Surgical Endoscopy (2020) 34:1343–1352
https://doi.org/10.1007/s00464-019-06913-9

Laparoscopic pancreaticoduodenectomy for periampullary tumors: lessons learned from 500 consecutive patients in a single center

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Received: 3 December 2018 / Accepted: 11 June 2019 / Published online: 18 June 2019

Abstract

Background Laparoscopic pancreaticoduodenectomy (LPD) is a feasible option in selected patients. However, its use has not yet been generalized since it is time-consuming, physically demanding, and technically challenging. It might be essential to share the experience of high-volume centers to understand its use.

Methods We retrospectively reviewed the data of 500 consecutive patients who underwent LPD at a single institution between January 2007 and December 2017.

Results The patients included 272 women and 228 men (mean age, 57.1 years). The most common indication for LPD was intraductal papillary neoplasm ($n = 104$, 20.8%). Overall and major (Clavien–Dindo grades III–V) complication rates were 37.2% and 4.8%, respectively. Fifty-four patients (10.8%) had clinically relevant (grade B/C) pancreatic fistulas. There were 3 (0.6%) 90-day mortalities. The most common late complication was bilioenteric stricture (25, 5%). Two hundred thirty patients were diagnosed with periampullary cancer. The 5-year overall survival rates of pancreatic cancer, common bile duct cancer, ampulla of Vater cancer, and duodenal cancer were 37.4, 63.2, 78, and 88.9%, respectively. We analyzed learning curves of first-generation and second-generation surgeons. A risk-adjusted cumulative sum analysis demonstrated a learning curve of 55 cases for LPD with the first-generation surgeon and earlier competency with the second-generation surgeon.

Conclusions LPD has the potential to become an alternative surgery to open pancreaticoduodenectomy for periampullary tumors with acceptable outcomes. We could reduce the steep learning curve with structured training, close supervision, and well-trained operation teams. Perioperative and oncologic outcomes of LPD will be optimized after overcoming the learning curve.

Keywords Laparoscopic pancreaticoduodenectomy · Survival · Complications · Learning curve

Pancreaticoduodenectomy has been considered one of the most challenging abdominal surgeries. Because of the complexity of the techniques used in this procedure, surgeons require more training time than that required for other abdominal surgery, in order to gain adequate experience. Over the past 2 decades, advances in pancreatic surgery including laparoscopic surgery have resulted in major improvements in patient outcomes. Recent studies in the literature describe the benefits of laparoscopic pancreaticoduodenectomy (LPD), including comparable oncological outcomes, less pain, quicker recovery, and shorter hospital stays than with open pancreaticoduodenectomy (OPD) [1–4]. We herein assessed the demographic and pathological findings of 500 patients with LPD and evaluated operative-related complications, oncologic outcomes, and the learning curve over an 11-year period.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00464-019-06913-9) contains supplementary material, which is available to authorized users.

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Methods

Patient population

Between January 2007 and December 2017, 3746 patients underwent pancreaticoduodenectomy at Asan Medical Center, Seoul, South Korea. Of these patients, 552 were treated by minimally invasive pancreaticoduodenectomy (500 laparoscopic approaches and 52 robotic approaches) and 3194 by an open technique. Whether to undergo LPD or OPD was decided according to the preference of patients and surgeons after discussing the advantages and disadvantages of both approaches. We retrospectively reviewed the data for 500 patients who underwent LPD after approval from the Institutional Review Board.

Data collection

Demographic data collected included age, sex, comorbidities, body mass index, and American Society of Anesthesiologists score. Operative details included operative time (incision to closure of the wound), estimated blood loss, packed red blood cell transfusion, and type of pancreatic anastomosis. Pathologic specimen details collected included the final pathologic diagnosis, size of the largest tumor, tumor staging details according to the American Joint Committee on Cancer 7th edition staging system for malignant tumors, and margin status. Outcomes used to assess the oncologic adequacy of LPD included oncologic surrogates and survival outcomes. The resection margin was considered R0 when clearance was complete on microscopic examination and within 1 mm from the tumor margin. R1 status was defined as incomplete tumor clearance with a residual tumor on microscopic examination located less than 1 mm from the tumor. We evaluated the perioperative results, long-term complications, oncologic outcomes, and rate of receiving the chemotherapy postoperatively. Abdominal computed tomography and blood tests, including for the tumor markers, were assessed during follow-up, every 3 months for the first 2 years after the primary surgery and then every 3–6 months thereafter.

Surgery-related complications were tracked for a median follow-up time of 29.3 months after surgery and were graded according to the Clavien–Dindo system [5]. We divided the postoperative complications into in-hospital and late complications. Minor complications were defined as grades I and II, whereas major complications were defined as grades III–V. The final overall complication grade assigned was the highest grade of complication experienced by each patient. Postoperative pancreatic fistula (POPF) was defined according to the 2016 International Study Group of Pancreas Surgery consensus definitions [6]. Clinically relevant POPF was defined as grade B/C POPF. Delayed gastric emptying was defined according to the grading system of the International Study Group of Pancreatic Surgery [7].

Surgical techniques

During the 10-year period, we have modified the technique. Our recent technique for LPD is as follows. The patient is placed in a supine position. The operator and second assistant, who hold the laparoscope, stand to the right of the patient, with the first assistant and the scrub nurse positioned to the left of the patient. The procedure can be performed using five trocars, including two 12-mm trocars and three 5-mm trocars. The trocar locations are shown in Fig. 1. The gastrocolic omentum is divided with an ultrasonic shear to allow entry into the lesser sac. The duodenum can be transected just distal to the pylorus using a laparoscopic stapling device. The stomach is placed in the left upper abdomen, providing better surgical view around the pancreatic head. The duodenum was kocherized until the anterior surface of the venous cava and a part of the aorta were exposed. After identifying the portal vein/superior mesenteric vein, we divided small vein branches including the gastrocolic trunk. The portal vein was easily identified behind the triangle of the common hepatic artery, gastroduodenal artery, and upper border of the pancreas, and was thus targeted for division of the pancreas.

The ultrasonic shear is very useful for dividing the pancreas. Ultrasonic energy allows for good hemostasis and a clear line of dissection. The dissection is continued up to the region of the pancreatic duct. Once clearly identified, the pancreatic duct is usually divided with scissors.

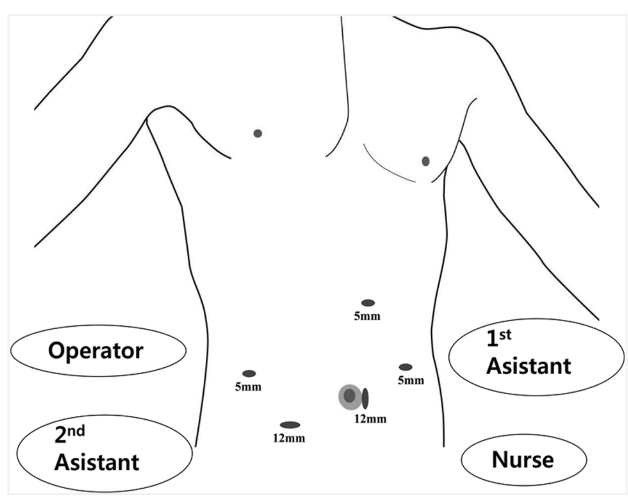

Fig. 1 Placement of trocars for laparoscopic pancreaticoduodenectomy

The common bile duct is divided, and its proximal part is clamped with a surgical bulldog clamp to avoid the spillage of bile during the remaining steps of the procedure. The jejunum is transected 15 cm distal to the ligament of Treitz with the lineal stapler. Dissection of the pancreatic head and uncinate process from the superior mesenteric vein, portal vein, and superior mesenteric artery is one of the most difficult steps of LPD. During the procedure, encircling the portal vein and superior mesenteric vein with a vessel loop allows for retraction of the vein as well as the potential need for vascular control. In patients with AoV cancer or distal CBD cancer, we performed standard lymphadenectomy (supra- and infra-pyloric lymph nodes, lymph nodes along the common hepatic artery, the bile duct and the cystic duct, lymph nodes around the head of the pancreas). In patients with pancreatic cancer, we performed additional concomitant resection of the superior mesenteric artery lymph nodes and selectively the enlarged paracaval lymph nodes above the renal artery, between the aorta and the inferior venous cava. Pancreaticojejunostomy (PJ) was created using either the dunking technique or the duct-to-mucosa technique. We initially used the end-to-side dunking method for convenience, but have begun using the duct-to-mucosa method stenting with a temporary silastic stent in the pancreatic duct. For choledochojejunostomy, we usually perform anterior and posterior continuous suturing in large-sized common bile duct. If the common bile duct is small, we may perform interrupted suturing on both sides. Duodenojejunostomy and jejunojejunostomy are performed intracorporeally or extracorporeally using the specimen extraction site of the umbilical port.

Statistical analysis

Categorical data are reported as a number with percentage of the whole. Continuous data are reported as a mean with range. Significance of the categorical data was tested using a two-tailed Fisher's exact test or Chi square test. Significance of continuous data was tested using the *t* test to compare the two means. A p value < 0.05 was used to determine significance.

Overall survival (OS) was defined as the time interval between the date of surgery and the date of death, and was censored at the last follow-up date for patients who were alive. All patients were accounted for in the follow-up period. Recurrence-free survival (RFS) was defined as the time interval between the date of surgery and the date of recurrence or death, whichever came first, and was censored at the last follow-up date for patients who were alive without recurrence. Statistical analyses were performed using SPSS 24.0 statistical software (IBM Corp., Armonk, NY). We analyzed the learning curve using the cumulative sum (CUSUM), which was defined as $\mathrm{CUSUM} = \Sigma(X_i - X_o)$. X_i is an individual attempt and assigned scores of 0 or 1 for successful surgery and surgical failure, respectively. X_o is the predetermined acceptable failure rate for the procedure; the acceptable failure rate and targeted success rate were set at 10% and 90%, respectively, based on previous reports [8, 9]. The positive and negative slopes of the CUSUM plot indicate failure and success, respectively. Failure was defined as when the operative time exceeded the mean operative time, which was individually calculated in each surgeon. Furthermore, the risk factors for longer operation time were investigated using univariate and multivariate analyses [10]. After calibrating the risk factors for longer operative time, the risk-adjusted CUSUM was used again [11]. The CUSUM was presented graphically, and completion of the learning phase was depicted as a continual fall in the curve after reaching a peak [9, 12, 13].

Results

Patient demographics and pathologic findings

Patient and tumor characteristics for all 500 patients are shown in Table 1. The patients included 272 women and 228 men with a mean age of 57.1 years (standard deviation [SD], 13.9), mean body mass index (kg/m^2) of 23 (SD, 2.8), and mean American Society of Anesthesiologists score of 1.9 (SD, 0.4). The histologic diagnosis of periampullary tumor was confirmed in all patients. The most common indication for LPD was intraductal papillary neoplasm ($n = 104$, 20.8%), followed by ampulla of Vater cancer in 80 patients (16%), pancreatic cancer in 76 patients (15.2%), and distal common bile duct (dCBD) cancer in 61 patients (12.2%).

Perioperative outcomes

The mean operative time and estimated blood loss were 402.4 min (SD, 103.6) and 409 mL (SD, 336), respectively. Of 500 patients, 154 patients underwent PJ by the duct-to-mucosa method and 346 by the dunking method. The mean length of the postoperative hospital stay was 13.3 days (SD, 10.8). In-hospital complications are summarized and graded by the Clavien–Dindo classification in Table 2. Conversion rate of LPD to OPD was 2.3% (12/512). The common reasons for conversion to OPD included accompanying severe pancreatitis and the need for unplanned vascular resection. The overall complication rate was 37.2%. Major morbidity (Clavien–Dindo grades III/IV/V) occurred in 24 (4.8%). POPF was the most frequent complication (54.6%) and 10.8% (54 cases) of patients had clinically relevant POPF. Twelve patients (12, 2.4%) had delayed gastric emptying. The most common life-threatening postoperative complication was bleeding (13, 2.6%). Twelve patients needed

Table 1 Patient demographics and pathologic data

Patients, no.	500
Age, mean (SD), years	57 (13.9)
Sex, female:male, no.	227:273
Body mass index, mean, (SD), kg/m^2	23 (2.8)
ASA score, mean (SD)	1.9 (0.4)
Diagnosis	Number (%)
Pancreatic cancer	76 (15.2)
Pancreatic ductal adenocarcinoma	70
Other pancreatic cancer	6
AoV cancer	80 (16)
Distal common bile duct cancer	61 (12.2)
Duodenal cancer	13 (2.6)
Metastatic renal cell carcinoma	1 (0.2)
IPMN	104 (20.8)
Low-grade dysplasia	53
Intermediate-grade dysplasia	38
High-grade dysplasia	13
PNET	61 (12.2)
Grade 1	37
Grade 2	23
Grade 3	1
Solid pseudopapillary neoplasm	47 (9.4)
Serous cystic neoplasm	18 (3.6)
Mucinous cystic neoplasm	3 (0.6)
Duodenal GIST	12 (2.4)
Low risk	7
Intermediate risk	1
High risk	4
AoV NET	4 (0.8)
AoV adenoma	5 (1)
Other benign peripancreatic tumor	15 (3)

No. number, *SD* standard deviation, *ASA* American Society of Anesthesiologists, *AoV* Ampulla of Vater, *IPMN* intraductal papillary mucinous neoplasm, *PNET* pancreatic neuroendocrine tumor, *GIST* gastrointestinal stromal tumor, *NET* neuroendocrine tumor

reoperations with open approach because of postoperative complications (2.6%). The 90-day mortality rate was 0.6% (3 cases) because of postoperative bleeding (1 case) and sepsis (2 cases, colonic ischemia and small bowel perforation). We performed 23 LPD (4.6%) with portal vein/superior mesenteric vein resection during the study period.

Late complications

Late complications are graded according to the Clavien–Dindo classification in Table 2. Ninety-nine patients were readmitted to our department after discharge during a median follow-up time of 29.3 months of observation. Eighty-five patients had surgery-related complications. Of these, complications were classified as Clavien–Dindo grade II in 39 patients and grade III in 56 patients. The most common late complication after LPD was bilioenteric stricture (BES) with cholangitis or intrahepatic hepatic duct stone (25/85, 29.4%). Most patients (23/25, 92%) with BES had a normal or small bile duct less than 7 mm in diameter. The management of BES was primarily dilatation and percutaneous transhepatic biliary stenting, which was performed in 14 patients, 5 by endoscopic ultrasound-guided hepaticogastrostomy with stenting, 5 patients by conservative management with antibiotic therapy, and 1 patient by surgical revision of bilioenteric anastomosis because of complete obstruction of the site of bilioenteric anastomosis. Of 25 patients, repetitive intervention therapies were required in 18 patients (72%). Symptomatic PJ stricture (e.g., abdominal pain and pancreatitis) was observed in 12 patients who underwent LPD. Operative PJ revisions in patients with pancreatitis with severe pain were performed in 2 patients. Three patients underwent endoscopic ultrasound-guided pancreaticogastrostomy. The other 7 patients were treated by conservative management without intervention or surgery. Five (41.7%) of the total patients with PJ stricture also had initial pancreatic duct dilatation (more than 4 mm) before LPD. Most patients (11/12, 91.7%) who developed PJ stricture received PJ anastomosis with the dunking method. Five patients were diagnosed with a marginal ulcer with perforation. All patients received primary repair of the perforation site with use of a proton-pump inhibitor and gastric mucosal protective agent. Interestingly, 12 patients were readmitted because of afferent loop obstruction with a median follow-up time of 42 days after initial LPD. Among them, 10 patients required a second operation. After these accidental complications, we started to suture 3 points evenly between the afferent loop and opening of the mesocolon of the colon to close the mesocolon opening and prevent migration of the afferent loop.

Oncologic outcomes for malignant disease

Of the 500 patients who underwent LPD, 230 patients were diagnosed with periampullary cancer (pancreatic cancer, Ampulla of Vater cancer, dCBD cancer, and duodenal cancer). Pathologic and survival data by each disease are shown in Table S1. The mean tumor size was 2.4 cm (SD, 1 cm), and the mean number of lymph nodes retrieved was 16.4 (SD, 8.1). R0 resection was possible in 87.8%, and it was accomplished in 59 patients (77.6%) with pancreatic cancer. Regional lymph node metastases were identified in 96 of the 230 patients (41.7%). The 5-year OS rates of pancreatic cancer, dCBD cancer, Ampulla of Vater cancer, and duodenal cancer were 37.4, 63.2, 78, and 88.9%, respectively (Fig. 2). The median OS and RFS following LPD for pancreatic cancer were 32.4 and 14.9 months, respectively.

Table 2 Complications of the patients who underwent LPD

	In-hospital complication (*N* = 500)	Late complication (*N* = 497)
No complication, numbers (%)	314 (62.8)	414 (82.8)
Grade I	69 (13.8)	
Chylous ascites with low long-chain triglyceride diet	67	
Superficial wound infection with bedside care	1	
Delayed gastric emptying	1	
Grade II	93 (18.6)	39 (7.8)
POPF grade B with antibiotic therapy	38	
Intraabdominal fluid collection with antibiotic therapy	27	9
Delayed gastric emptying	11	
Postoperative bleeding with transfusion	10	
Bile leakage with conservative management	3	
Pancreatitis and PJ stricture with conservative management		10
Cholangitis with antibiotic therapy	1	5
Ileus	1	4
Diarrhea	1	
Pneumonia	1	
Afferent loop obstruction with conservative management		2
Portal vein thrombus with anticoagulant therapy		2
Poor oral intake and general weakness		2
Liver abscess with antibiotic therapy		1
Gastric ulcer bleeding with conservative management		1
Ascites with conservative management		1
Gastritis with reflux esophagitis		1
Tractitis at the drain insertion site with antibiotic therapy		1
Grade III	19 (3.8)	46 (9.3)
Grade IIIa	10	26
Intraabdominal fluid collection with drainage	3	1
Pseudoaneurysmal bleeding with embolization or stent insertion	3	4
Bile leakage with interventional therapy	3	
Wound dehiscence	1	
Choledochojejunostomy site stricture with intervention		20
Gastric ulcer bleeding with bleeding control by gastroscopy		1
Grade IIIb	9	20
Postoperative bleeding with reoperation	8	
POPF grade C with pancreaticojejunostomy revision	1	
Afferent loop obstruction with operation		10
Marginal ulcer perforation with operation		5
Mechanical ileus by band with operation		1
PJ revision because of PJ stricture with pancreatitis		2
CJ revision because of complete obstruction of the CJ site		1
Incisional hernia repair		1
Grade IV (intensive care unit management)	2 (0.4)	0
POPF grade C with pancreaticojejunostomy revision	1	
Postoperative bleeding with reoperation	1	
Grade V (death)	3 (0.6)	0
Septic shock with colonic ischemia	1	
Postoperative bleeding with sepsis	1	

Table 2 (continued)

	In-hospital complication ($N=500$)	Late complication ($N=497$)
POPF grade C and small bowel perforation with sepsis	1	
POPF according to 2016 ISGPS		
No POPF	227 (45.4)	
Biochemical leakage	219 (43.8)	
Grade B	51 (10.2)	
Grade C	3	

LPD laparoscopic pancreaticoduodenectomy, *POPF* postoperative pancreatic fistula, *ISGPS* International Study Group of Pancreas Surgery, *PJ* pancreaticojejunostomy, *CJ* choledochojejunostomy

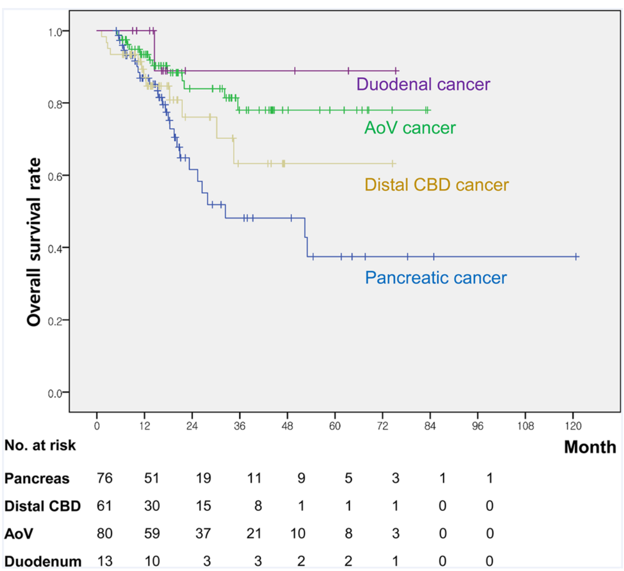

Fig. 2 Overall survival rates of periampullary cancers

Learning curves for LPD

We analyzed the learning curve of the most experienced first-generation surgeon, who performed 289 cases. We found risk factors for a longer operative time such as elderly patients aged older than 60 years ($p=0.036$), male sex ($p<0.001$), body mass index > 25 kg/m^2 ($p=0.022$), and larger blood loss ($p=0.009$). Multivariate analysis showed that male sex was the independent prognostic factor for a longer operative time (OR 3.367, 95% CI 0.181–0.564, $p=0.001$). We investigated the risk-adjusted CUSUM plot. The learning curve comprised 4 periods based on the changes of consecutive successes or failures [14, 15]. The first phase (case numbers 1–55) showed a learning period, and the second phase (case numbers 56–100) showed a stable period after competence of the learning curve. In third phase (case numbers 101–180), the surgeon expanded the surgical indication to include pancreatic cancer. Meticulous dissection of regional lymph nodes was the reason for the longer operative time. The fourth phase (case numbers 181–289) was stable even after the extended operative indication (Fig. 3A). Table 3 shows the trends of results in LPD focused on the first-generation surgeons, which was compatible with Fig. 3A. Because the accumulated learning curves of 5 surgeons may show confusing results, we analyzed the trends of results in LPD focused on the first-generation surgeons.

We evaluated the learning curve of the two main surgeons. Even though the other three surgeons have performed LPD, the number was too small to properly evaluate the

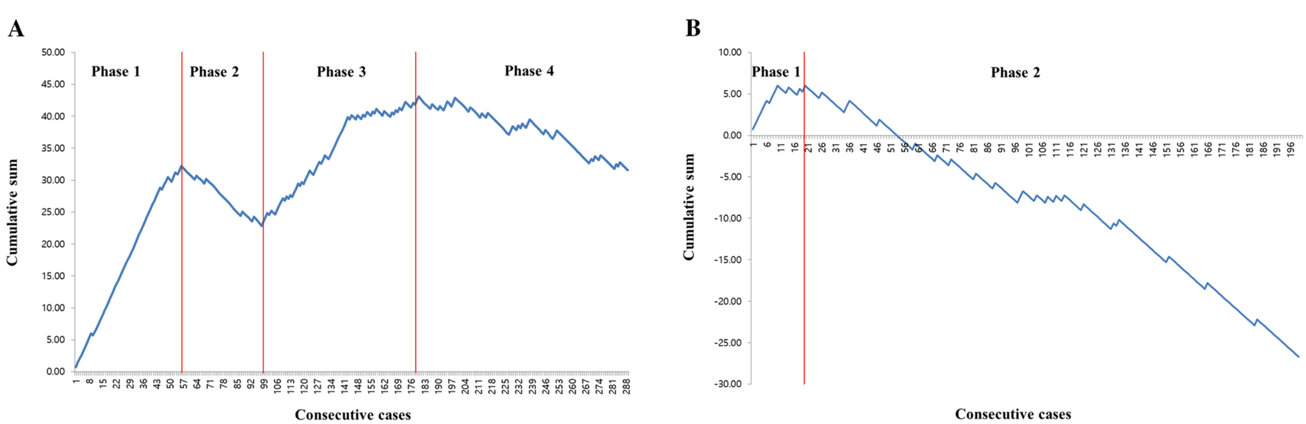

Fig. 3 Cumulative sum curves by operator. **A** First-generation surgeon. **B** Second-generation surgeon

Table 3 Comparison of perioperative outcome of LPD performed by first-generation surgeon according to the period

	Period 1 ($n=55$)	Period 2 ($n=45$)	Period 3 ($n=80$)	Period 4 ($n=109$)	p value Overall	p value (1 vs. 2)	p value (2 vs. 3)	p value (3 vs. 4)
OP time (min)	564.9 ± 99.3	394.5 ± 66.7	462.2 ± 85.2	393.9 ± 64.1	<0.001	<0.001	<0.001	0.001
EBL (mL)	595.9 ± 480.0	393.3 ± 30.1	307.2 ± 270.8	364.3 ± 294.0	<0.001	0.016	0.104	0.174
Malignant tumor (no.)	5 (9.1)	13 (28.9)	22 (27.5)	41 (37.6)	<0.001	0.010	0.868	0.145
Complications (no.)	32 (58.2)	9 (20.0)	30 (37.5)	33 (30.3)	0.011	<0.001	0.043	0.298
Hospital stay (days)	17.7 ± 11.1	11.2 ± 5.3	13.7 ± 10.0	10.4 ± 4.1	<0.001	<0.001	0.132	0.003
Readmission (no.)	17 (30.9)	13 (28.9)	16 (20.0)	7 (6.4)	<0.001	0.636	0.258	0.005
Late complications (no.)	17 (30.9)	10 (22.2)	14 (17.5)	7 (6.4)	<0.001	0.389	0.520	0.017

ASA American Society of Anesthesiologists, *OP* operative, *EBL* estimated blood loss, *no.* number, *vs.* versus

learning curves in this study. The second main surgeon received training from the first main surgeon, and was thus referred to as the second generation. Therefore, we compared the learning curves of the first main surgeon (Fig. 3A) with that of the second main surgeon (Fig. 3B). The CUSUM of second-generation surgeon showed early competency even with the same operative indication.

Discussion

Historically, the first LPD was performed in 1994 by Michel Gagner et al. [16]. They published a series of 10 cases in which the mean operative time was 8.5 h and the conversion rate was 40%, and they concluded that the advantages of LPD were questionable [17]. LPD has attracted little enthusiasm over the ensuing decade since then. Recently, Dokmak et al. [18] reported that LPD is associated with higher morbidity, mainly due to more severe POPF, and LPD is not indicated for treatment of all resectable periampullary tumors. In the present study, only 14.7% of the total patients underwent LPD (including robotic approach). Since LPD is more time-consuming, physically demanding, and technically challenging than OPD, most pancreatic surgeons in our hospital might regard OPD as the standard surgery for right-sided pancreatic tumors. Therefore, unlike laparoscopic distal pancreatectomy, which has been gradually recognized as the standard operation for left-sided pancreatic tumors, LPD has not yet become generalized. There have been several consecutive reports on the feasibility, safety, and effectiveness of LPD in large-volume centers [19, 20]. We also reported on enhancing the experience of the surgery [21]. LPD may be considered safe and acceptable when performed by experienced surgeons in selected patients.

In Boggi et al.'s systemic literature review of LPD, the most common complication after LPD was POPF [22]. According to their study, the incidence of clinically relevant POPF, as defined by 2016 International Study Group of Pancreas Surgery, was 10.5%. This result was similar to that of the current study (10.8%). There have been many studies on the risk factors of POPF after OPD [23–25]. Soft pancreatic texture, small pancreatic duct, high body mass index, and male sex are well-known risk factors. However, there have been no reports about the unique risk factors of POPF for LPD.

Hemorrhage after pancreaticoduodenectomy is a potentially fatal complication. The most common cause of early postoperative hemorrhage (postoperative period < 1 week) was bleeding from the pancreatic stump site of PJ (i.e., bleeding from the dorsal or inferior pancreatic artery). That of delayed hemorrhage (postoperative period ≥ 1 week) was pseudoaneurysmal bleeding. As with the previous reports in OPD [26–29], early detection of sentinel bleeding, diagnostic or therapeutic angiography, and proper surgical treatment are important for the treatment of postoperative bleeding in LPD. Delayed gastric emptying is usually not a life-threatening complication, but this condition results in prolonging the hospital stay and increasing the cost of hospitalization with an incidence of between 5 and 81% [30]. In the present study, only 2.2% of patients developed serious delayed gastric emptying. Zhao et al. reported that it decreased in LPD compared with OPD in meta-analysis [31]. Although the mechanism is not clear, minimizing manipulation in LPD may be related to the early recovery of bowel movement and the reduced occurrence of postoperative adhesion and delayed gastric emptying.

To the best of our knowledge, this is the first report to evaluate late complications after LPD. Our results show that the incidence of symptomatic BES with readmission and treatment was 5% during a median follow-up of 29.3 months. There have been several reports of the incidence of BES, which varies from 2.6 to 8% [32–34]. The discrepancy of incidences of BES in each study seems to be due to different surgical indications and observation periods. Zhu et al. [34] reported that surgeon's volume (≤ 30 cases) was associated with BES, while large-sized bile ducts (> 6 mm) had a negative association with BES. There have been few studies about how laparoscopic surgery affects the development of BES. There is no reason for the incidence of BES to be different between open and laparoscopic bilioenteric anastomosis, because there is no methodological difference between the two. It can be assumed that there is a relationship between the initial size of the bile duct and BES, because most cases of BES occurred in patients with a small bile duct in several studies including present study [34, 35]. Well-designed studies are needed to identify the risk factors for postoperative BES in the future, and surgeons must continue to try to reduce technical faults during bilioenteric anastomosis. The treatment of choice of symptomatic BES was interventional therapy (primarily dilatation and percutaneous transhepatic biliary stenting, and endoscopic ultrasound-guided hepaticogastrostomy with stenting). Most papers recommend interventional therapies as a treatment choice for BES such as the method used in our hospital [33, 36, 37].

The incidence of published PJ stricture after OPD varies from 2 to 11% [32, 38, 39], and 2.4% of cases of PJ stricture following LPD in our hospital are within the range of reported results. In the early period, we have performed side-to-side dunking invagination PJ, which is technically easy and takes less time than the duct-to-mucosa method. However, we had several cases of stenosis of anastomosis in PJ during the follow-up periods. Also, an experimental study reported that the rate of PJ stenosis is higher in the dunking method than the duct-to-mucosa method [40]. Based on our experience of PJ stricture with the dunking method, we modified the PJ procedure from the dunking method to the duct-to-mucosa method. When we compared the PJ leak and PJ stenosis rates between the duct-to-mucosa and the dunking groups, the PJ stenosis rate was higher in the dunking group, albeit without statistical significance.

Pancreaticoduodenectomy employs afferent limb of the jejunum for reconstruction of the pancreatic and biliary drainage. Afferent loop obstruction is a rare complication with the open procedure, and it occurs during the long-term follow-up period due to small bowel obstruction by recurrence or adhesion. However, afferent loop obstruction following LPD is mainly caused by internal herniation. Based on our experience, we have modified the procedure by suturing the jejunal limb to the transverse mesocolon at three evenly placed points to close the mesocolic window. After the modifications, there has been no case of afferent loop obstruction.

In order for LPD to be a reasonable surgical modality for periampullary cancers, it should have non-inferior oncologic outcomes compared to OPD. Several studies have reported that there were no differences in oncologic outcomes between the two groups [1, 20, 41, 42]. In the present study, the mean number of lymph nodes retrieved was 16.4, and R0 resection was possible in 87.8% of the patients with periampullary cancers. Several papers reported that short-term oncologic surrogates of LPD were reasonable, but there have been few studies of the long-term oncologic outcomes with large numbers of patients with periampullary cancer [22]. More research studies with long-term data are needed to solve this controversy. Our institution introduced LPD relatively early. Our study reports the oncologic outcome data from more than 11 years of follow-up, and showed acceptable OS and RFS in patients with periampullary cancer compared to those of previous studies [20, 42, 43]. These findings could warrant continued implementation of laparoscopic approaches for patients with periampullary cancer.

Even though our center gradually expanded the indication for LPD, LPD was performed in only 13.3% of all pancreaticoduodenectomy cases. This shows that even though we have performed over 500 cases of LPD, OPD remains as the standard procedure of pancreaticoduodenectomy, and that LPD has been selected based on limited medical indication and surgeon preference.

The surgical indication is extremely important to reduce morbidity and mortality, especially during the initial phase of LPD. In the initial period, the ideal candidates for LPD should be patients with benign or low-grade malignant tumors. With growing experience, LPD could be offered for all periampullary cancers. Generally, pancreatic ductal adenocarcinoma (PDAC) is the most common malignant disease for which pancreaticoduodenectomy is performed. However, PDAC is often accompanied with severe pancreatitis and multivisceral invasion. In addition, it is difficult to obtain a safe superior mesenteric artery margin. Performing LPD in PDAC is more technically challenging than in other periampullary tumors. On the other hand, LPD for Ampulla of Vater cancer is relatively easy to perform because it has relatively little multivisceral invasion and combined pancreaticobiliary dilatation, which makes it easy to perform pancreatico-enteric and biliary-enteric anastomosis. Therefore, we considered Ampulla of Vater cancer to be the best indication of LPD among periampullary cancers in the initial period.

The present study provided a multidimensional evaluation of the learning curve in LPD by addressing multiple indicators of surgical performance. Learning curves for surgical methods have been used to indicate how much experience is needed to obtain reliable surgical outcomes, but there is still debate over whether they can be applied to all surgeons equally. The learning curve of LPD is bound to differ depending on the surgeon's experience with OPD and intensity and quality of laparoscopic training. In this study, the multiple phases of the learning curve of the first-generation surgeon showed his surgical competency, pushing limits, and final steady state. It is reported that experience on 30–60 cases are usually needed to overcome the learning curve for LPD [44, 45]. During the learning curve period, guidance of an experienced surgeon can be very helpful for reducing the learning curve time. The CUSUM of the second-generation surgeon showed early competency. It has been reported that the accumulation of surgical experience and incorporation of expertise from high-volume centers may enable satisfactory outcomes to be achieved after pancreaticoduodenectomy in low-volume clinical settings [46]. Inexperienced operators trained in high-volume centers can perform LPD safely and efficiently with a short operative time and reliable perioperative outcomes. In addition to overcoming the learning curve of the surgeon, tacit cooperation among the surgical team is essential to reducing the operative time and improving perioperative outcomes. Therefore, structured training of LPD, close supervision by an expert, and cooperation with another well-trained assistant may be possible strategies to reduce the steepness of the learning curve.

There are several limitations to this study. The results of the present study may have limited generalizability because the outcomes were based on retrospectively collected data from a single center. In addition, this study did not examine the impact of laparoscopic approach compared with open approach. A multicenter, prospective, randomized, controlled trial to compare LPD and OPD should be carried out to draw a firm conclusion.

Conclusions

Over the 11 years of experience with 500 cases of LPD in our center, LPD showed that it has the potential to become an alternative surgery to OPD in selected patients with periampullary tumors with acceptable outcomes. We could reduce the steep learning curve with structured training, close supervision, and well-trained operation teams. Perioperative and oncologic outcomes of LPD will be optimized after overcoming the learning curve in selected patients.

Funding This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health & Welfare, South Korea (Grant Number: HI14C2640).

Compliance with ethical standards

Disclosures Ki Byung Song, Song Cheol Kim, Woohyung Lee, Dae Wook Hwang, Jae Hoon Lee, Jaewoo Kwon, Guisuk Park, Yejong Park, and Seung Jae Lee have no conflicts of interest or financial ties to disclose.

References

1. Conrad C et al (2017) Comparable long-term oncologic outcomes of laparoscopic versus open pancreaticoduodenectomy for adenocarcinoma: a propensity score weighting analysis. Surg Endosc 31(10):3970–3978
2. Shin SH et al (2015) A comparative study of laparoscopic vs. open distal pancreatectomy for left-sided ductal adenocarcinoma: a propensity score-matched analysis. J Am Coll Surg 220(2):177–185
3. Khaled YS et al (2018) Matched case-control comparative study of laparoscopic versus open pancreaticoduodenectomy for malignant lesions. Surg Laparosc Endosc Percutan Tech 28(1):47–51
4. Maher H et al (2017) The prospective of laparoscopic pancreaticoduodenectomy for cancer management. Chin Clin Oncol 6(1):8
5. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240(2):205–213
6. Bassi C et al (2017) The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 161(3):584–591
7. Wente MN et al (2007) Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 142(5):761–768
8. Forbes TL et al (2004) Cumulative sum failure analysis of the learning curve with endovascular abdominal aortic aneurysm repair. J Vasc Surg 39(1):102–108
9. Choi DH et al (2009) Learning curves for laparoscopic sigmoidectomy used to manage curable sigmoid colon cancer: single-institute, three-surgeon experience. Surg Endosc 23(3):622–628
10. Nomi T et al (2015) Learning curve for laparoscopic major hepatectomy. Br J Surg 102(7):796–804
11. Kim CW et al (2015) Learning curve for single-incision laparoscopic anterior resection for sigmoid colon cancer. J Am Coll Surg 221(2):397–403
12. Lee W et al (2016) Comparison of learning curves for major and minor laparoscopic liver resection. J Laparoendosc Adv Surg Tech A 26(6):457–464
13. Ramsay CR et al (2000) Assessment of the learning curve in health technologies. A systematic review. Int J Technol Assess Health Care 16(4):1095–1108
14. Tomassini F et al (2016) The single surgeon learning curve of laparoscopic liver resection: a continuous evolving process through stepwise difficulties. Medicine (Baltimore) 95(43):e5138
15. Lin CW et al (2016) The learning curve of laparoscopic liver resection after the Louisville statement 2008: will it be more effective and smooth? Surg Endosc 30(7):2895–2903
16. Gagner M, Pomp A (1994) Laparoscopic pylorus-preserving pancreatoduodenectomy. Surg Endosc 8(5):408–410
17. Gagner M, Pomp A (1997) Laparoscopic pancreatic resection: is it worthwhile? J Gastrointest Surg 1(1):20–25 **discussion 25–6**
18. Dokmak S et al (2015) Laparoscopic pancreaticoduodenectomy should not be routine for resection of periampullary tumors. J Am Coll Surg 220(5):831–838
19. Kendrick ML, Cusati D (2010) Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. Arch Surg 145(1):19–23
20. Croome KP et al (2014) Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? Ann Surg 260(4):633–638 **discussion 638–40**
21. Kim SC et al (2013) Short-term clinical outcomes for 100 consecutive cases of laparoscopic pylorus-preserving pancreatoduodenectomy: improvement with surgical experience. Surg Endosc 27(1):95–103
22. Boggi U et al (2015) Laparoscopic pancreaticoduodenectomy: a systematic literature review. Surg Endosc 29(1):9–23
23. Hu BY et al (2016) Risk factors for postoperative pancreatic fistula: analysis of 539 successive cases of pancreaticoduodenectomy. World J Gastroenterol 22(34):7797–7805

24. Akamatsu N et al (2010) Risk factors for postoperative pancreatic fistula after pancreaticoduodenectomy: the significance of the ratio of the main pancreatic duct to the pancreas body as a predictor of leakage. J Hepatobiliary Pancreat Sci 17(3):322–328
25. Callery MP et al (2013) A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg 216(1):1–14
26. Lee HG et al (2010) Management of bleeding from pseudoaneurysms following pancreaticoduodenectomy. World J Gastroenterol 16(10):1239–1244
27. Blanc T et al (2007) Hemorrhage after pancreaticoduodenectomy: when is surgery still indicated? Am J Surg 194(1):3–9
28. Ding X et al (2011) Therapeutic management of hemorrhage from visceral artery pseudoaneurysms after pancreatic surgery. J Gastrointest Surg 15(8):1417–1425
29. Treckmann J et al (2008) Sentinel bleeding after pancreaticoduodenectomy: a disregarded sign. J Gastrointest Surg 12(2):313–318
30. Imamura M et al (2016) Effects of antecolic versus retrocolic reconstruction for gastro/duodenojejunostomy on delayed gastric emptying after pancreatoduodenectomy: a systematic review and meta-analysis. J Surg Res 200(1):147–157
31. Zhao Z et al (2017) A systemic review and an updated meta-analysis: minimally invasive vs open pancreaticoduodenectomy. Sci Rep 7(1):2220
32. Reid-Lombardo KM et al (2007) Long-term anastomotic complications after pancreaticoduodenectomy for benign diseases. J Gastrointest Surg 11(12):1704–1711
33. House MG et al (2006) Incidence and outcome of biliary strictures after pancreaticoduodenectomy. Ann Surg 243(5):571–576 **discussion 576–8**
34. Zhu JQ et al (2017) Bilioenteric anastomotic stricture in patients with benign and malignant tumors: prevalence, risk factors and treatment. Hepatobiliary Pancreat Dis Int 16(4):412–417
35. Malgras B et al (2016) Early biliary complications following pancreaticoduodenectomy: prevalence and risk factors. HPB (Oxford) 18(4):367–374
36. Mauri G et al (2013) Biodegradable biliary stent implantation in the treatment of benign bilioplastic-refractory biliary strictures: preliminary experience. Eur Radiol 23(12):3304–3310
37. Kaffes A et al (2014) A randomized trial of a fully covered self-expandable metallic stent versus plastic stents in anastomotic biliary strictures after liver transplantation. Therap Adv Gastroenterol 7(2):64–71
38. Cioffi JL et al (2016) Pancreaticojejunostomy stricture after pancreatoduodenectomy: outcomes after operative revision. J Gastrointest Surg 20(2):293–299
39. Demirjian AN et al (2010) The inconsistent nature of symptomatic pancreatico-jejunostomy anastomotic strictures. HPB (Oxford) 12(7):482–487
40. Bai MD et al (2008) Experimental study on operative methods of pancreaticojejunostomy with reference to anastomotic patency and postoperative pancreatic exocrine function. World J Gastroenterol 14(3):441–447
41. Torphy RJ et al (2018) Comparing short-term and oncologic outcomes of minimally invasive versus open pancreaticoduodenectomy across low and high volume centers. Ann Surg. https://doi.org/10.1097/SLA.0000000000002810
42. Senthilnathan P et al (2015) Long-term results of laparoscopic pancreaticoduodenectomy for pancreatic and periampullary cancer-experience of 130 cases from a tertiary-care center in South India. J Laparoendosc Adv Surg Tech A 25(4):295–300
43. Stauffer JA et al (2017) Laparoscopic versus open pancreaticoduodenectomy for pancreatic adenocarcinoma: long-term results at a single institution. Surg Endosc 31(5):2233–2241
44. Wang M et al (2016) Learning curve for laparoscopic pancreaticoduodenectomy: a CUSUM analysis. J Gastrointest Surg 20(5):924–935
45. Lu C et al (2016) Analysis of learning curve for laparoscopic pancreaticoduodenectomy. J Vis Surg 2:145
46. Chedid AD et al (2015) Achieving good perioperative outcomes after pancreaticoduodenectomy in a low-volume setting: a 25-year experience. Int Surg 100(4):705–711