed as means and ranges, or percentages, when appropriate. The chi-square test was used to compare categorical variables. The independent *t*-test and the Mann-Whitney test were used to compare continuous variables. Values of $p < 0.05$ were considered significant. All statistical analyses were performed using SPSS version 20.0 (SPSS, Inc).

RESULTS

The comparison of the LPD and OPD groups (Table 1) showed no difference in age, sex, tumor size, or associated comorbidities, but the BMI was lower in the LPD group (23 vs 27 kg/m^2, $p < 0.001$). There was no difference in underlying disease, and pancreatic and ampullary carcinomas (58% and 56%, respectively) were the main indications for resection in both groups. Although the difference was not significant, a soft pancreas was more frequently noted in LPD patients (57% vs 47%, $p = 0.38$).

Surgical and pathologic data

Surgery lasted longer in the LPD group (342 vs 264 minutes, $p < 0.001$), but there was no difference in blood loss or transfusion rate (Table 1). Conversion and hand assistance were necessary in 3 (6.5%) and 1 (2.2%) cases, respectively. The reasons for conversion were vascular invasion (n = 1) and nonprogression (n = 2). The GDA was divided by ligation with clips (n = 20) or more recently, by vascular stapler (n = 26). In pure LPD (n = 42), the gastrojejunal anastomosis was performed by stapler (n = 18), or manually by a 4-cm midline incision (n = 24). In patients operated on for malignancy (36 in each group), there were no differences in mean size (2.51 vs 2.82 cm, $p = 0.27$), mean number of harvested (20 vs 23, $p = 0.62$) or invaded (2.4 vs 2, $p = 0.22$) LN, or the rate of R0 resection (80% vs 80%; $p = 1$) between the LPD and OPD groups, respectively.

Postoperative outcomes

Postoperative complications are summarized in Table 2. One death occurred on postoperative day 82 in a 74-year-old female patient who underwent LPD for T3N+ ampullary adenocarcinoma. She developed PF and bleeding requiring another intervention, and she died from early diffuse liver metastases. Overall and severe complications were more frequent in the LPD group. Although the differences were not significant for PF (48% vs 41%, $p = 0.52$), grade C PF (24% vs 6%, $p = 0.007$), bleeding (24% vs 7%, $p = 0.02$), and additional surgery (24% vs 11%, $p = 0.09$) were more frequent in the LPD group. Although the difference was not significant for Clavien III–IV complications (28% vs 20%, $p = 0.32$), however the number of patients who presented at least 2 Clavien III–IV complications was higher in the LPD group. There was no difference in other complications or in the length of the hospital stay.

In the LPD group, postoperative bleeding was observed in 11 patients due to bleeding from the stump of the GDA (n = 3), from a collateral of the SMA or the celiac trunk (n = 7), and from adhesions in a patient with cirrhosis (n = 1). It occurred early (<24 hours) in 1 patient and was delayed (>24 hours) in 10. Another operation was needed in 11 patients in the LPD group for bleeding and collections (n = 9), gastrojejunostomy leak (n = 1), and small bowel incarceration in the retromesenteric window (n = 1). The postoperative outcome in the 3 converted patients was uneventful (n = 1), marked by grade B PF (n = 1) and delayed gastric emptying (n = 1), with a hospital stay ranging from 15 to 23 days.

Prognostic factors for grades B + C pancreatic fistula

Many prognostic factors including age (≤50 years old vs >50 years old), sex (male vs female), BMI (≤25>kg/m^2 vs >25 kg/m^2), underlying disease (pancreatic adenocarcinoma vs other underlying disease), pancreatic texture (soft vs hard), and blood loss (≤400 mL vs >400 mL) were analyzed between patients who developed grade B + C

Table 1. Demographics and Operative Characteristics of Both Groups

Variables	Laparoscopic (n = 46)	Open (n = 46)	p Value
Demographic and radiologic data			
Age, y (range)	60 (27–85)	63 (47–81)	0.11
Sex, male, n (%)	26 (57)	28 (61)	0.67
BMI, kg/m^2, mean (range)	22.6 (17–30)	26.4 (19–42)	<0.001
Diabetes, n (%)	12 (26)	17 (39)	0.213
Hypertension, n (%)	11 (24)	17 (37)	0.182
Tumor size, cm, mean (range)	2.82 (1.2–4)	2.51 (1.5–4)	0.27
Main indications, n (%)			
Adenocarcinoma	15 (32)	14 (30)	0.82
Ampulloma	12 (26)	12 (26)	1
Benign IPMN	6 (13)	8 (17)	0.78
NET	6 (13)	5 (11)	0.91
Bile duct cancer	3 (7)	5 (11)	0.23
Other	4 (9)	2 (5)	1
Operative data			
Pancreatic texture, soft, n (%)	26 (57)	21 (47)	0.38
Operative time, min, mean (range)	342 (240–540)	264 (120–400)	<0.001
Blood loss, mL, mean (range)	368 (50–1,200)	293 (50–1,200)	0.16
Transfusion, n (%)	5 (11)	4 (9)	0.72

IPMN, intraductal papillary mucinous neoplasia; NET, neuroendocrine tumor.

PF (n = 20) and grade A or those who did not develop PF. Grade B + C PF was less frequent after PD for pancreatic adenocarcinoma (15% vs 85%, p = 0.025) and in the presence of a hard pancreas (20% vs 80%, p = 0.031).

Subgroup analysis in patients with pancreatic adenocarcinoma

The postoperative outcomes in patients who underwent surgery for pancreatic adenocarcinoma, summarized in Table 3, showed no difference between the 2 groups for mortality, complications, incidence and severity of PF, or length of hospital stay. Tumor size, the number of harvested LN, and the rate of R0 resection were also similar.

Comparison of 2 periods (learning curve)

The first 20 LPD were compared with the last 26. Table 4 shows a significant decrease in the duration of surgery (367 vs 323 minutes, p = 0.009) and blood loss (467 vs 291 mL, p = 0.02), but no difference in major complications including severe PF, bleeding, or additional surgery between the 2 groups. Although the rate of bleeding was similar, there was no bleeding from the stump of the GDA during the second period (60% vs 0%, p = 0.001)

DISCUSSION

Our experience shows that LPD is feasible, with low mortality but increased morbidity, compared with OPD. Indeed, clinically significant PF (44%), postoperative bleeding (24%), and reoperation (24%) were significantly more frequent after LPD than OPD. Moreover, we did not observe any reduction in the length of hospital stay compared with OPD. These results suggest that the laparoscopic approach does not improve the results of PD and should not be routinely indicated in patients at high risk of PF.

Laparoscopic pancreaticoduodenectomy is a long, technically difficult procedure. Indeed, as in other comparative studies, surgery was longer with LPD than with OPD (342 vs 264 minutes, p < 0.001).[20,21] As in other studies,[18,24,28] the length of the operation decreased with the learning curve. In the last 26 LPD, the mean length of surgery was shorter (323 vs 367 minutes, p = 0.009) but was still longer than OPD (264 minutes). This surgical time is shorter than times reported with the robotic approach, which varied from 476 to 568 minutes.[19,23,24] The influence of this long operative time on the postoperative outcome of the patient is unknown, but can be harmful, as recently reported with colonic laparoscopic surgery.[29] Additional studies are needed to evaluate the outcome of patients who have undergone LPD with a long operative time (>6 to 7 hours) to determine if a cut-off operative time (for conversion) is needed or not. We also found that blood loss with LPD was comparable to that with the open approach (368 vs 293 mL, p = 0.16), and it decreased significantly

Table 2. Postoperative Complications

Complication	Laparoscopic (n = 46)	Open (n = 46)	p Value
Mortality, n (%)	1 (2)	0	0.28
Overall morbidity, n (%)	34 (74)	27 (59)	0.12
Clavien III−IV, n (%)	13 (28)	9 (20)	0.32
Pancreatic fistula, n (%)	22 (48)	19 (41)	0.52
Grades of pancreatic fistula			
A	2 (4)	4 (9)	0.39
B	9 (20)	12 (26)	0.61
C	11 (24)	3 (6)	0.007
Delayed gastric emptying, n (%)	8 (17)	7 (15)	0.77
Bleeding, n (%)	11 (24)	3 (7)	0.02
Reintervention, n (%)	11 (24)	5 (11)	0.09
Biliary fistula, n (%)	2 (4)	2 (4)	1
Drained collections, n (%)	2 (4)	3 (7)	0.40
Gastroenteric anastomosis fistula, n (%)	1 (2)	1 (2)	1
Pulmonary complications, n (%)	5 (11)	4 (9)	0.74
Readmission, n (%)	4 (9)	4 (9)	1
Hospital stay, d, mean (range)	25 (6−104)	23 (7−115)	0.59

with the learning curve (467 vs 292 mL, p = 0.02). The use of mechanical staplers and Harmonic devices for 2-sided hemostasis, patient selection, and better visualization offered by the laparascopic approach can compensate for the increased blood loss that may be encountered in some cases, because bleeding can be more difficult to control in the laparoscopic approach. However, 2 comparative studies[20,25] reported decreased blood loss with the LPD approach. Our conversion rate (7%) was comparable to that in the literature (0% to 16%),[17-19,21,24] but was better than the rates reported for laparoscopic distal pancreatectomy, in which the conversion rate can reach 16%.[30] Although the reasons for conversion can be related to bleeding,[21,22] unsuspected vascular invasion or nonprogression,[19,20] in this study, conversion was not indicated for bleeding in any of our patients. The mortality rate (2%) observed after LPD was similar to that in previously studies, ranging from 1% to 7%.[17-21,24,25] Therefore the laparoscopic approach does not seem to influence the risk of death after PD. This is highly important because most resections are performed for malignant diseases.

This is the first comparative study to report a higher early morbidity with LPD. The main reason was the increased incidence of grade C PF with subsequent bleeding and reoperation. Our results are very similar to those from the recent noncomparative series of 22 LPD by Corcione and colleagues,[22] which reported similar overall rates of complications (64%), including PF (27%), bleeding (23%), reoperation (14%), and mean hospital stay of 23 days (range 12 to 35 days). There are several reasons for the increase in complications. First, to facilitate the procedure, for the laparoscopic approach we selected patients who had small lesions, which theoretically have an increased risk of PF due to a soft pancreas and nondilated main pancreatic duct. For example, although ampullary carcinomas are a good technical indication for LPD,[17,22,23] as in our study (26% of our indications), the risk of PF is increased because the texture of the pancreas is soft and the main pancreatic duct is nondilated.[31] On the other hand, only 15% of the patients with pancreatic adenocarcinoma, in which the texture of the pancreas is hard (87% of cases), developed grade C PF. Second, laparoscopic pancreatic anastomoses are probably less effective than manual anastomoses, and more complex pancreatic anastomoses such as 2-layered or with an external drain,[32-34] which have a lower risk of PF but are more difficult to perform by laparoscopy. We found that PF after LPD were characterized by early occurrence and high output, possibly because laparoscopy results in fewer adhesions. Although certain studies have reported a low rate of PF after LPD (6% to 26%), a high rate of collections (18% to19%) or readmission (30%) were also noted,[19,20,25,28] which might have been due to misdiagnosed or internal PF. The risk of bleeding in our series was markedly higher for LPD than for OPD (24% vs 7%, p = 0.02). This rate can be explained by the more severe PF, less effective hemostasis with the Harmonic than with ligations or staples, and less effective peripancreatic drainage. The endovascular stapler effectively prevented bleeding from the stump of the GDA in the second half of our experience, even with severe

Table 3. Postoperative Outcomes in Patients Operated for Pancreatic Adenocarcinoma*

Variables	Laparoscopic (n = 15)	Open (n = 14)	p Value
Size, cm, mean (range)	2.4 (1.5–4)	2.8 (2.5–4)	0.16
Pancreatic texture, hard, n (%)	13 (87)	10 (71)	0.38
Mortality, n (%)	0 (0)	0 (0)	1
Overall morbidity, n (%)	8 (53)	5 (36)	0.34
Major morbidity, n (%)	2 (13)	0 (0)	0.09
Pancreatic fistula, n (%)	3 (20)	4 (29)	0.59
Delayed gastric emptying, n (%)	3 (20)	1 (7)	0.31
Bleeding, n (%)	1 (7)	1 (7)	0.98
Reintervention, n (%)	2 (13)	0 (0)	0.09
Hospital stay, d, mean (range)	15 (6–53)	14 (7–32)	0.38
Harvested LN, n, mean (range)	20 (8–59)	25 (8–47)	0.80
Invaded LN, n, mean (range)	4.7 (0–32)	2.2 (0–12)	0.26
R0, n (%)	9 (60)	7 (50)	0.58

LN, lymph node; PF, pancreatic fistula.
*These patients were at low risk for pancreatic fistula.

PF. A recent multicenter randomized trial reported higher rates of severe complications and mortality due to abdominal complications if no drains were used, suggesting the importance of peripancreatic drainage after pancreatectomy.[35] This difference in morbidity could be more important because the BMI was higher with the OPD (27 vs 23 kg/m^2, $p < 0.001$), which is a bias in favor of the laparoscopic approach.

Because of the increased rate of complications, and also because patients with PF all remained hospitalized until they had completely healed, the hospital stay was not reduced and was even longer after LPD. On the other hand, the rate of readmission was very low (9%).

Two larges series on LPD were recently published. The first non-comparative one from the University of Pittsburgh Medical Center reported on 132 robotic LPD for all indications. In this study, the outcome was marked by Clavien III–IV (21%), readmission (28%), hospital stay of 10 days (range 4 to 87 days), and a decrease in severe complications was observed only in the last 40 patients (30% vs 16%, $p < 0,05$).[36] The second series was from the Mayo Clinic; oncologic outcomes of 108 LPD were compared with 214 OPD, and only in the setting of pancreatic adenocarcinoma. In this study, the first 10 LPD were excluded and LPD was associated with similar major morbidity (5.6% vs 13.6%, $p = 0.17$), but less delayed gastric emptying (9% vs 18%, $p = 0,03$) and shorter hospital stay (6 vs 9 days, $p < 0,001$).[37] Although these 2 teams were pioneers in the development of this technique, we note that the major morbidity in the first study was similar to our results, and the favorable outcome in the second study can be related to the low risk of PF with pancreatic adenocarcinoma.

As with any new surgical procedure, morbidity can be influenced by a learning curve. Although our comparison

Table 4. Postoperative Outcomes in 2 Consecutive Periods*

Variables	Laparoscopic (first 20 cases)	Laparoscopic (last 26 cases)	p Value
Operative duration, min, mean (range)	367 (260–540)	323 (240–450)	0.009
Blood loss, mL, mean (range)	468 (50–1,200)	292 (50–1,200)	0.02
Intraoperative transfusion, n (%)	4 (20)	1 (4)	0.08
Major morbidity, n (%)	7 (35)	6 (23)	0.37
Pancreatic fistula (grade B + C), n (%)	10 (50)	10 (39)	0.21
Delayed gastric emptying, n (Ù)	3 (15)	5 (19)	0.70
Bleeding, n (%)	5 (25)	6 (23)	0.88
Reintervention, n (%)	5 (25)	6 (23)	0.88
Hospital stay, d, mean (range)	29 (7–104)	23 (6–70)	0.29
Readmission, n (%)	1 (5)	3 (12)	0.43

*These data show the learning curve.

between the beginning and end of our study (first 20 vs last 26 cases) showed a significant decrease in operative time and blood loss, this did not affect severe complications or hospital stay. These results are similar to those in a recently published study,[28] which showed a significant decrease in operative time and blood loss, but no benefit to morbidity in relation to the learning curve. This suggests that postoperative morbidity is not only related to the technical factors of LPD but also the underlying disease. Therefore, patient selection may be the most important factor to optimize the advantages of laparoscopic approach with this complex surgical procedure. For example in our group, LPD was performed by an experienced surgeon who had performed more than 400 OPD and 240 laparoscopic pancreatic resections including central and total pancreatectomies.[38,39]

In our study, the postoperative outcomes for LPD in patients with pancreatic adenocarcinoma were similar to those with the open approach. Based on the underlying disease, pancreatic adenocarcinoma had theoretically the lowest risk of PF because hard pancreas and dilated main pancreatic duct are more frequently encountered compared with other periampullary diseases. These results suggest that severe complications were related to the incidence and severity of PF and not specifically to the laparoscopic approach. Limiting LPD to selected patients with pancreatic adenocarcinoma is also supported by oncologic rules for laparoscopic approach determined by the mean number of harvested LN (20; range 8 to 59) or the rate of R0 resection (60%). A recent study in pancreatic ductal adenocarcinoma showed that LPD was better than OPD, with more rapid adjuvant therapy and a better progression free survival.[37] Therefore, limiting LPD to pancreatic adenocarcinoma does not seem to be related to oncologic considerations or postoperative morbidity, but only to technical aspects including tumor size and vascular involvement. These aspects could evolve in the near because since LPD with venous resection has been described.[40,41]

Our case-control study had certain limitations, including its retrospective design and the small number of patients. However, our LPD program is ongoing only in patients at lower risk of PF, and the results will be evaluated in the first 20 patients operated on according to our new selection criteria. In the subgroup of patients at high risk of PF (ampullary carcinoma, neuroendocrine tumor, benign IPMN, and main bile duct cancer) and especially in obese patients, specific preventive measures such as omental flap wrapping,[42] external main pancreatic duct drainage,[32,33] or new somatostatin analogs[43] should be evaluated to decrease both the incidence and consequences of this complication.

CONCLUSIONS

In conclusion, LPD was associated with a low and acceptable mortality rate, but an increased rate of complications, related to the increased incidence and severity of PF. From the results of our experience, the laparoscopic approach is not indicated for treatment of all resectable periampullary tumors. We believe that prospective evaluation should be done and only in very experienced units and in the subgroup of patients at lower risk of PF in order to evaluate the safety of this approach.

Author Contributions

Study conception and design: Dokmak, Ftériche, Aussilhou, Bensafta, levy, Ruszniewski, Belghiti, Sauvanet
Acquisition of data: Dokmak, Ftériche, Aussilhou, Bensafta
Analysis and interpretation of data: Dokmak, Ftériche, Aussilhou, Bensafta, Belghiti, Sauvanet
Drafting of manuscript: Dokmak, Ftériche, Aussilhou, Bensafta, Belghiti, Sauvanet
Critical revision: Dokmak, Ftériche, Aussilhou, Bensafta, Levy, Ruszniewski, Belghiti, Sauvanet

Acknowledgment: The authors would like to thank D Roche for her editorial assistance and correction of the article.

REFERENCES

1. Schmidt CM, Powell ES, Yiannoutsos CT, et al. Pancreaticoduodenectomy: a 20-year experience in 516 patients. Arch Surg 2004;139:718—725; discussion 725—727.
2. DeOliveira ML, Winter JM, Schafer M, et al. Assessment of complications after pancreatic surgery: A novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. Ann Surg 2006;244:931—937; discussion 937—939.
3. Balzano G, Zerbi A, Capretti G, et al. Effect of hospital volume on outcome of pancreaticoduodenectomy in Italy. Br J Surg 2008;95:357—362.
4. van der Gaag NA, Rauws EA, van Eijck CH, et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med 2010;362:129—137.
5. Figueras J, Sabater L, Planellas P, et al. Randomized clinical trial of pancreaticogastrostomy versus pancreaticojejunostomy on the rate and severity of pancreatic fistula after pancreaticoduodenectomy. Br J Surg 2013;100[12]:1597—1605.
6. Wellner UF, Sick O, Olschewski M, et al. Randomized controlled single-center trial comparing pancreatogastrostomy versus pancreaticojejunostomy after partial pancreatoduodenectomy. J Gastrointest Surg 2012;16:1686—1695.
7. Duffas JP, Suc B, Msika S, et al. French Associations for Research in Surgery. A controlled randomized multicenter trial of pancreatogastrostomy or pancreatojejunostomy after pancreatoduodenectomy. Am J Surg 2005;189:720—729.

8. Bassi C, Falconi M, Molinari E, et al. Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. Ann Surg 2005;242:767—771.
9. Gangavatiker R, Pal S, Javed A, et al. Effect of antecolic or retrocolic reconstruction of the gastro/duodenojejunostomy on delayed gastric emptying after pancreaticoduodenectomy: a randomized controlled trial. J Gastrointest Surg 2011;15:843—852.
10. Eshuis WJ, van Dalen JW, Busch OR, et al. Route of gastroenteric reconstruction in pancreatoduodenectomy and delayed gastric emptying. HPB (Oxford) 2012;14:54—59.
11. Nimura Y, Nagino M, Takao S, et al. Standard versus extended lymphadenectomy in radical pancreatoduodenectomy for ductal adenocarcinoma of the head of the pancreas: long-term results of a Japanese multicenter randomized controlled trial. J Hepatobiliary Pancreat Sci 2012;19:230—241.
12. Farnell MB, Pearson RK, Sarr MG, et al, Pancreas Cancer Working Group. A prospective randomized trial comparing standard pancreatoduodenectomy with pancreatoduodenectomy with extended lymphadenectomy in resectable pancreatic head adenocarcinoma. Surgery 2005;138:618—628.
13. Pessaux P, Varma D, Arnaud JP. Pancreaticoduodenectomy: superior mesenteric artery first approach. J Gastrointest Surg 2006;10:607—611.
14. Sanjay P, Takaori K, Govil S, et al. 'Artery-first' approaches to pancreatoduodenectomy. Br J Surg 2012;99:1027—1035.
15. Gagner M, Pomp A. Laparoscopic pylorus-preserving pancreatoduodenectomy. Surg Endosc 1994;8:408—410.
16. Gagner M, Palermo M. Laparoscopic Whipple procedure: review of the literature. J Hepatobiliary Pancreat Surg 2009;16:726—730.
17. Palanivelu C, Rajan PS, Rangarajan M, et al. Evolution in techniques of laparoscopic pancreaticoduodenectomy: a decade long experience from a tertiary center. J Hepatobiliary Pancreat Surg 2009;16:731—740.
18. Kendrick ML, Cusati D. Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. Arch Surg 2010;145:19—23.
19. Zeh HJ, Zureikat AH, Secrest A, et al. Outcomes after robot-assisted pancreaticoduodenectomy for periampullary lesions. Ann Surg Oncol 2012;19:864—870.
20. Asbun HJ, Stauffer JA. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. J Am Coll Surg 2012;215:810—819.
21. Chalikonda S, Aguilar-Saavedra JR, Walsh RM. Laparoscopic robotic-assisted pancreaticoduodenectomy: a case-matched comparison with open resection. Surg Endosc 2012;26:2397—2402.
22. Corcione F, Pirozzi F, Cuccurullo D, et al. Laparoscopic pancreaticoduodenectomy: experience of 22 cases. Surg Endosc 2013;27:2131—2136.
23. Boggi U, Signori S, De Lio N, et al. Feasibility of robotic pancreaticoduodenectomy. Br J Surg 2013;100:917—925.
24. Kim SC, Song KB, Jung YS, et al. Short-term clinical outcomes for 100 consecutive cases of laparoscopic pylorus-preserving pancreatoduodenectomy: improvement with surgical experience. Surg Endosc 2013;27:95—103.
25. Bao PQ, Mazirka PO, Watkins KT. Retrospective comparison of robot-assisted minimally invasive versus open pancreaticoduodenectomy for periampullary neoplasms. J Gastrointest Surg 2014;18:682—689.
26. 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.
27. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138:8—13.
28. Speicher PJ, Nussbaum DP, White RR, et al. Defining the learning curve for team-based laparoscopic pancreaticoduodenectomy. Ann Surg Oncol 2014;21:4014—4019.
29. Bailey MB, Davenport DL, Vargas HD, et al. Longer operative time: deterioration of clinical outcomes of laparoscopic colectomy versus open colectomy. Dis Colon Rectum 2014;57: 616—622.
30. Daouadi M, Zureikat AH, Zenati MS, et al. Robot-assisted minimally invasive distal pancreatectomy is superior to the laparoscopic technique. Ann Surg 2013;257:128—132.
31. Yeo CJ, Cameron JL, Maher MM, et al. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Ann Surg 1995; 222:580—588.
32. Berger AC, Howard TJ, Kennedy EP, et al. Does type of pancreaticojejunostomy after pancreaticoduodenectomy decrease rate of pancreatic fistula? A randomized, prospective, dual-institution trial. J Am Coll Surg 2009;208:738—747.
33. Pessaux P, Sauvanet A, Mariette C, et al, Fédération de Recherche en Chirurgie (French). External pancreatic duct stent decreases pancreatic fistula rate after pancreaticoduodenectomy: prospective multicenter randomized trial. Ann Surg 2011;253:879—885.
34. Poon RT, Fan ST, Lo CM, et al. External drainage of pancreatic duct with a stent to reduce leakage rate of pancreaticojejunostomy after pancreaticoduodenectomy: a prospective randomized trial. Ann Surg 2007;246:425—433.
35. Van Buren G 2nd, Bloomston M, Hughes SJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. Ann Surg 2014;259:605—612.
36. Zureikat AH, Moser AJ, Boone BA, et al. 250 robotic pancreatic resections: safety and feasibility. Ann Surg 2013;258: 554—559; discussion 559—562.
37. Croome KP, Farnell MB, Que FG, et al. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? Ann Surg 2014;260:633—640.
38. Dokmak S, Aussilhou B, Ftériche FS, et al. Pure laparoscopic middle pancreatectomy: single-center experience with 13 cases. Surg Endosc 2014;28:1601—1606.
39. Dokmak S, Aussilhou B, Sauvanet A, et al. Hand-assisted laparoscopic total pancreatectomy: a report of two cases. J Laparoendosc Adv Surg Tech A 2013;23:539—544.
40. Kendrick ML, Sclabas GM. Major venous resection during total laparoscopic pancreaticoduodenectomy. HPB (Oxford) 2011;13:454—458.
41. Awad ZT. Totally laparoscopic pancreaticoduodenectomy for pancreatic head cancer with involvement of the superior mesenteric vein-portal vein confluence. Ann Surg Oncol 2014;2:34—39.
42. Rosso E, Lopez P, Roedlisch MN, et al. Double omental flap reduced perianastomotic collections and relaparotomy rates after pancreaticoduodenectomy with pancreaticogastrostomy. World J Surg 2012;36:1672—1678.
43. Allen PJ, Gönen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. N Engl J Med 2014;370:2014—2022.