



Laparoscopic versus open pancreaticoduodenectomy for pancreatic neuroendocrine tumors: a single-center experience

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Abstract

Background The efficacy and outcomes of laparoscopic resection for pancreatic neuroendocrine tumors (PNETs) are well established; however, specific data regarding the outcomes of laparoscopic pancreaticoduodenectomy (L-PD) are limited. The purpose of the present study was to compare the clinical and oncological outcomes following L-PD versus open PD (O-PD) in patients with PNETs.

Methods This retrospective study included 149 patients with PNETs who underwent PD at the Asan Medical Center between January 2006 and December 2017. In 58 patients, a laparoscopic approach was used (L-PD group), and in 91, an open technique was used (O-PD group).

Results The mean operative time was longer in the L-PD group than in the O-PD group (417.4 min vs. 362.2 min; $p=0.002$), and the mean duration of postoperative stay was shorter in the L-PD group (12.6 days vs. 17.8 days; $p<0.001$). The estimated blood loss (433.2 ml vs. 415.0 ml; $p=0.824$) and the overall complication rate (34.5% vs. 38.5%; $p=0.624$) did not significantly differ between the two groups. Regarding the oncological outcomes, there were no significant differences in the resection margins, tumor size, tumor grading, or T/N stage. The number of harvested lymph nodes in the L-PD group was lower than that in the O-PD group (7.1 vs. 10.8; $p=0.002$). The 3-year overall survival rate was 91.9% in the L-PD group and 93.6% in the O-PD group ($p=0.974$). The 3-year disease-free survival rate was 94.8% in the L-PD group and 86.7% in the O-PD group ($p=0.225$).

Conclusions L-PD is feasible for the treatment of PNETs in selected patients and has the advantages of short recovery time and reduced hospital stay. The survival rate was similar in both groups; however, due to the difference in the harvested lymph nodes, a randomized trial should confirm the oncological safety of L-PD for PNETs.

Keywords Pancreatic NET · Laparoscopy · Pancreaticoduodenectomy

Pancreatic neuroendocrine tumors (PNETs) represent 1–2% of all tumors arising in the pancreas, with an incidence of < 1 per 100,000 individuals per year [1]. The incidence of PNETs has been steadily increasing, possibly because of the increased detection on endoscopic and cross-sectional

images [2]. PNETs comprise a heterogeneous group of tumors with extremely diverse biological behavior, ranging from relatively indolent to very aggressive [3–5]. In the recent years, PNETs have been incidentally detected during an evaluation for other conditions or unrelated symptoms; thus, many of these tumors are often found at an early stage [6].

Surgery plays a central role in the curative treatment of localized PNETs. Early detected PNETs are often small and single tumors of less aggressive biological behavior, which makes them ideal for treatment with laparoscopic surgery. Since the first laparoscopic resection of a PNET by Gagner and Pomp [7], the number of these procedures has progressively increased. The safety, efficacy, and outcomes of laparoscopic pancreatic resection have been proven by recent systematic reviews and meta-analyses [8–10]. This approach

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has many advantages over the open surgical approach, including reduced blood loss during surgery, reduced postoperative pain, accelerated recovery, earlier return to normal bowel function and oral intake, and early hospital discharge [11, 12]. Therefore, many centers with high-level skilled personnel have started to perform laparoscopic pancreatic resection for PNETs [13–15]. In the recent years, laparoscopic pancreaticoduodenectomy (L-PD) is also performed more often for benign and malignant lesions, because its feasibility, safety, and good oncological outcomes have been confirmed in several studies [16, 17]. However, L-PD is not yet widely performed or accepted as the gold standard treatment for PNETs. Furthermore, there are few studies that compare L-PD with the open PD (O-PD) for the treatment of PNETs.

The purpose of the present study was to compare the clinical and oncological outcomes following L-PD versus open PD in patients with PNETs.

Materials and methods

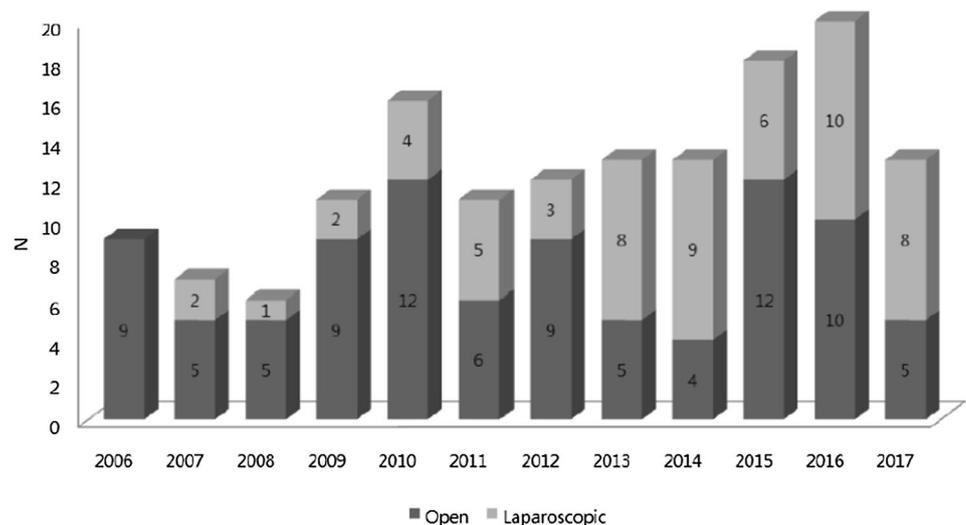
We reviewed and retrospectively analyzed the medical records of 163 patients with PNETs who underwent an O-PD or L-PD at the Asan Medical Center between January 2006 and December 2017. The study period included 2006, which was a year before L-PD began to be performed for PNETs at our center. Nine patients with liver metastases treated with hepatectomy or radiofrequency ablation, two patients with other combined operations, and one patient who underwent a robotic PD were excluded. Two patients who required a conversion to open surgery due to bleeding during the laparoscopic surgery were also excluded, and per-protocol analysis was performed. Finally, 149 patients with PNETs who underwent PD were included in the study.

Of these, 58 patients underwent L-PD and 91 underwent O-PD (Fig. 1). The type of surgery (L-PD or O-PD) was determined according to the patients' and surgeons' preference, after discussing the advantages and disadvantages of both approaches. The two groups were compared in terms of the clinical and oncological outcomes. The present study was approved by the Institutional Review Board of the Asan Medical Center.

The following clinical characteristics were analyzed: age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status score, and comorbidities. The collected operative data included the operating time, amount of blood loss, postoperative complications, the start of oral intake, and length of postoperative hospital stay. The postoperative surgical complications were described according to the classification proposed by Clavien and colleagues [18]. Pancreatic fistulas, the most important postoperative complication following pancreatic surgery, were classified according to the system of the International Study Group of Pancreatic Surgery [19]. Readmission was defined as rehospitalization within 30 days of discharge.

The pathology data were also analyzed, and the tumor size was defined as the maximum cross-sectional diameter determined by the pathologist. All PNETs were classified according to a grading scheme based on the mitotic count or Ki67 index, as follows: G1 (mitotic count < 2/10 high-power fields (HPF) and/or $\leq 2\%$ Ki67 index); G2 (mitotic count 2–20/10 HPF and/or 3%–20% Ki67 index); and G3 (mitotic count > 20/10 HPF and/or > 20% Ki67 index). The 8th edition of the American Joint Committee on Cancer (AJCC) recommends that the tumor–node–metastasis staging system be used for tumor staging. Primary tumor lymphovascular invasion (LVi), perineural invasion (PNi), and resection margins were also evaluated in the pathological samples. The survival status was determined from the national registries.

Fig. 1 Laparoscopic and open pancreaticoduodenectomy cases for pancreatic neuroendocrine neoplasms by year for the period from 2006 to 2017



Death certificates and time of death were confirmed through the National Health Insurance. All patients were followed up periodically according to the tumor grade to monitor for tumor recurrence. Patients with G1 grade PNETs were followed up at 3 months after surgery and annually thereafter. Those with G2 grade PNETs were followed up at 3 months after surgery, every 6 months for 2 years, and then annually thereafter. The follow-up was every 3 months for 2 years, then every 6 months for 5 years, and then annually thereafter for patients with G3 grade PNETs. The end of the follow-up was in July 2018. Overall survival (OS) was defined as the interval between the date of surgery and the date of death, and disease-free survival (DFS) was defined as the duration between the primary resection and the first documented recurrence of the disease on CT or PET during regular follow-up.

Surgical procedure

In L-PD, the operator and second assistant, who held the laparoscope, stood to the right of the patient and the first assistant and the scrub nurse positioned to the left. We used five trocars, including two 12-mm trocars and three 5-mm trocars. The gastrocolic omentum was separated using a harmonic scalpel to allow exposure of the lesser sac, avoiding injury to the colon. To clearly expose the operative field, the right colon was thoroughly mobilized from the liver and duodenum. Kocher maneuver was performed with traction of the duodenum toward the opposite side by the assistant surgeon. Using an endoscopic linear stapler, the duodenum was divided 2 cm distal to the pylorus. Dissection of the hepatoduodenal ligament and isolation of the common bile duct were performed. A cholecystectomy was performed separately. The common bile duct was divided 2 to 3 cm proximal to the duodenum. The common hepatic artery was dissected from the pancreas, and the gastroduodenal artery and the right gastric artery were transected. The pancreas was divided at the neck using a harmonic scalpel. After retracting the pancreatic head toward the right side of the patient, the intrapancreatic portal vein was dissected. The jejunum was divided 10 to 15 cm distal to the ligament of Treitz using an endoscopic linear stapler. An endoscopic linear stapler or ultrasonic shear was used to divide the soft tissue and the superior mesenteric artery branches between the uncinate process of the pancreas and the superior mesenteric artery to complete the resection. Pancreaticojejunostomy was performed using the double-layered, end-to-side dunking method in normal-sized ducts, or the duct-to-mucosa method in dilated pancreatic ducts. Intracorporeal laparoscopic choledochojejunostomy was performed using interrupted absorbable sutures for very small duct and continuous suturing for dilated duct. Duodenojejunostomy and jejunojejunostomy were performed intra- or extracorporeally using

the specimen extraction site on the umbilical port place. Closed suction drains were placed.

In O-PD, the patient was placed in the supine position and a long midline or an inverted L incision was done. All reconstructions were performed in the same way as in L-PD.

Statistical analysis

Continuous variables are expressed as the median and range or the mean \pm standard deviation. L-PD was compared with O-PD using the χ^2 test and Mann–Whitney *U* test for continuous variables. Categorical variables are reported as numbers and percentages. The OS and DFS were calculated using the Kaplan–Meier method. The log-rank test was used to make group comparisons. Statistical analyses were performed using the SPSS software (ver. 22.0; SPSS Inc. Chicago, IL, USA). Cox regression analysis was performed to identify the factors independently associated with the prognosis. The multivariate analysis included the clinically important parameters identified in the univariate analysis and those with $p < 0.050$. Hazard ratios (HRs) and 95% confidence intervals (CI) are presented for all variables.

Results

Patients' characteristics

The patients' clinical characteristics are listed in Table 1. The patients in the L-PD group were younger (49.5 years vs. 56.0 years, $p = 0.001$) and weighed less (BMI, 23.1 kg/m² vs. 24.5 kg/m², $p = 0.013$). There were no significant differences in the ASA score or previous abdominal operation history between the two groups. With respect to the comorbidities, the O-PD group had more cases of hypertension than the L-PD group (33.0% vs. 13.8%, $p = 0.009$).

Perioperative results

The mean operative time was significantly longer in the L-PD group than in the O-PD group (417.4 min vs. 362.2 min; $p = 0.002$). The estimated blood loss was similar in both groups (433.2 mL vs. 415.0 mL; $p = 0.824$). The mean time to sips of water and the duration of the postoperative hospital stay were shorter in the L-PD group than in the O-PD group (3.8 days vs. 4.9 days; $p = 0.031$, and 12.6 days vs. 17.8 days, respectively; $p < 0.001$). The perioperative findings are summarized in Table 2.

The early postoperative complications in the two groups are also presented in Table 2. The overall complication rate did not significantly differ between the two groups ($p = 0.624$). The rates of clinically relevant postoperative pancreatic fistulas (POPFs) were 5.2% in the L-PD and 4.4%

Table 1 The patients' demographic characteristics and preoperative comorbidities

	L-PD (<i>n</i> =58)	O-PD (<i>n</i> =91)	<i>p</i>
Age (years) mean ± SD	49.5 ± 12.0	56.0 ± 10.5	0.001
Gender, male:female	18:40	42:49	0.067
BMI (kg/m ²) mean ± SD	23.1 ± 2.5	24.5 ± 3.6	0.013
ASA score, <i>n</i> (%)			0.167
1	15 (25.9)	14 (15.4)	
2	43 (74.1)	75 (82.4)	
3	0	2 (2.2)	
Previous operation history	10 (17.2)	26 (28.6)	0.115
CEA (ng/mL) mean ± SD	1.4 ± 0.9	1.9 ± 1.6	0.086
CA19-9 (U/mL) mean ± SD	11.7 ± 12.1	18.7 ± 40.4	0.220
Comorbidities, <i>n</i> (%)			
Hypertension	8 (13.8)	30 (33.0)	0.009
Diabetes	3 (5.2)	13 (14.3)	0.080
Other cardiovascular disease	1 (1.7)	6 (6.6)	0.171
Other pulmonary disease	2 (3.4)	6 (6.6)	0.406
Other	1 (1.7)	4 (4.4)	0.377

L-PD laparoscopic pancreaticoduodenectomy, O-PD open pancreaticoduodenectomy, SD standard deviation

in the O-PD group ($p=0.827$). Delayed gastric emptying (DGE) rates were similar in both groups (3.4% vs. 8.8%,

$p=0.203$). In addition, there were no statistically significant differences in the reoperation and readmission rates between the two groups ($p=0.563$, $p=0.286$, respectively).

Pathology results

Table 3 shows the pathology results for the patients of both groups. The mean tumor size was 2.6 cm in the L-PD group and 2.8 cm in the O-PD group ($p=0.390$). The surgical resection margin and positive lymph nodes (LNs) in the resected specimens did not differ between the two groups (R1 rate, 5.2% vs. 3.3%, $p=0.570$; N1 rate, 11.3% vs. 16.3%, $p=0.419$). The number of LNs in the resected specimens in the L-PD group was lower than that in the O-PD group ($p=0.002$), and the rate of PN_i was also higher in the O-PD group than in the L-PD group ($p=0.004$). However, the WHO grading, AJCC 8th classification, and the rate of LV_i were similar in both groups ($p=0.485$, $p=0.503$, and $p=0.116$, respectively).

Survival analysis

The median follow-up duration in the L-PD and O-PD groups was 39.2 and 66.3 months, respectively. The 3-year OS rate in the L-PD and O-PD groups was 91.9 and 93.6%, respectively ($p=0.974$) (Fig. 2). The 3-year DFS rate in the

Table 2 Comparison of the perioperative results between the two groups

	L-PD (<i>n</i> =58)	O-PD (<i>n</i> =91)	<i>p</i>
Operation time (min) mean ± SD	417.4 ± 102.7	362.2 ± 106.5	0.002
Estimated blood loss (mL) mean ± SD	433.2 ± 394.0	415.0 ± 533.7	0.824
Gas out (day) mean ± SD	4.3 ± 0.8	4.5 ± 1.1	0.318
Sip of water start (day) mean ± SD	3.8 ± 3.4	4.9 ± 2.8	0.031
Diet start (day) mean ± SD	5.1 ± 4.1	5.7 ± 3.8	0.345
Postoperative hospital stay (day) mean ± SD	12.6 ± 6.1	17.8 ± 9.1	< 0.001
All complications, <i>n</i> (%)	20 (34.5)	35 (38.5)	0.624
Complications by Clavien–Dindo classification, <i>n</i> (%)			0.898
I	6 (10.3)	7 (7.7)	
II	12 (20.7)	21 (23.1)	
IIIA	1 (1.7)	3 (3.3)	
IIIB	1 (1.7)	3 (3.3)	
V	0	0	
Major complication, <i>n</i> (%)	2 (3.4)	6 (6.6)	0.415
Pancreatic fistula by ISGPF, <i>n</i> (%)			0.948
Biochemical leak	21 (36.2)	35 (38.5)	
Grade B	3 (5.2)	4 (4.4)	
Grade C	0	0	
Clinically relevant postoperative pancreatic fistula, <i>n</i> (%)	3 (5.2)	4 (4.4)	0.827
Delayed gastric emptying, <i>n</i> (%)	2 (3.4)	8 (8.8)	0.203
Reoperation, <i>n</i> (%)	1 (1.7)	3 (3.3)	0.563
Readmission, <i>n</i> (%)	4 (6.9)	3 (3.3)	0.286

L-PD laparoscopic pancreaticoduodenectomy, O-PD open pancreaticoduodenectomy, SD standard deviation, ISGPF International Study Group of Pancreatic Fistula

Table 3 Comparison of the pathology results between the two groups

	L-PD (<i>n</i> = 58)	O-PD (<i>n</i> = 91)	<i>p</i>
Tumor size (cm) mean ± SD	2.6 ± 1.3	2.8 ± 1.9	0.390
No. of positive LN, mean ± SD	0.1 ± 0.3	0.2 ± 0.4	0.422
Total no. of LN, mean ± SD	7.1 ± 5.7	10.8 ± 7.7	0.002
Grade, WHO classification (<i>n</i> = 128)			0.485
Grade 1	32 (58.2)	37 (50.7)	
Grade 2	21 (38.2)	30 (41.1)	
Grade 3	2 (3.6)	6 (8.2)	
T stage, <i>n</i> (%)			0.166
T1	23 (39.7)	40 (44.0)	
T2	27 (48.6)	28 (30.8)	
T3	8 (13.8)	22 (24.2)	
T4	0	1 (1.1)	
N stage (<i>n</i> = 139), <i>n</i> (%)			0.419
N0	47 (85.8)	72 (83.7)	
N1	6 (11.3)	14 (16.3)	
AJCC 8th classification (<i>n</i> = 139), <i>n</i> (%)			0.503
I	21 (39.6)	36 (41.9)	
II	26 (49.1)	35 (40.7)	
III	6 (11.3)	15 (17.4)	
Lymphovascular invasion	12 (28.2)	29 (32.6)	0.116
Perineural invasion	6 (10.5)	26 (31.0)	0.004
Resection margin	3 (5.2)	3 (3.3)	0.570

L-PD laparoscopic pancreaticoduodenectomy, O-PD open pancreaticoduodenectomy, SD standard deviation, LN lymph nodes, WHO World Health Organization, AJCC American Joint Committee on Cancer

L-PD group was 94.8%, whereas that in the O-PD group was 86.7% ($p = 0.225$) (Fig. 3). We performed an analysis of the prognostic factors influencing the patients' survival. In the multivariate analysis, grade 3 (HR 14.93, $p < 0.001$) and the resection margin (HR 4.99, $p = 0.043$) were significantly associated with decreased OS. Factors significantly associated with a poor DFS were grade 3 (HR 2.92, $p = 0.044$), AJCC III (HR 2.97, $p = 0.024$), LNi (HR 5.34, $p = 0.002$), and the resection margin (HR 4.99, $p = 0.043$). The variables associated with the OS or DFS are shown in Tables 4 and 5, respectively.

Discussion

In the recent years, many studies have confirmed that laparoscopic pancreatic resection is feasible and safe in patients with PNETs [13–15]. According to the latest statistics, enucleation is performed in 65% of the cases, distal pancreatic resection in 34%, and central pancreatectomy, total resection, or PD in the remaining 1% [20]. Due to the complex anastomoses and substantial dissection around major blood vessels, L-PD is a difficult procedure for surgeons to perform. There have been few large-sized studies comparing the outcomes of L-PD and O-PD in patients with PNETs, since

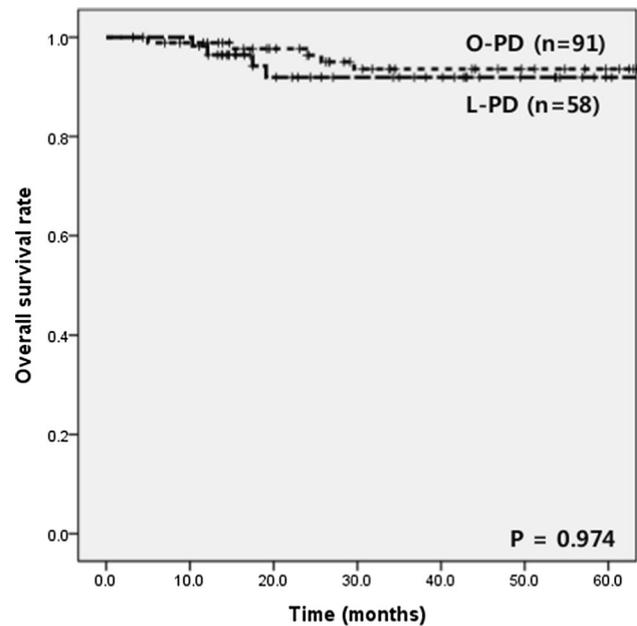


Fig. 2 Comparison of the overall survival of the patients with PNETs between the L-PD and O-PD groups (*n* = 151)

the prevalence of these tumors is low, and L-PD requires advanced laparoscopic skills. To the best of our knowledge,

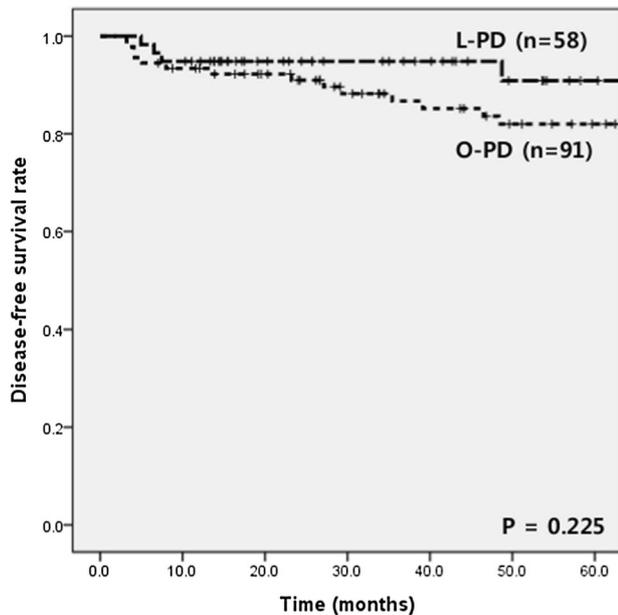


Fig. 3 Comparison of the disease-free survival of the patients with PNETs between the L-PD and O-PD groups ($n = 151$)

this is the first study to compare the clinical and oncological outcomes of L-PD and O-PD for PNETs. In our previous study, we demonstrated that L-PD is technically safe and feasible, and has favorable oncological outcomes in comparison with O-PD in patients with periampullary tumors [16]. Therefore, in the present study, we focused on patients with PNETs who underwent PD.

Laparoscopic pancreatic surgery has been associated with significantly shorter times to first flatus, return to oral intake,

return to bowel movement, and resumption of oral diet as compared with open surgery [9]. It has also gained rapid acceptance due to its relatively high feasibility, decreased postoperative pain, and shorter hospital stay [10]. In the present study, the time to first flatus and resumption of oral diet were similar between the two groups. The patients who underwent L-PD had a shorter time to water intake. Another study showed that the operative time was substantially longer in the L-PD group than in the O-PD group [21]. Similarly, the mean operative time was longer in the L-PD group in the present study. Although L-PD is known to be a time-consuming procedure, it was found to significantly reduce the postoperative hospital stay by 5 days in the present study. In addition, the overall complication rate was similar in both groups, at 34.5% and 38.5%, respectively. POPFs and DGE are common complications in pancreatic surgery. In the present study, the overall rate of POPFs was similar in the two groups. In terms of clinically significant pancreatic fistulas (ISGPF B or C), only 3 (5.2%) patients had grade B pancreatic fistula, and there were no grade C pancreatic fistulas in the L-PD group. DGE was also similar in the two groups. Therefore, our results indicate that there is no significant difference between the two approaches in terms of short-hospital stay and postoperative complications.

Most of the concerns related to the laparoscopic approach refer to its oncological safety. Several variables have been demonstrated as markers for comparing the outcomes in patients with PNETs undergoing O-PD. We found that there were no significant differences in the resection margin, tumor size, tumor grading, or T/N stage between the two groups. In addition, there were no significant differences concerning the 3-year OS or 3-year DFS between the

Table 4 Univariate and multivariate analysis results of the overall survival ($n = 149$)

	Univariate			Multivariate		
	HR	95% CI	<i>p</i>	HR	95% CI	<i>p</i>
Age (> 60 years)	0.726	0.200–2.640	0.627			
Symptomatic	1.805	0.589–5.553	0.302			
Nonfunctioning tumors	0.813	0.105–6.269	0.843			
Op time (> 360 min)	1.385	0.453–4.237	0.568			
Blood loss (> 400 mL)	0.487	0.149–1.585	0.232			
Postoperative hospital stay (> 15 days)	0.528	0.161–1.729	0.292			
L-PD	1.020	0.307–3.389	0.974			
Grade 3	14.413	4.640–44.707	< 0.001	14.930	4.751–46.918	< 0.001
Positive lymph nodes	1.836	0.502–6.714	0.358			
AJCC III	1.768	0.484–6.460	0.389			
Lymphovascular invasion	3.298	1.103–9.857	0.033			
Perineural invasion	1.638	0.489–5.490	0.424			
Resection margin	4.614	1.020–20.881	0.047	4.990	1.055–23.603	0.043

L-PD laparoscopic pancreaticoduodenectomy, *HR* hazard ratio, *CI* confidence interval, *AJCC* American Joint Committee on Cancer

Table 5 Univariate and multivariate analysis results of the disease-free survival ($n = 149$)

	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Age (> 60 years)	0.650	0.242–1.742	0.391			
Symptomatic	1.233	0.538–2.824	0.621			
Nonfunctioning tumors	0.152	0.008–2.790	0.204			
Op time (> 360 min)	1.430	0.625–3.273	0.397			
Blood loss (> 400 mL)	0.845	0.376–1.901	0.684			
Postoperative hospital stay (> 15 days)	1.120	0.480–2.614	0.794			
L-PD	0.545	0.201–1.474	0.232			
Grade 3	8.021	2.868–22.432	< 0.001	2.919	1.030–8.276	0.044
Positive lymph nodes	7.206	2.805–18.508	< 0.001			
AJCC III	6.985	2.745–17.772	< 0.001	2.973	1.154–73.660	0.024
Lymphovascular invasion	9.034	3.536–23.077	< 0.001	5.340	1.899–15.013	0.002
Perineural invasion	5.470	2.245–13.327	< 0.001			
Resection margin	5.086	1.500–17.244	0.009	4.990	1.055–23.603	0.043

L-PD laparoscopic pancreaticoduodenectomy, HR hazard ratio, CI confidence interval, AJCC American Joint Committee on Cancer

two groups ($p = 0.974$ and $p = 0.225$, respectively). However, the number of harvested LNs in the L-PD group was lower than that in the O-PD group. In our previous study, we reported that the number of LNs in the resected specimens in patients with periampullary cancer did not differ between the open and laparoscopic approach groups [16]. It is unclear whether the low sampling rate of LNs in L-PD in the present study results from an incomplete pathological evaluation, incomplete surgery without adequate lymphadenectomy, or a combination of both. In contrast, Asbun and colleagues reported that there was a considerably increased number of overall LNs retrieved in the patients who underwent L-PD as compared with those who underwent O-PD (23.4 vs. 16.8) [22], proposing that the increased lymph node retrieval in the L-PD group is directly related to the resection technique with a more aggressive lymphadenectomy. Since the lymph node status of patients with resectable pancreatic ductal adenocarcinoma is an important predictor of survival, standard lymphadenectomy for pancreaticoduodenectomy should strive to resect lymph node stations no. 5, 6, 8a, 12b1, 12b2, 12c, 13a, 13b, 14a, 14b, 17a, and 17b [23]. However, the definition of standardized lymphadenectomy in L-PD for PNETs has not been established yet. In addition, the impact of the lymph node metastases on the survival of patients with PNETs remains debated; certain studies have demonstrated the prognostic importance of the nodal metastases in PNETs, whereas others have failed to find this association [24–26]. Justin and colleagues found that LNs are not evaluated in many major pancreatic resections for PNETs, and many patients may be understaged and undergo a potentially inadequate resection [27]. Thus, the number of harvested LNs as a parameter for comparing the oncological outcomes

between L-PD and O-PD may be limited. Therefore, not only standardization of the lymphadenectomy, but also the impact of the lymph node metastases on survival, will further verify the oncological safety of L-PD with respect to O-PD for PNETs in a randomized multicenter study.

Our study has several limitations. First, the number of study patients was small, the study was retrospective and analyzed data from only a single center, and the follow-up period was relatively short. Second, L-PD for PNETs commenced in our center in 2007, whereas O-PD has been performed for PNETs since 1990. Although we analyzed all the data since 2006, there may be confounding factors related to these limitations that affected the results. Finally, functioning tumors are usually detected early due to the symptoms caused by hormone production, and the biological behavior of the nonfunctioning and functioning tumors is different; however, we included both functioning and nonfunctioning tumors in the study. Thus, a selection bias may have occurred in the present study.

Conclusion

L-PD is feasible in selected patients for the treatment of PNETs and has the advantages of a short recovery time and reduced hospital stay. However, the experience with L-PD for PNETs remains limited, and long-term follow-up data are required to clearly define the oncological safety. It may be necessary to conduct a multicenter, well-designed, randomized study to assess the oncological outcomes of the patients undergoing L-PD for PNETs.

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Compliance with ethical standards

Disclosures Hanbaro Kim, Ki Byung Song, Dae Wook Hwang, Jae Hoon Lee, Shadi Alshammary, and Song Cheol Kim have no conflicts of interest or financial ties to disclose.

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