Annals of Medicine and Surgery 69 (2021) 102742

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cohort Study

Efficacy of laparoscopic-assisted pancreaticoduodenectomy in Vietnamese patients with periampullary of Vater malignancies: A single-institution prospective study☆

Tran Que Son [a,b], Tran Hieu Hoc [a,*], Nguyen Tien Quyet [c], Tran Bình Giang [d], Nguyen Ngoc Hung [e], Tran Thanh Tung [b], Tran Thu Huong [f]

[a] Department of Surgery, Hanoi Medical University, Hanoi, Viet Nam
[b] Emergency Center (A9), Bachmai Hospital, Hanoi, Viet Nam
[c] Organ Transplantation Center, Vietduc University Hospital, Hanoi, Viet Nam
[d] Director of Laparoscopic Surgical Centre, Emergency Abdominal Surgery Department, Viet Nam
[e] Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Bach Mai Hospital, Hanoi, Viet Nam
[f] Department of pharmacy, Bachmai Hospital, Hanoi, Viet Nam

ARTICLE INFO

Keywords:
Results
Laparoscopic
Periampullary tumours
Laparoscopic-assisted pancreatoduodenectomy
Whipple procedure

ABSTRACT

Introduction: Minimally invasive pancreaticoduodenectomy is a technically complex technique, that is being used to treat periampullary malignancy. We provide our experience with laparoscopic-assisted pancreaticodu odenectomy (LAPD) with statistics on the outcomes of periampullary cancer patients.

Material and method: Thirty patients underwent surgery between June 1, 2016 and May 30, 2020, with 21 undergoing classical PD and 9 undergoing pylorus-preserving pancreaticoduodenectomy (PPPD). Prospectively gathered data on surgical outcomes and long-term oncological results are given.

Results: The median operative time was 277.5 min (range, 258.7–330 min), and the median intraoperative estimated blood loss was 319.5 mL (range, 241.2–425 mL). The rate of conversion to OPD, surgical reintervention, and mortality was 20%, 13.3%, and 10% respectively. Cumulative surgery-related morbidity was 33.4%, including bleeding (n = 4), severe POPF (n = 4), biliary fistula (n = 1), DGE (n = 2), and intestinal obstruction (n = 1). Pathologic diagnoses were AoV cancer (n = 23), distal CBD cancer (n = 4), PDAC (n = 2), and AoV NET (n = 1). The mean survival time of the LAPD group was 29.9 months. The long-term survival time of the N0 group was 36.8 months, which was significantly longer than that of the N1 group. The long-term survival times of stages I–B, II-A, and II-B were 36.9, 26.5, and 15.7 months, respectively (p = 0.016).

Conclusion: LAPD has a high rate of conversion to OPD, morbidity, and mortality. However, LPD is feasible technique for highly selected patients. Lymph node metastasis and stage of disease are the risk factors for long-term survival.

1. Introduction

Most of tumours that develop in the periampullary of the Vater region are malignant. Since Whipple et al. originally described pancreaticoduodenectomy (PD) in 1935, it has developed into the preferred therapy for periampullary illness needing resection [1]. Survival is determined by the type of tumour, its location, and the stage of the disease. Ampullary of Vater (AoV) and duodenal cancer have a favourable prognosis, with a median survival time of 4–5 years. Cholangiocarcinoma has a median survival time of approximately 3 years, and pancreatic cancer has a median survival time of approximately 1 year following PD [2,3].

Due to the numerous advantages of laparoscopic surgery over conventional open surgery, it is frequently used to treat a variety of digestive issues. However, laparoscopic pancreaticoduodenectomy (LPD) remains the most challenging procedure in laparoscopic surgery, not only due to the complexity of the surgical method and reconstruction of the gastrointestinal tract but also due to the high number of potential

☆ Tran Que Son and Tran Hieu Hoc contributed equally to this work either as first authors.

* Corresponding author. Tran Hieu Hoc – Hanoi Medical University, 1 Ton That Tung Street, Khuong Thuong Ward, Dong Da District, Hanoi city, Viet Nam.
E-mail address: tranhieuhoc.hmu@gmail.com (T.H. Hoc).

https://doi.org/10.1016/j.amsu.2021.102742
Received 25 July 2021; Received in revised form 13 August 2021; Accepted 15 August 2021
Available online 27 August 2021
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morbidities and mortality. Many researchers are interested in the advantages of LPDs, such as less blood loss, postoperative pain relief, early movement, and short hospital stays. However, the benefits of LPD over open surgery are still not clear because the indications for surgery have been restricted (such as tumours at an early stage, small size, and no major vascular invasion). The incidence of complications and conversion to open pancreaticoduodenectomy (OPD) is still frequent. Some complications, such as postoperative pancreatic fistula (POPF) and severe postpancreatoduodenectomy haemorrhage (PPH), can be fatal in rare cases. As a result, this procedure is performed only in tertiary care hospitals by surgeons who are proficient in both open and laparoscopic surgery [4–7].

Total laparoscopic pancreaticoduodenectomy (TLPD) remains a complex and difficult procedure in Vietnam due to technical and equipment restrictions. Therefore, the number of patients receiving surgery is negligible, and there are no international reports. Due to the complexity of this operation, we initially evaluated its effectiveness using LAPD with a preoperative selection of minor tumours, early stage, and good patient condition.

This prospective review aimed to analyse the outcomes of 30 cases of LAPD performed for cancer treatment. The paper's results will serve as a great resource and will be extremely beneficial for surgical institutions in the preliminary phase of the LPD training curve.

2. Methods and materials

2.1. Patient population

Between January 2000 and May 2020, 535 patients underwent PD at Bachmai Hospital, Hanoi, Vietnam. Of these patients, 30 consecutive patients were treated with LAPD for periampullary Vater malignancy from June 1, 2016, to May 30, 2020.

Inclusion criteria: A prospective study database was performed. The selection criteria were patients with small periampullary cancer (<4 cm) without vascular invasion, body mass index (BMI) < 30.0 kg/m^2, and no comorbidities eligible for LAPD (ASA I or II). Resectability criteria following the National Comprehensive Cancer Network (NCCN) guidelines were utilized [8]. The inclusion criterion for this study was resection performed for malignant disease on final histopathology (30 cases).

Exclusion criteria: Any cases who had a history of major upper abdominal surgery; patients with other combined cancers; and patients with advanced-stage and benign diseases were excluded from the study (6 cases).

2.2. Data collection

Routine preoperative evaluations, including blood tests, abdominal computed tomography (CT) scans, magnetic resonance cholangiopancreatography (MRCP), upper GI endoscopy and/or endoscopic ultrasound (EUS), were performed to clearly define the tumour location. Demographic data collected included age, sex, comorbidities, body mass index, indication for surgery, and ASA score. Operative details included operative time, estimated blood loss, packed red blood cell transfusion, complications during surgery and type of pancreatic anastomosis. Postoperative factors included the day return to diet, hospitalization, morbidity, and mortality**.** Pancreas-specific complications were assessed and graded according to the recommendations of the International Study Group on Pancreatic Surgery (ISGPS).

2.3. Operative techniques

All patients were treated by a team of digestive and gastro-hepatobiliary surgeons with more than 30 OPDs experienced by each person at Bachmai Hospital. In all cases, PPPD or the classic Whipple procedure was performed using pancreaticojejunostomy (PJ) anastomosis.

In LAPD, patients were placed in a supine position, and 5 to 6 trocars were placed in a U-shape towards the hepatobiliary tract (Fig. 1). Our technique consists of two phases. **The first phases** of LAPD involve laparoscopic mobilization, organ dissection, lymph node transection (around the hepatoduodenal ligament, around the common hepatic artery, and on the right side of the SMA), and specimen removal. This technique following "clockwise" dissection: The duodenum is elevated from the retroperitoneum with the Kocher manoeuvre **(Video S0)**. The gastroduodenal artery (GDA) is ligated and divided at its origin by Ligasure or Lapro-Clips, with dissection of the lymph nodes along the common and separate hepatic arteries. The duodenum is transected 2–3 cm distal to the pylorus when the duodenum is not involved; otherwise, the antrum is divided using Ligasure or Hamonic ShearTM (Ethicon Endo-Surgery). The jejunum is divided 10–15 cm distal to the duodenojejunal flexsure. The proximal jejunal and duodenal vessels are ligated **(Video S1)**. A retropancreatic tunnel is created between the dorsal surface of the pancreas and the superior mesenteric vein (SMV). After the pancreatic neck is separated from the SMV posteriorly, parenchymal transection is performed with ultrasonic shears and endoscissors, followed by dissection of the uncinate process and mesopancreas (Fig. 2a and b). Finally, cholecystectomy and transected distal CBD are performed, and hepatoduodenal ligament lymph nodes are dissected (Fig. 3). **The second phase** is followed by reconstruction of three anastomoses via laparoscopy or a small upper midline incision (5–8 cm) (Fig. 1). Various techniques for the creation of PJ, hepaticojejunostomy and gastrojejunostomy are utilized in OPD based on the surgeon's preference and judgement during surgery (Fig. 2c), **(Video S2)**. Pathologists with over 5 years of experience examined the macroscopic and histopathology of the pancreaticoduodenal mass (Figs. 2d and 3)

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amsu.2021.102742.

2.4. Follow-up

The drained fluid volume and characteristics were recorded. After a progressive decrease in amylase concentration in the drainage with an amount less than 100 cm^3 and no indications of POPF or intraabdominal infection, the drain was withdrawn for at least 5 days. From the fourth postoperative day, patients were allowed to eat and drink liquids. Considerations for discharge were fine condition, tolerable pain with oral analgesics, and proper resumption of oral diet. Patients returned to the outpatient department 30 days after discharge to evaluate their general condition, withdraw the other drains (bile duct or pancreatic duct drain) and then every 3–6 months for a health checkup. Histopathology was used to establish the postoperative chemotherapy regimen.

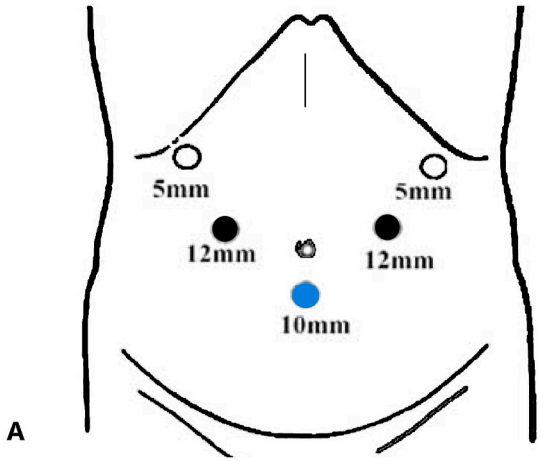

Fig. 1. The trocar positions.

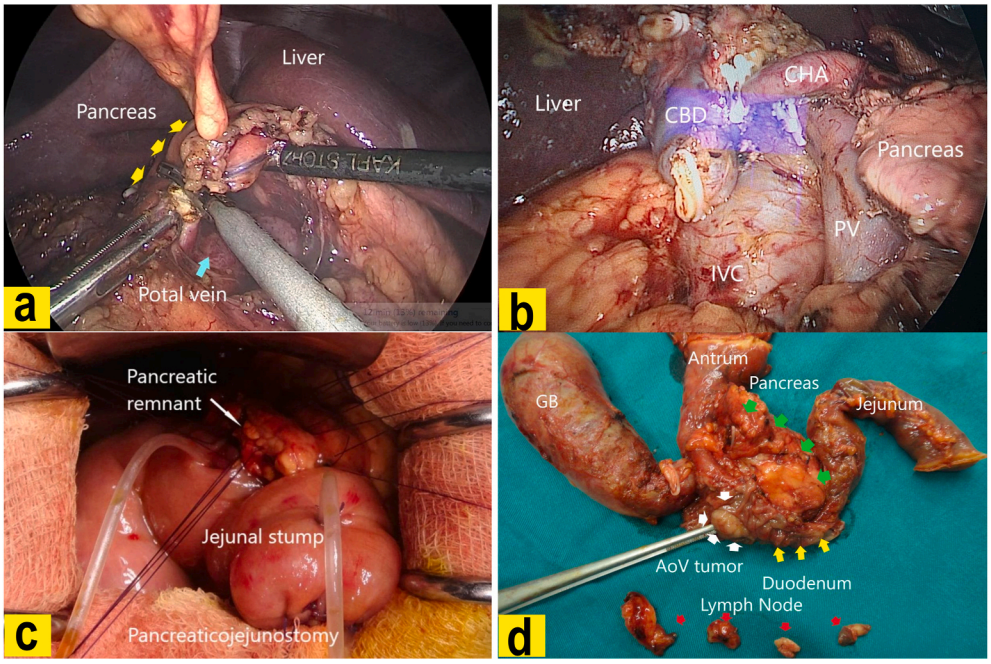

Fig. 2. The first phases of LAPD involve laparoscopic mobilization, organ dissection, lymph node transection. **a**, a tunnel was dissected posterior to the pancreatic neck and the pancreatic transection was made on the neck. **b**, completed pancreaticoduodenal dissection. **c**, two-layer duct-to-mucosa pancreaticojejunostomy using hand technique through abdominal wall incision with 5–8 cm length. **D**, pancreaticoduodenal mass (ampullary of Vater cancer – white arrow; pancreatic head – green arrow; duodenum – yellow arrow; lymph nodes – red arrow). IVC inferior vena cava, PV portal vein, CHA common hepatic artery, CBD common bile duct. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

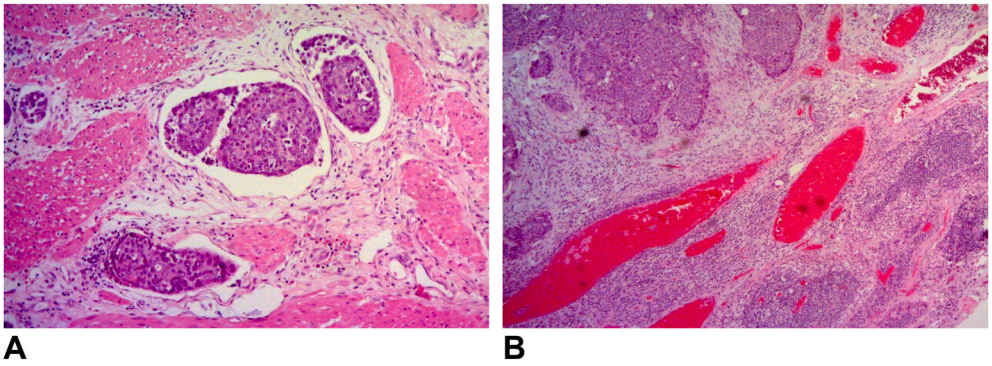

Fig. 3. Histopathology of the pancreaticoduodenal mass.

AoV cancer and distal CBD cancer at T3-4 or N1 were treated with gemcitabine alone (papillary cancer), capecitabine alone (biliary cancer), or FOLFOX with 5-FU, oxaliplatin, and leucovorin (enteric type). Patients diagnosed with pancreatic cancer were treated with one of three chemotherapy regimens: GEMOX (gencitabin, oxaliplatin), FOLFIRINOX (5-FU, irinotecan, oxaliplatin), or Gem-Abraxan (gemcitabine, paclitacel).

At least once a year, patients were subjected to a thorough clinical examination, blood tests including CA 19-9, and imaging in the form of an abdominal CT scan. The last follow-up time was on May 30, 2020. On the day before the last recorded follow-up, the data for missing persons were processed for survival analysis and were considered alive.

2.5. Definitions

The operational time for LAPD was from the insertion of the first trocar to skin closure. Estimated blood loss (EBL) was calculated from skin incision to final closure of skin. Quantity = (total fluid in the aspirator + weight of gauze sponges and meches with blood) – (total amount of washed serum + number of gauze sponges x P_1 + number of meches x P_2). (P_1 and P_2 are the weight (grams) of gauze sponges and meches, respectively). Postoperative blood transfusion was from the last skin closure to hospital discharge. A consultant surgeon investigated the texture (soft vs. firm) of the resected material based on the margin. The pancreatic duct diameter was measured to be < 3 mm or more at the position at which the portal vein passes posterior to the pancreatic neck. Conversion was defined as the transition to open surgery before dissection of the meso-pancreatic tissue, regardless of the level of the laparotomy.

Postoperative complications were evaluated according to the Clavien-Dindo classification system [9] and included POPF [10], bile leakage (BL) [11], and PPH [12]. Delayed gastric emptying (DGE) was established by the American College of Surgeons (ACS NSQIP). The definitions were assigned grade B or C by the ISGPS [13,14]. Reoperation was defined as a secondary operation due to severe complications within 30 days following LAPD.

Bottle of albumin = Human Albumin Baxter 20% 50 mL. Bottle of lipid = Lipofundin MCT/LCT 10% Brawn (c/250 ml) 10 S. Bottle of aminoplasma = Aminoplasmal® B. Braun 5% E 500 mL. Three Chamber Bags = Liquid Smofkabiven 1026 ml (For Clinical, Fresenius Kabi) or NuTRIflex® Lipid plus 1250 mL (B. Braun) or Combilipid Peri Injection 1440 ml (Choongwae Pharma Corp, Korea). Pain relief medication = Paracetamol Kabi 1000/100 mL (Fresenius Kabi, Bidiphar, Vietnam) and/or Nefopam 20 mg/2 mL (Vidipha, Vietnam) and/or morphine hydrocloride 10 mg/ml, Vidipha, Vietnam). Sandostatin = Sandostatin® (octreotide/octreotida) 0.2 mg/mL, Novatis Pharma. Antibiotic

administration (cephalospotin II, III 1 g and/or metronidazole Kabi 500 mg/10 mL and/or carbapenem (imipenem, meropenem, ertapenem)).

Morbidity and mortality were defined as any problems or deaths occurring during or within 90 days following surgery.

The final pathologic diagnosis was determined using the AJCC Cancer Staging Manual, which included staging, the total number of harvested lymph nodes, the resection margin status, lymph node invasion status, and mass size [15]. R0 resection assumed that no evidence of cancer was discovered in any of the resection margins, whereas R1 resection indicated the presence of malignancy in at least one of the resection margins on a permanent section [15].

The quality of life (QoL-C30) of cancer patients participating followed the criteria of the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30, version 3.0–2001) and included 4 levels: excellent (90–100 pts), good (80–90 pts), average (70–80 pts) and bad (<70 pts) [16]. Overall survival (OS) was defined as the time interval between the date of surgery and the date of death. Long-term survival was described using the Kaplan-Meier method.

2.6. Statistical analyses

Categorical data were summarized using the number and percentage of cases. Median and IQR, or percentages, are used to convey values. Mean and standard deviation (SD) are used for continuous variables. The OS of periampullary cancer patients was determined using the Kaplan-Meier algorithm, and group comparisons were assessed using the log-rank test, which was statistically significant when $p < 0.05$. All statistical analyses were performed using SPSS 20.0 software (SPSS Inc., Chicago, IL). All patients were informed about the procedure, risks, and advantages of LPD and OPD. Written informed consent was obtained from all patients in our study, which was approved by the Hanoi Medical University Institutional Ethical Review Board, Vietnam (Decision no. 04/HĐĐĐ ĐHYHN, on January 6, 2017).

This study is reported in line with the STROCSS 2019 criteria [17].

3. Results

A total of 30 LAPDs were carried out. There were 17 males and 13 females with a mean age of 53.7 years (range, 37 to 68 y) and a median body mass index of 20.9 kg/m^2 (range, 19.7–22.4). All patients had no important organ dysfunctions. The patient demographic characteristics were collected and analysed as shown in Table 1. In 6 cases (20%), there was a conversion from planned hybrid laparoscopy to OPD. Causes for conversion are listed in Table 2. The most common cause was vascular complications, including uncontrollable bleeding (n = 3) and difficult dissection (n = 3). The median operative time was 277.5 min (range, 258.7–330 min). The median estimated blood loss was 319.5 mL (range, 241.2–425 mL). The intraoperative details are given in Table 3

In our study, overall complications were 33.4%. Complications were classified following Clavien-Dindo classification, in which severe complications ≥ III accounted for 13.4%. The number of patients with more than one complication was 3 patients (10%) (including one patient with POPF + DGE; one patient with Meckel hernia + gastrojejunostomy stenosis; and one patient with PJ anastomosis bleeding + POPF). Four instances required surgical reintervention related to intra-abdominal haemorrhage (Patient No. 14), bile leakage (Patient No. 23), bleeding from the PJ anastomosis (Patient No. 28), and Meckel's diverticulum (1st time) + gastrojejunostomy stenosis (2nd and 3rd times) (Patient No. 29). At three months following surgery, 26 patients were evaluated for their QoL-C30 (except for 3 patients who died within 30 days and 1 patient who lost information). The results indicated most patients were rated excellent (73.1%) and good (11.5%) (Table 4). AoV cancer was most cases (76.7%). The oncologic information of the 30 patients with tumours is shown in (Table 5). The median size of the tumour was 14.5 mm. The resection margin free from disease was 93.3% on pathologic examination. The number of harvested lymph nodes was 15 (range, 11–17).

The mean duration of survival in this study was 29.9 months (Table 6). The survival probabilities at 1, 2, and 3 years were 65.8%, 62.1%, and 62.1%, respectively (Fig. 4A). The difference in long-term survival between pT2 and pT3 was not statistically significant (p = 0.560). However, regional lymph node metastasis (pN1) and cancerous

Table 1
Clinical characteristics and preoperative outcomes for LAPD groups.

Age, mean (SD)	53.7 ± 9.5
Sex, n (%) (Male/Female)	17 (56.7)/13 (43.3)
ASA, n (%) (I, II)	23 (76.7)/7 (23.3)
BMI, median (IQR), kg/m^2	20.9 (19.7–22.4)
CA 19-9, median (IQR)	101.1 (10.4–220.5)
Comorbidities, n (%)	
Diabetes	4 (13.3)
Hypertension	2 (6.7)
Cardiovascular	1 (3.3)
Chronic bronchitis	1 (3.3)
ENBD or PTCD, n (%)	5 (16.7)
Pancreatic duct width (≤3 mm), n (%)	19 (63.3)
Preoperative initial symptoms, n (%)	
Jaundice	26 (86.7)
Epigastric pain	3 (10)
Severe haemorrage	1 (3.3)
Method or technique, n (%)	
Pylorus-preserving PD	9 (30)
Classical PD (cPD)	21 (70)
Pancreaticojejunostomy anastomosis, n (%)	
Single-layer	15 (50)
Two-layer (Blumgart's anastomosis)	15 (50)
Pancreatic duct stent, n (%)	15 (50)
Hepaticojejunostomy, n (%)	12 (40)
Continuous suture/Interupted suture	26 (86.7)/4 (13.3)
Biliary drainage	12 (40)
Gastrojejunostomy	
Anterior-mesocolic/posterior-mesocolic	23 (76.7)/7 (23.3)
Continuous suture/interrupted suture	20 (66.7)/10 (33.3)

ASA American Society of Anaesthesiologists, BMI body mass index, CA 19-9 carbohydrate antigen 19-9, ENBD endoscopic nasal biliary drainage, PTCD percutaneous transhepatic cholangial drainage.

Table 2
Reasons for conversion to open surgery.

Reasons for conversion	Number of patients, n
Mesenteric jejunal artery bleeding	1
Superior mesenteric artery rupture	1
Gastroduodenal artery bleeding	1
Postoperative adhesion	1
Inflammatory intestinal adhesion post-acute pancreatitis	1
Inflammatory intestinal adhesion in tumour surrounding	1
Total	6

Table 3
Intraoperative and postoperative data of the LAPD.

OT, median (IQR), min	277.5 (258.7–330)
EBL, median (IQR), mL	319.5 (241.2–425)
Postoperative blood transfution, median (IQR), mL	500 (0–787.5)
Postoperative LOS, median (IQR), days	13 (12–18.2)
Albumin, median (IQR), bottles	4 (3 - 7)
Aminoplasma, median (IQR), bottles	11 (11 - 16)
Lipid, median (IQR), bottles	8 (5.5–13.5)
Three Chamber Bags, median (IQR), bags	7.5 (5 - 10)
Antibiotic, median (IQR), days	12 (9 - 18)
Sandostatin, median (IQR), days	8 (6 - 12)
Pain relief medication, median (IQR), days	4 (3.75–6)
Oral intake, median (IQR), days	5(5 - 6)
Withdraw abdominal drainage, median (IQR), days	6 (5.75–7.25)
Withdraw biliary drainage, median (IQR), days	30 (17.5–30)

SD Standard Deviation; PD pancreaticoduodenectomy; OT operative time, EBL estimated blood loss, LOS length of hospital stays.

Table 4
Short-term outcomes by operative method.

Grade B/C POPF, n (%)	4 (13.4)
DGE, n (%)	2 (6.7)
Postpancreatectomy haemorrhage PPH, n (%)	2 (6.7)
Abdominal bleeding	1 (3.3)
Gastrojejunostomy anastomosis bleeding	1 (3.3)
Biliary fistula, n (%)	1 (3.3)
Postoperative intestinal obstruction, n (%)	1 (3.3)
Overall morbidity, n (%)	10* (33.4)
Number of patients with more than 1 complication, n (%)	3 (10)
Clavien – Dindo, n (%), n (%)	
Grade I-II	4 (13.4)
Grade ≥ III	6 (20)
Re-operation, n (%)	4 (13.3)
30-Day mortality, n (%)	3 (10)
Quality of life (QoL)	26 (100)
Excellent	19 (73.1)
Good	3 (11.5)
Moderate	2 (7.7)
Poor	2 (7.7)

DGE delayed gastric emptying, POPF postoperative pancreatic fistula, PPH postpancreatectomy haemorrhage.

Table 5
Baseline characteristics of all pathologic results of the LAPD groups.

Pathology, n (%)	
AoV cancer	23 (76.7)
Pancreatic ductal adenocarcinoma	2 (6.7)
Distal common bile duct cancer	4 (13.3)
AoV NET (Grade 1)	1 (3.3)
TNM staging, n (%)	
T2N0M0	12 (40)
T2N1M0	5 (16.7)
T3N0M0	6 (20)
T3N1M0	7 (23.3)
Tumour differentiation, n (%)	
Well-differentiated	1 (3.3)
Moderately differentiated	26 (86.7)
Poorly differentiated	3 (10)
Lesion major diameter, median (range), cm	14.5 (12–16.5)
No. lymph nodes collected, median (IQR)	15 (11 - 17)
Node positive, n (%)	12 (40)
R0 resection, n (%)	28 (93.3)
AoV Ampulla of Vater, NET neuroendocrine tumour	

Table 6
Long-term survival in patients for periampullary of Vater manignancies

Factors	Number of patient (n)	Survival time (months)			p
		Mean	SD	95% CI	
LAPD patients	30	29.9	3.2	(23.6–36.4)	–
pT2	17	28.1	4.5	(19.3–37.1)	0.560
pT3	13	24.2	3.0	(18.3–30,1)	
pN0	18	36.8	3.5	(29.9–43.7)	0.012
pN1	12	15.7	3.1	(9.5–21.8)	
I–B staging	12	36.9	4.2	(28.6–45.2)	0.042
II–A staging	6	26.5	4.5	(17.6–35.3)	
II–B staging	12	15.7	3.1	(9.5–21.8)	

stage (as defined by TNM) are risk factors for long-term survival. Table 6 and Fig. 4B, C, D illustrate the extra survival time.

4. Discussion

Gargner and Pomp published the first successful LPD in 1994 [18]. This is an extremely difficult procedure, and the efficacy has not been proven to be superior to open surgery [7,19–21]. To accomplish LPDs, many authors mention a difficult learning curve [6,22].

Accurate selection of patients is essential for a safe and successful operation for LPD. Clinical reality suggests that there are several instances in which preoperative diagnosis is extremely difficult due to the invasiveness of the tumour, leaving the determination of the lesion margin impossible. Based on our preliminary experience, early ampullary adenocarcinomas and cholangiocarcinomas are most likely to enable a laparoscopic approach. Furthermore, patients with early pancreatic head carcinoma without vascular involvement and tumours smaller than 3 cm are candidates for laparoscopic surgery [6,23,24]. Some authors found that most periampullary and pancreatic head tumours can be treated with LPD, except in situations of severe comorbidities, numerous prior abdominal operations, borderline resectability, or vascular invasion. After a few years of practice, they discovered that obese individuals may also be treated with LPD [3,25,26].

Although the preoperative selection criteria are stringent (small tumour, no vascular invasion, pT2-T3), abdominal exploration is the initial step in determining the invasiveness and mobility the pancreatic head and duodenum.

This is the most essential method to determine whether the pancreatic duodenal mass can be removed through laparoscopy. First, we assessed the presence of peritoneal metastases. Has the tumour spread to the colonic mesentery? Next, we carefully opened the minor omentum to determine whether the longitudinal lymph nodes of the hepatic artery were large or small. Infiltrates should be seen along the hepatic peduncle and upper pancreatic border. From the right border of the duodenum, we performed the Kocher technique to determine the degree of tumour invasion into the inferior vena cava (IVC) and superior mesenteric vascular bundles (SMV, SMA). If the pancreatic duodenal tumour can be moved to expose the left renal vein, it can be separated laparoscopically. When adhesions to the pancreatic head are present, the Kocher procedure becomes more difficult; the superior pancreatic border is infiltrated; the hepatic peduncle is oedematous; the tumour is adherent to the colonic mesentery; the tumour infiltrates the SMV; and the procedure should be converted to OPD.

The anterior first approach is a well-established technique for PD that is now used in both laparoscopic and open surgery, as Sanjay summarized in 2012 [27]. Before resection, the arteries coming from the visceral celiac artery (for example, GDA) and SMA (for example, IPDA, JA1) were dissected and ligated. In this study, we reversed the sequence of the surgical steps. This method has several advantages, including less intraoperative blood loss, dredging lymph nodes around the great artery, ensuring radicalization, and enabling vascular transplantation.

The conversion rate to open surgery varies according to the authors, ranging from 0% to 40%, with an average of 9.1% [5,19,28,29]. The literature discusses several reasons for conversion to OPD, including tumour adhesion or invasion into the PV or SMV, bleeding from the PV, adhesion inflammation caused by acute pancreatitis, adhesion inflammation of the peritoneum, failure of the robotic surgery system, acidosis caused by the CO_2 pump, and damage to the hepatic artery. However, many cases are related to tumour adhesion to the peripancreatic vessel (PV, SMV, CHA) and uncontrolled bleeding following LAPD [5]. Six patients (20%) required conversion to OPD, three of which included vascular injuries (Table 2). Patient #1 bleeding from JA1 at the mesenteric arteries near the Treitz angle. Patient #6's SMA had ruptured. This was a very severe complication during mesopancreatic resection and group dissection of 14 lymph nodes. We needed to connect the distal SMA to the inferior abdominal aorta through anastomosis. There was bleeding from the GDA and pyloric arteries in patient #22. When the laparoscopic prognosis is uncertain, we suggest that open surgery should be performed to assure a safe procedure.

All three anastomoses were made by a 5–8 cm long abdominal incision. The rates of single-layer and two-layer PJ anastomosis are comparable. The pancreatic stump is extended approximately 1.5–3 cm in length to allow for anastomosis, thus avoiding bleeding or necrosis of the pancreatic remnant. The technique used to perform PJ anastomosis is determined by the surgeon's own opinions. If adapting a single layer, we utilize Safil 3.0 thread (B. Braun, Spain) and tighten the thread just

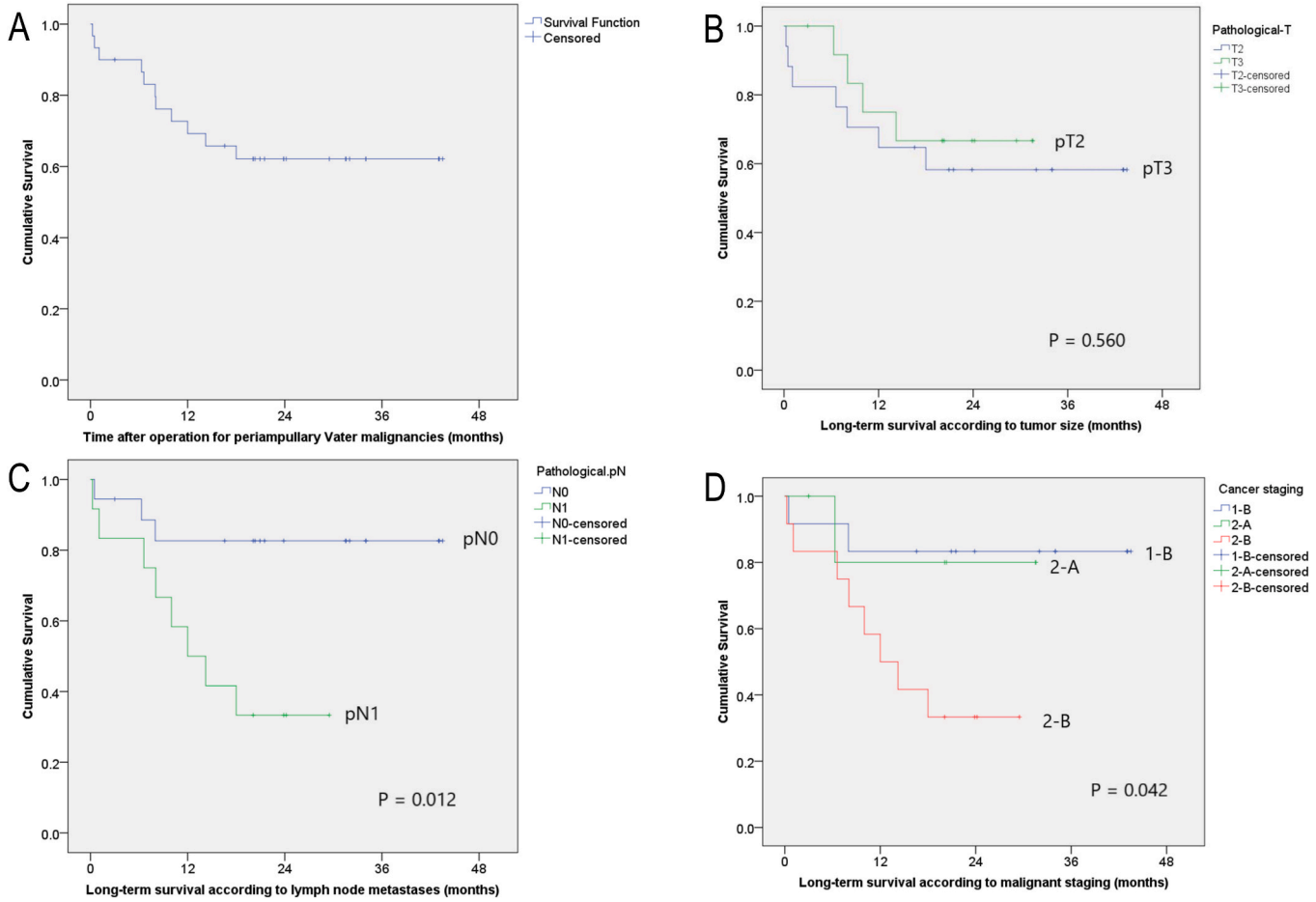

Fig. 4. Overall survival in patients with malignant disease. **A**, long-term survival for periampullary Vater malignancies; **B,** Overall survival according to tumour size; **C,** Overall survival according to lymph node metastases and **D,** overall survival followed to cancerous staging. p-value derived from the log-rank test.

enough to avoid tearing the pancreatic parenchyma, particularly in situations of soft parenchyma. We employ the modified Blumgart anastomosis technique developed by Fuji when splicing two layers [30]. Fang (2007), Lee (2013), and Zhu (2013) all support the pancreaticogastrostomy method because it is a safe method with low mortality and a complication rate ranging from 0 to 3.7% [1,31,32]. However, Peng (2002), Kleespspies (2009), and Fujii (2014) prefer PJ anastomosis and all report beneficial results, with pancreatic fistula rates ranging from 2.5 to 36% depending on the kind of anastomosis performed [30,33,34].

In almost all cases, we used PDS TM 4-0 (Ethicon, Johnson & Johnson). Hepatojejunostomy is challenging in individuals with abdominal fat and a deep surgical field. Because all three anastomoses were on the same small intestine loop, the surgeons still drained both the pancreatic duct and biliary drainage outside to decrease anastomosis pressure. However, some studies show that biliary drainage is unnecessary because it causes dehydration, electrolyte loss, and bile leakage following draining [35]. Nutrition is critical for the patient following PD. Intravenously, nutritional preparations were supplemented with blood transfusions and fresh frozen plasma. The median duration of oral refeeding was five days (Table 3). Hwang's study demonstrated the efficacy of early enteral feeding, a shorter hospital stay (25.9 8.5 vs 32.3 16.3 days, p = 0.01), a lower rate of anastomosis (1.2% vs 16%, p = 0.001), and a lower rate of reoperation (3.7% vs 20%, p = 0.01) than the other group [36]. The median duration of hospitalization was 13 days (range, 12–18.2), which is comparable to some studies in Asia (13 days) and North America (9.4 days), but less than a finding in Europe (21.9 days) [5].

The most common surgical complication was POPF, followed by DGE, PPH, fluid collection or abscess, wound infection, and bile leakage. The total POPF rates vary substantially between 3.8% and 50% observed in all systematically reviewed studies. Grade C POPFs are the primary causes of reoperation and death [37,38]. In Boggi's study from Asian, European, and American studies, the rate of pancreatic fistula was 21.6% (ranging from 17.7% to 24.4%), and that of mortality was 2.1% (1.1%–3.4%). There was no difference in the rates of conversion to OPD, overall complications, POPF or mortality in studies of ≥30 cases and 29 LPDs [5]. In this research, the total complication rate was 33.4%, and problems occurred in all three anastomoses. Severe POPF, DGE, and PPH were 13.4%, 6.7%, and 6.7%, respectively. Other potential risks include intra-abdominal haemorrhage (3.3%), bile leakage, and intestinal obstruction after surgery.

Two cases of severe POPF resulted in death. The initial instance of POPF drained a significant amount of necrotic pancreatic juice up to the third week. The patient died, most likely because of peritonitis or toxic septic shock. The second case of pancreatic fistula after surgical intervention occurred because of anastomosis haemorrhage. Although the patient was kept alive until the 32nd day, bile and pancreatic juice continued to flow through the drainage and abdominal incision. We inserted suction equipment into the subhepatic location through the incision. The volume of digestive juices consumed each day was 600–1000 mL; the patient's condition deteriorated due to multiorgan failure and death. We discovered that if the pancreas's large volume increases, it is essential to perform reoperation [39].

Senthilnathan's rate of reoperation was 3.84% [25], Deichmann's rate was 6.5% [40], and Wellner's rate was 21% [19]. In this study,

reoperation occurred at a rate of 13.3% (4 patients), which is significantly higher than that in previous studies worldwide. Severe intra-abdominal haemorrhage, peritonitis due to bile leakage anastomosis, bleeding at the PJ anastomosis, and constriction of the gastro-enteric anastomosis are all indications for these patients.

The postoperative mortality in the LPD case series was in the range of 1.6%–8%. Three patients died in the first 30 days (10%). Other case series had varying mortality rates of 1.53% (Senthilnathan et al. [25]), 1.5% (Kendrick and Cusati [4]), and 5.7% (Asbun and Stauffer [41]). Postoperative haemorrhage, pulmonary complications, myocardial infarction, and sepsis have all been implicated as important causes of mortality.

Chapman reported a median tumour size of 1.9 cm, an average of 19 lymph nodes removed, and a 100% R0 resection status [42]. Croome et al. reported a median tumour size of 3.3 cm and a median number of 21.4 lymph nodes harvested with R0 resection possible in 77.8% of patients [3]. Wellner et al. found a median tumour size of 2.5 cm and a median number of 15 lymph nodes removed, with 86% of resections being margin-free [19]. Although several other studies have reported 100% R0 resections, very few of them have analysed uncinate margin and SMV margin positivity, which are critical aspects of pathological evaluation to achieve oncological radicality.

On May 30, 2020, 13 patients were alive (54.2%), 10 patients died (41.6%), and one patient lost information. The laparoscopic support group had an average survival duration of 29.9 months. Lymph node metastases and disease stage are independent predictors of postoperative survival. Croome found no difference in mean survival time between groups of patients with pancreatic cancer following laparoscopic or open surgery (23 versus 21.8 months, $p = 0.12$); however, the laparoscopic surgery group had a longer disease-free survival ($p = 0.03$) [3]. This evidence is similar to Dellito's and Chapman's studies [42,43]. Tumour size, R1, lymph node metastasis, and late chemotherapy time beyond 3 months are risk factors for reducing survival time [3]. Local recurrence and distant metastases are typically the cause of mortality [23]. According to Deichmann et al., the group of patients who begin chemotherapy early is a predictive indicator for survival extension [40].

This clinical research study had some limitations. The number of patients was limited, and the research ended at the level of description without comparison to the control group (OPD group). Despite our efforts and ongoing attempts to enhance oncological radicality, pancreatic cancer continues to have a poor prognosis. Many patients are not surgical candidates and have a median survival of a few months. In the future, it will be important to assess the survival benefit of chemotherapy or surgery alone and suggest follow-up interventions as well as determine the reasons for death. A randomized controlled trial vs an open surgery group was conducted to determine the efficacy of laparoscopic support throughout the first 30 operations.

5. Conclusion

Our study revealed that LAPD has a high rate of complications, conversion to OPD, and mortality at the first 30 patients. However, LAPD is feasible method and can provide acceptable oncological results with careful patient selection for the management of periampullary malignancies. Experience, learning curve, and high-volume centre might have influenced the results.

Acknowledgements

We many thanks to Hung TM, Truong TV, Anh H, Quang N.V, Long VD, Kien CT who participated in surgery.

We also many thanks the AJE Team (www.aje.com) for editing a draft of this manuscript.

Abbreviations

PD	Pancreaticoduodenectomy
PPPD	Pylorus-preserving pancreaticoduodenectomy
OPD	Open pancreaticoduodenectomy
LPD	Laparoscopic pancreaticoduodenectomy
TLPD	Total laparoscopic pancreaticoduodenectomy
LAPD	Laparoscopic-assisted pancreaticoduodenectomy
POPF	Postoperative pancreatic fistula
PPH	Postpancreatectomy haemorrhage
DGE	Delayed gastric emptying
CBD	Common Bile Duct
PDAC	Pancreatic ductal adenocarcinoma
AoV	Ampullary of Vater
NET	Neuroendocrine tumour
PDAC	Pancreatic ductal adenocarcinoma
GI	Gastrointestinal
AJCC	The American Joint Committee on Cancer
IPDA	Inferior Pancreaticoduodenal Artery
JA1	The first jejunal artery
SMV	Superior mesenteric vein
PV	Portal vein
CHA	Common hepatic artery
IQ	Interquartile Range

Provenance and peer review.

Not commissioned, externally peer-reviewed.

Declaration of interest statement

Authors declare no conflict of interest.

Ethical approval

Written informed consent was obtained from all the patients in our study, which was approved by Hanoi Medical University Institutional Ethical Review Board, Vietnam (Decision no. 04/HĐĐĐ ĐHYHN, on January 01, 2017).

Please state any sources of funding for your research

None.

Author contribution

Tran Que Son: main surgeon, conceived the idea, designed the study, conducted literature search, data collection, data analysis & interpretation, drafted the manuscript, and created the illustrations. **Tran Hieu Hoc**: main surgeon, conceived the idea, designed the study, conducted literature search, data collection, data analysis & interpretation, drafted the manuscript, and created the illustrations. **Tran Thu Huong**: data analysis & interpretation, and edit English language. **Tran Binh Giang**: conceived the idea, conducted literature search. **Nguyen Tien Quyet**: conceived the idea, conducted literature search. **Nguyen Ngoc Hung**: study concept, interpretation. **Tran Thanh Tung:** study concept, interpretation. All authors read and approved the final manuscript.

Please state any conflicts of interest

Authors declare no conflict of interest.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

1. Name of the registry: researchregistry.com
2. Unique Identifying number or registration ID: researchregistry6999
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#home/registrationdetails/60fcde432f84c1001ee94bc6/

Guarantor

Assoc. Prof. Ph.D. Tran Hieu Hoc.

Appendix. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amsu.2021.102742.

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