



저작자표시 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.
- 이차적 저작물을 작성할 수 있습니다.
- 이 저작물을 영리 목적으로 이용할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#) 

의학석사 학위논문

Laparoscopic assisted
pancreaticoduodenectomy
: Experience with 90 consecutive
cases and analysis of the learning
curve

복강경 보조하 췌십이지장 절제술
: 90례의 사례 분석과 학습 곡선 분석

2018 년 2 월

서울대학교 대학원

임상의과학과

김 성 호

Laparoscopic assisted
pancreaticoduodenectomy
: Experience with 90 consecutive
cases and analysis of the learning
curve

지도 교수 한 호 성

이 논문을 의학석사 학위논문으로 제출함
2017 년 10 월

서울대학교 대학원
임상의과학과
김 성 호

김성호의 의학석사 학위논문을 인준함
2018 년 1 월

위 원 장 황 진 혁 (인)

부위원장 윤 유 석 (인)

위 원 한 호 성 (인)

Abstract

Laparoscopic assisted pancreaticoduodenectomy: Experience with 90 consecutive cases and analysis of the learning curve

Sungho Kim

Department of Clinical Medical Sciences

The Graduate School

Seoul National University

Introduction

Recent advances in minimally invasive techniques have led to increased efforts and interest in laparoscopic pancreatic surgery. Laparoscopic distal pancreatectomy is a widely accepted procedure for left-sided pancreatic lesions, but the adoption of laparoscopic pancreaticoduodenectomy for other lesion types has been hindered by concerns regarding the technical complexity of laparoscopic reconstruction. Laparoscopy-assisted pancreaticoduodenectomy (LAPD), in which pancreaticoduodenal resection is performed laparoscopically while reconstruction is completed via a small upper midline minilaparotomy, combines the efficacy of the open approach with the benefits of the laparoscopic approach. The purpose of this study

was to report our experience with LAPD and define the learning curve.

Methods

Ninety patients with benign and malignant periampullary lesions who underwent LAPD by the same surgeon between March 2003 and May 2017 were reviewed retrospectively. The clinicopathologic variables were prospectively collected and analyzed. The learning curve for LAPD was assessed using the cumulative sum (CUSUM) and risk-adjusted (RA)-CUSUM methods.

Results

The most common histopathology was pancreatic ductal adenocarcinoma (n = 27, 30.0%); followed by carcinomas of the ampulla of Vater (n = 16, 17.8%) and common bile duct (n = 14, 15.6%); and intraductal papillary mucinous neoplasm (n = 13, 14.4%). The median operation time was 556 (range, 300–865) minutes, and the median estimated blood loss was 546 (range, 50–2000) ml. The mean hospital stay was 21.4 days. Complications developed in 33 patients (36.7%), of whom 12 (13.2%) had clinically significant pancreatic fistula (International Study Group on Pancreatic Surgery grade B/C). Based on the CUSUM and RA-CUSUM analyses, the learning curve for LAPD was divided into three phases: phase I (cases 1–26), phase II (cases 27–69), and phase III (cases 70–90). The surgical indications were significantly different between phases I and II ($p = 0.001$).

Conclusions

LAPD is technically feasible and safe for select patients. This procedure incorporates the benefits of both the open and the minimally invasive laparoscopic approaches, and may be a stepping stone for transition from open to pure pancreaticoduodenectomy.

Keywords: laparoscopy, pancreaticoduodenectomy, learning curve

Student number: 2016-22224

Table of Contents

| | |
|--|----|
| Introduction | 1 |
| Methods..... | 3 |
| Study population..... | 3 |
| LAPD surgical procedure | 4 |
| Statistical analysis | 6 |
| CUSUM and RA–CUSUM analyses | 7 |
| Results | 8 |
| Baseline characteristics..... | 8 |
| Operative outcomes..... | 8 |
| Oncologic outcomes of cases of invasive periampullary malignancy | 9 |
| Complications | 9 |
| Analysis of the learning curve | 10 |
| Discussion | 22 |
| Conclusion | 27 |
| References | 28 |
| Abstract in Korean..... | 33 |

List of Tables

| | |
|--|----|
| Table 1. Demographics and clinical findings of patients who underwent laparoscopy–assisted pancreaticoduodenectomy | 12 |
| Table 2. Cases of conversion to the open procedure | 14 |
| Table 3. Perioperative outcomes of 58 patients with periampullary malignancies | |

| | |
|---|----|
| | 15 |
| Table 4. Postoperative complications | |
| | 16 |
| Table 5. Comparisons of preoperative parameters among the phases | |
| | 17 |
| Table 6. Comparisons of perioperative parameters among the phases | |
| | 18 |

List of Figures

| | |
|---|----|
| Figure 1. Cumulative sum plot for operation time | |
| | 20 |
| Figure 2. Risk-adjusted cumulative sum plot for operation failure | |
| | 21 |

Introduction

Surgery is currently the gold standard of treatment for pancreatic head tumors, which are a leading cause of cancer-related deaths worldwide. The first pancreaticoduodenectomy was described by Whipple et al. [1] as a highly complex, challenging, and demanding abdominal procedure that can be safely performed only by highly expert surgeons. In addition, serious postoperative complications frequently develop in association with this complex procedure, ranging from those that prolong hospital stay (such as delayed gastric emptying [2]) to those that are potentially life threatening (such as postpancreatectomy hemorrhage [3] and pancreatic fistula [4]).

The field of minimally invasive surgery has expanded dramatically since 1994, when Cuschieri [5] reported the first laparoscopic distal pancreatectomy and Gagner and Pomp [6] reported the first laparoscopic pancreaticoduodenectomy. Laparoscopic distal pancreatectomy is now considered a safe and feasible technique and has therefore been widely adopted for lesions of the pancreatic body and tail [7-10]. However, even though minimally invasive pancreaticoduodenectomy was reported as early as 1994, most surgeons have been reluctant to perform the procedure.

Pancreaticoduodenectomy poses a particular challenge. During the procedure, extensive retroperitoneal dissection is required around anatomically complex and hazardous structures, with prolonged reconstruction that includes three technically demanding anastomoses. With regard to the surgical technique, there are two trends in laparoscopic

pancreatoduodenectomy, pure laparoscopic pancreatoduodenectomy [11-14] and the hybrid approach (laparoscopy-assisted pancreaticoduodenectomy; LAPD), in which the dissection is performed laparoscopically and reconstruction is conducted via a small laparotomy [15-19].

To our knowledge, few studies have reported experience with LAPD. The present study examined our experience with LAPD, which has the advantages of minimal invasiveness and safe formation of biliary and gastro-jejunal anastomoses.

Methods

Study population

A total of 90 patients who had undergone LAPD for pancreatic head tumor at Seoul National University Bundang Hospital, South Korea between March 2003 and December 2016 were enrolled in this study. A retrospective chart review was performed on prospectively and retrospectively collected data, including clinical, operative, and pathologic information.

The preoperative variables examined included sex, age, body mass index, comorbidities, and the American Society of Anesthesiologists (ASA) score. The operative variables included the type of procedure, estimated blood loss (ml), operation time (min), total packed red blood cells transfused during the operation, resection margin status, and number of lymph nodes harvested. Postoperative complications were collected and scored according to the Clavien–Dindo classification [20]. Readmission and complications occurring up to 90 days after surgery were recorded.

Pancreatic fistula [4], delayed gastric emptying [2], and post-pancreatectomy hemorrhage [3] were defined according to the International Study Group of Pancreatic Surgery (ISGPS) definitions. Patient selection for the laparoscopic procedure was based on the patient's preferences. The advantages, disadvantages, and possible complications were clearly discussed with the patients. Patients with lesions that were likely to require major vessel resection (portal vein and superior mesenteric vein) or who had a risk of positive resection margins were not offered LAPD. All patients

underwent abdominal computed tomography 5 days after surgery to evaluate possible complications.

This retrospective study conformed to the ethical guidelines of the Declaration of Helsinki. The Investigational Review Board or Ethics Committee of Seoul National University Bundang Hospital approved the study.

LAPD surgical procedure

The patient is placed in the lithotomy position modified with the reverse Trendelenburg position to expose the operative field. The operator and scrub nurse stand to the right of the patient, while the first assistant stands on the opposite side, and the second assistant, who holds the laparoscope, is positioned between the legs of the patient. An open technique is used to establish the pneumoperitoneum through a 12-mm umbilical trocar. Pneumoperitoneum is maintained at a pressure below 13 mmHg. If no contraindications for resection are found after inspection of the abdominal cavity, four additional trocars are inserted in a semicircular pattern centered on the head of the pancreas. The gastrocolic ligament is divided using an energy device to visualize the anterior surface of the pancreas, avoiding injury to the colon. The right gastroepiploic vessels are isolated and transected. Mobilization of the duodenum is performed by traction of the duodenum toward the opposite side by the first assistant. This Kocher maneuver is performed until reaching the left peritoneal fold opened during duodenojejunal junction dissection, freeing the anterior surface of the

inferior vena cava, aorta, and left renal vein.

After cholecystectomy, the hepatoduodenal ligament is dissected, and a complete hilar lymphadenectomy is performed to skeletonize the portal triad, with precautions taken to avoid injury to the main vessels, especially the aberrant right hepatic artery arising from the superior mesenteric artery. The duodenum which was cleared with transection of the right gastric artery is transected 2–3 cm distal to the pylorus using an endoscopic linear stapler in the case that the duodenum is not involved. Otherwise, the classic Whipple's procedure is performed. After transection of the duodenum, dissection is continued along the suprapancreatic portion to isolate the common hepatic artery, from which the gastroduodenal artery can be traced, which is doubly ligated using endoclips. The common bile duct (CBD) is transected above the cystic duct junction using an endoscopic bulldog clip on the proximal side.

Then, careful dissection of the inferior border of the pancreas is performed. Using this procedure, the superior mesenteric vein and splenic vein should be visualized at confluence. A retropancreatic tunnel can be created by blunt dissection using a laparoscopic suction device and LigaSureTM technology. After complete formation of the retropancreatic tunnel, parenchymal transection is performed using ultrasonic shears and endoscissors. The proximal jejunum is transected 10–15 cm distal to the ligament of Treitz using an endoscopic linear stapler. Dissection between the pancreatic head and superior mesenteric vessels is carried out from the

caudal to the cephalad aspect of the patient, while ensuring an adequate margin. The specimen is placed in an endoscopic retrieval bag.

A 10- to 15-cm upper midline incision is created for reconstruction and specimen extraction. The specimen is sent for frozen section pathologic examination of the margins. Reconstruction is performed in a manner similar to that used with the open procedure. The transected end of the proximal jejunum is brought up to the right upper quadrant through a defect in the transverse mesocolon. A two-layer duct-to-mucosa pancreaticojejunostomy is constructed in the Blumgart fashion using a polyethylene internal stent in situ. Then, end-to-side choledochojejunostomy (or hepaticojejunostomy) and end-to-side duodenojejunostomy are performed. After application of fibrin glue and hemostasis, two closed suction drains are placed near the pancreaticojejunostomy and choledochojejunostomy.

Statistical analysis

Continuous variables are presented as the mean \pm standard deviation or median with interquartile range. Categorical variables were compared using the χ^2 test or Fisher's exact test, and continuous variables were compared using the nonparametric Mann-Whitney U test. P values < 0.05 were considered statistically significant. SPSS version 24.0 for Mac (SPSS, Chicago, IL, USA) was used for all analyses.

In this study, we analyzed the learning curve for LAPD using the cumulative sum (CUSUM) and risk-adjusted (RA)-CUSUM methods.

CUSUM and RA-CUSUM analyses

The surgeries were ordered chronologically from the earliest to the latest. The CUSUM analysis for operation time (CUSUM_{OT}) was defined as follows:

$$\text{CUSUM}_{\text{OT}} = \sum_{i=1}^n (x_i - \mu),$$

where x_i is the operation time for an individual patient, and μ is the mean operation time. The mean surgical time was extracted from each time record to create the plot.

The RA-CUSUM method was applied to further assess the learning curve, and because several risk factors related to surgical failure might confound the outcomes using the simple CUSUM method. Surgical failure was defined as occurrence of at least one relevant parameter: postoperative complications (Clavien-Dindo grade ≥ 3) or conversion to the open method.

RA-CUSUM was defined as follows:

$$\text{RA-CUSUM} = \sum_{i=1}^n (x_i - \tau) + (-1)^{x_i} P_i,$$

where $x_i = 1$ indicates surgical failure; otherwise, $x_i = 0$, and τ represents the actual event rate and P_i the expected rate of LAPD failure, which was calculated using the logistic regression model.

Results

Baseline characteristics

During the study period, 90 patients underwent LAPD. The patient demographic characteristics, surgical indications, and procedures are summarized in Table 1. The patients comprised 46 males (51.1%) and 44 females (48.9%), with a mean age of 61.0 years. The mean body mass index was 22.5 kg/m². The median ASA score was 2. The most common histopathology was pancreatic ductal adenocarcinoma (n = 27, 30.0%), followed by carcinomas of the ampulla of Vater (n = 16, 17.8%) and CBD (n = 14, 15.6%); and intraductal papillary mucinous neoplasm (n = 13, 14.4%). Solid pseudopapillary neoplasm, serous cystic neoplasm, neuroendocrine tumor, and others made up the remaining 24% of patient histopathologies.

Operative outcomes

Of the 90 patients, 67 underwent pylorus-preserving pancreaticoduodenectomy (74.4%) and 23 underwent Whipple's procedure (25.6%). The overall mean operation time was 556.8 minutes, and the mean estimated blood loss was 546 ml; 21 patients (23.3%) required an intraoperative transfusion. In six patients, the portal vein was invaded by the tumor and thus was resected, and an end-to-end anastomosis was

performed. There were five cases of conversion to the open procedure, the reasons for which are listed in Table 2.

Oncologic outcomes of cases of invasive periampullary malignancy

The perioperative outcomes of the patients with periampullary malignancy are summarized in Table 3. Invasive malignant disease was found in 58 patients, including 27 with pancreatic ductal adenocarcinoma, 16 with ampullary carcinoma, 14 with CBD carcinoma, and 1 with duodenal carcinoma. The mean tumor size was 3.1 cm, and the mean number of harvested lymph nodes was 14.4. Among the 58 patients, 25 (42.4%) had lymph node metastasis, and 7 had positive R1 resection margins, even though the intraoperative frozen sections were negative.

Complications

Table 4 lists the postoperative complications, which developed in 33 patients (36.7%). Using the Clavien–Dindo classification, the clinically relevant complication rate was 32.2% (grade III/IV, n = 29). There were 12 cases (13.2%) of clinically significant pancreatic fistula (ISGPS grade B/C) and 10 cases of bile leakage. Grades B and C postpancreatectomy hemorrhage occurred in two (2.2%) and two (2.2%) patients, respectively. Two and three patients had ISGPS grades A and B delayed gastric emptying,

respectively. Four patients experienced postoperative ileus and six patients pulmonary complications, which were managed conservatively. The mean and median hospital stays were 21.4 days and 13 days, respectively (range, 5–200 days).

Analysis of the learning curve

We analyzed the learning curve using CUSUM methods. In a plot of $CUSUM_{OT}$ versus the number of patients treated (Fig. 1), there are three peaks. Four groups of patients can be differentiated from this plot: phase I (cases 1–10), phase II (cases 11–38), phase III (cases 39–68), and phase IV (cases 69–90). After the stabilization period of phase II, phase III shows a constant increase in operation time, followed by a steep decrease in phase IV.

The simple CUSUM method assesses operation time but does not indicate the efficacy or success of the operation. Therefore, the learning curve was assessed using the RA-CUSUM method (Fig. 2). Combining the results from the $CUSUM_{OT}$ and RA-CUSUM analyses, three phases were finally determined: phase I (cases 1–26), phase II (cases 27–69), and phase III (cases 70–90). No significant differences among the three phases were detected in terms of the baseline characteristics of the patients (Table 5).

A comparison of perioperative outcomes among the three phases of patients is shown in Table 6. There was no significant difference in operation time between phases 1 and 2. However, in phase 3, the operation time was decreased to 486 minutes, which was statistically different from those of phases 1 and 2 ($p < 0.001$). The same trend was detected in intraoperative estimated blood loss, which was not significantly different between phases 1 and 2 but was reduced by half in phase 3 ($p < 0.001$) compared with phase 1. The postoperative hospital stay was significantly shorter in phase 3 ($p = 0.018$).

Significant differences were detected in the pathologic diagnosis. In the early learning phase (phase 1), 38.5% of cases were found to have malignancies, while 78.0% and 69.6% of cases were found to have malignancies in phases 2 and 3, respectively. The number of harvested lymph nodes increased steadily. There were no statistically significant differences among the phases in terms of transfusion rate, simultaneous organ resection rate, or resected tumor size.

There were no significant differences among the learning phases in terms of severe postoperative complications according to the expanded Accordion Severity Grading System, except between phases 1 and 3 ($p = 0.049$).

Table 1. Demographics and clinical findings of the patients who underwent laparoscopy-assisted pancreaticoduodenectomy

| Patients (n = 90) | | |
|--|-------------|------|
| | N | % |
| Patient demographics | | |
| Sex | | |
| Male | 46 | 51.1 |
| Female | 44 | 48.9 |
| Age at diagnosis (years) | 61.0 ± 14.9 | |
| BMI (kg/m ²) | 22.5 ± 3.3 | |
| ASA score | | |
| I | 40 | 44.4 |
| II | 41 | 45.6 |
| III | 9 | 10.0 |
| Perioperative data | | |
| Procedure | | |
| PPPD | 67 | 74.4 |
| Whipple | 23 | 25.6 |
| Operation time (min), mean (± SD) | 556.8 ± 104 | |
| Estimated blood loss (ml), mean (± SD) | 546.1 ± 366 | |
| Hospital stay (days), mean (± SD) | 21.4 ± 2.5 | |
| Transfusion | 21 | 23.3 |
| Simultaneous resection | 7 | 7.8 |

| | | |
|----------------------------------|----|------|
| Portal vein resection | 6 | 6.7 |
| Conversion to open procedure | 5 | 5.6 |
| Histologic diagnosis | | |
| IPMN | 13 | 14.4 |
| SPN | 8 | 8.9 |
| PNET | 4 | 4.4 |
| Serous cystic neoplasm | 3 | 3.3 |
| Pancreatic ductal adenocarcinoma | 27 | 30.0 |
| AoV cancer | 16 | 17.8 |
| CBD cancer | 14 | 15.6 |
| Others | 5 | 5.6 |

Table 2. Cases of conversion to the open procedure

| Patient no. | Sex | Age (years) | OP time (min) | Blood loss (ml) | Reason |
|-------------|--------|-------------|---------------|-----------------|--------------------------------|
| 1 | Female | 58 | 575 | 550 | Severe pancreatitis |
| 2 | Female | 68 | 680 | 1850 | Gastroduodenal artery bleeding |
| 3 | Female | 78 | 430 | 500 | Portal vein injury |
| 4 | Female | 38 | 460 | 1600 | Portal vein injury |
| 5 | Male | 52 | 585 | 1600 | Inferior vena cava injury |

Table 3. Perioperative outcomes of 58 patients with periampullary malignancies

| Variables | |
|---------------------------------------|-----------------|
| Mean tumor size (cm, \pm SD) | 3.1 \pm 1.5 |
| Mean lymph nodes harvested (n, range) | 14.4 \pm 10.8 |
| Regional lymph node metastasis (n, %) | 25 (42.4%) |
| Negative resection margins (n, %) | 52 (88.1%) |
| TNM stage | |
| 1A | 14 (23.7%) |
| 1B | 10 (16.9%) |
| 2A | 11 (18.6%) |
| 2B | 22 (37.3%) |
| 3 | 2 (3.4%) |

Table 4. Postoperative complications

| Variables | |
|---------------------------------------|------------|
| Overall morbidity (n, %) | 33 (36.7%) |
| Clavien–Dindo classification (n, %) | |
| I | 3 (3.3%) |
| II | 1 (1.1%) |
| IIIa | 25 (27.8%) |
| IIIb | 2 (2.2%) |
| IV | 2 (2.2%) |
| Mortality (n, %) | 0 (0%) |
| Pancreatic fistula (n, %) | |
| Grade B | 8 (8.8%) |
| Grade C | 4 (4.4%) |
| Post-pancreatectomy hemorrhage (n, %) | |
| Grade B | 2 (2.2%) |
| Grade C | 2 (2.2%) |
| Delayed gastric emptying (n, %) | |
| Grade A | 2 (2.2%) |
| Grade B | 3 (3.3%) |
| Ileus | 4 (4.4%) |
| Bile leakage | 10 (11.1%) |
| Pulmonary complications | 6 (6.7%) |
| Wound infection/dehiscence | 7 (7.8%) |

Table 5. Comparisons of preoperative parameters among the phases

| Variables | Phase I Cases 1-26 | Phase II Cases 27-67 | Phase III Cases 68-90 |
|--------------------------|-----------------------|-------------------------|--------------------------|
| Sex (M/F) | 9 / 17 | 27 / 14 | 10 / 13 |
| Age (years) | 50.8 | 65.2 | 64.9 |
| BMI (kg/m ²) | 22.6 | 22.6 | 22.1 |
| ASA | 16 / 9 / 1 | 18 / 19 / 4 | 6 / 13 / 4 |
| ECOG | 20 / 5 / 1 / 0 | 8 / 23 / 8 / 2 | 4 / 18 / 1 / 0 |

Table 6. Comparisons of perioperative parameters among the phases

| Variables | Phase I Cases 1– 26 | Phase II Cases 27–67 | Phase III Cases 68–90 | p value | | |
|---------------------------------|---------------------------|----------------------------|-----------------------------|---------|---------|---------|
| | | | | Phase | | |
| | | | | 1 vs. 2 | 1 vs. 3 | 2 vs. 3 |
| Operation time (min) | 581.3 ± 95 | 580.9 ± 90 | 486.0 ± 108 | 0.959 | 0.001 | 0.001 |
| Estimated blood loss (ml) | 576.9 ± 363 | 651.2 ± 399 | 323.9 ± 178 | 0.154 | 0.001 | 0.001 |
| Hospital stay (days) | 20.7 | 21.8 | 13.3 | 0.579 | 0.018 | 0.077 |
| Transfusion | 7 (26.9%) | 10 (24.4%) | 4 (17.4%) | 0.816 | 0.425 | 0.516 |
| Simultaneous resection | 2 (7.7%) | 2 (4.9%) | 3 (13.0%) | 0.636 | 0.537 | 0.243 |
| Open conversion | 3 (11.5%) | 0 (0%) | 2 (8.7%) | 0.026 | 0.743 | 0.055 |
| Periampullary malignancy | 10 (38.5%) | 32 (78.0%) | 16 (69.6%) | 0.001 | 0.029 | 0.453 |
| Tumor size | 3.26 | 3.03 | 3.06 | 0.626 | 0.857 | 0.737 |

| | | | | | | |
|---------------------------------|--------------|---------------|--------------|-------|-------|-------|
| (cm) | | | | | | |
| Number of harvested lymph nodes | 7.8 | 16.4 | 18.1 | 0.001 | 0.001 | 0.785 |
| Clavien-Dindo ≥ 3 | 7 (26.9%) | 17 (41.5%) | 5 (21.7%) | 0.226 | 0.674 | 0.111 |

Figure 1. [Fig. 1 is not referenced in the main text.] Cumulative sum plot for operation time

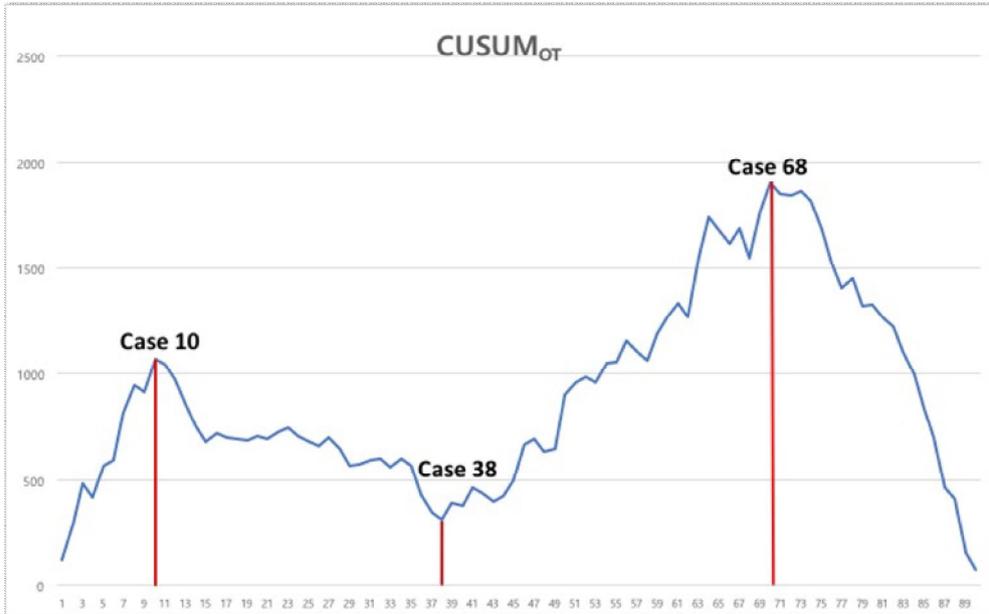
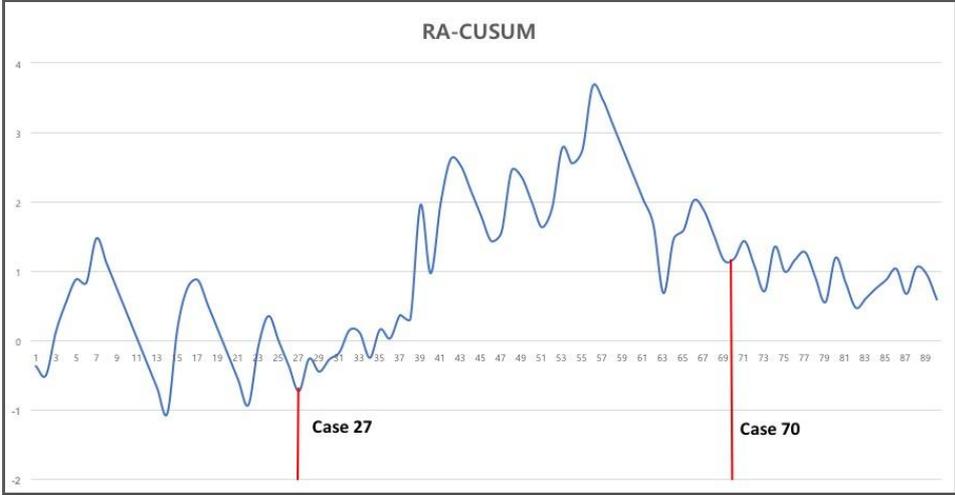


Figure 2. Risk-adjusted cumulative sum plot for operation failure



Discussion

With the development of laparoscopic techniques, a laparoscopic approach to distal pancreatectomy has been widely adopted for various pancreatic lesions [21–23]. In addition, dissection and resection of complex and hazardous structures around the pancreas have become easier and safer with the development of laparoscopic instruments such as the LigaSure™ and Harmonic scalpel™.

Since the first report of laparoscopic pancreaticoduodenectomy by Gagner and Pomp [6] in 1994, several studies [11, 24, 25] have reported that the laparoscopic approach is associated with less blood loss, higher numbers of harvested lymph nodes, and no significant difference in postoperative morbidity compared with the open approach [13, 26–28]. Furthermore, Langan et al. [29] reported the quality of life of patients who underwent LAPD versus open pancreaticoduodenectomy. More favorable quality-of-life scores and perioperative outcomes were observed in those who underwent HLAPD.

Despite these advantages of, and improvements in, the laparoscopic approach, only technically expert laparoscopic surgeons have adopted this procedure. There are several reasons why the laparoscopic approach for periampullary tumors is not generally accepted, including extensive retroperitoneal dissection around anatomically complex and hazardous structures, and prolonged reconstruction that includes three technically demanding anastomoses.

To overcome these limitations of the laparoscopic procedure, LAPD was introduced, and several surgeons have since reported their experiences [15-18]. However, compared with pure laparoscopic pancreatoduodenectomy, few studies involving small patient numbers have been conducted. In our previous study, we compared the perioperative outcomes and complications between the LAPD and open pancreatoduodenectomy groups [19]. There were no significant differences in complications or perioperative outcomes, except for the operation time, which was 530 minutes and 357 minutes in the LAPD and open pancreatoduodenectomy groups, respectively ($p < 0.001$).

Here, we report our experience with 90 consecutive cases of LAPD and describe the learning curve. To our knowledge, this is the largest series of patients treated with LAPD at a single center. Cho A et al. [17] reported 15 cases of LAPD and compared their perioperative outcomes with those who underwent the open procedure. The factors of operation time, intraoperative blood loss, incidence of postoperative complications, and hospital stay were similar between the LAPD and open groups. In addition, they found no significant differences between the two groups regarding the surgical margins or number of retrieved lymph nodes. Wellner et al. [30] compared perioperative outcomes between LAPD (40 cases) and the open procedure (40 cases) and reported favorable outcomes in terms of fewer transfusion requirements, shorter operation time, less delayed gastric emptying, and a reduced hospital stay. Wang et al. [31] reported significantly lower intraoperative blood loss and shorter hospital stay in the LAPD group than

in the open pancreatoduodenectomy group.

The mean operation time of this study (556.8 minutes) was longer than those in other similar studies. However, the operation time gradually decreased with accumulation of experience, as the mean operation time in phase III was 486.0 minutes, which was significantly different from those in phases I and II (phase I vs. phase III: $p = 0.001$; phase II vs. phase III: $p = 0.001$). Wellner et al. [30] also reported a reduction in the operation time, from 433 minutes in the first 20 cases to 313 minutes in the next 20 cases ($p = 0.002$). The mean hospital stay was 21 days and was shorter in phase III (13.3 days), which was either similar or shorter than those reported in other studies.

In previous studies, mortality rates of 0%–8% have been reported [17, 18, 29, 30]. Cho et al. [17] reported 2 cases (13%) of pancreatic fistula, 1 case (7%) of biliary leak, and 1 case (7%) of delayed gastric emptying among 15 cases of LAPD. Wellner et al. [30] reported 7 cases (18%) of pancreatic fistula, 5 cases (13%) of post-pancreatectomy hemorrhage, and 5 cases (13%) of delayed gastric emptying among 40 patients. Wang et al. [31] reported 2 cases (15%) of major complications (Clavien–Dindo III/IV) and 4 cases of pancreatic fistula among 13 cases, and Lee et al. [18] reported a complication rate of 35.7% (15/42).

In the present study, the overall morbidity rate was 36.7% (33/90), and the clinically relevant complication rate was 32.2% (grade III, IV, $n = 29$). Among the 90 patients, 12 cases (13.2%) of significant pancreatic fistula

(ISGPS grade B/C) and 10 cases of bile leakage were detected. However, no postoperative mortalities relevant to the perioperative complications occurred.

Speicher et al. [32] analyzed the learning curve for laparoscopic pancreatoduodenectomy. The first 23 cases were performed using the hybrid procedure, and the next 25 cases were performed using the pure laparoscopic procedure. After accumulating experience with approximately 50 cases, the operation time and estimated blood loss were lower than those of the open procedure. Wellner et al. [29] analyzed the learning curve by dividing their patients into two groups, the first 20 cases of LAPD and the next 20 cases of LAPD, and reported that the operation time was shorter for the latter 20 cases than the first 20 cases ($p = 0.002$). Although these studies analyzed the learning curve for LAPD, no studies have assessed the learning curve for LAPD using the CUSUM and RA-CUSUM methods.

In the plot of $CUSUM_{OT}$, there were three peak points marked by the 10th, 38th, and 68th cases, and two stabilizing points were observed around the 27th and 70th cases in the RA-CUSUM plot. Three phases were finally determined by combining the results of these two analyses. The operation time, EBL, and hospital stay were stable in phase III, and the number of harvested lymph nodes was significantly increased in phase II compared with phase I. No significant difference in postoperative complications was observed. In the RA-CUSUM plot (Fig. 2), although the lowest point was seen with case 14, the values between cases 14 and 27 fluctuated, so these

cases were assigned to phase I. Wang et al. [33] also evaluated the learning curve for laparoscopic pancreatoduodenectomy using the CUSUM_{OT} and RA-CUSUM methods and reported that experience with a minimum of 40 cases is required before favorable perioperative outcomes are achieved.

In the RA-CUSUM plot (Fig. 2), after minimizing surgical failure (phase I), an increase in surgical failure was observed. This phenomenon can be explained by the increase in surgical indications. The number of periampullary malignancy cases was dramatically increased in phase II compared with phase I [10 (38.5%) vs. 32 (78.0%), phase I vs. phase II, $p = 0.001$].

The main limitation of this study was the absence of comparisons with the open procedure. In addition, we did not report oncologic outcomes such as survival rate or recurrence rate. However, the aim of this study was to report our experience with LAPD. In addition, because we perform LAPD routinely for periampullary lesions, the number of open procedure cases was relatively small. Otherwise, the strength of this study was that it analyzed a homogenous procedure in the largest LAPD case series to date.

Conclusion

LAPD is a technically feasible and safe procedure in select patients. This procedure incorporates the benefits of both the open and minimally invasive laparoscopic procedure and could be a stepping stone for the transition from open to pure pancreaticoduodenectomy. To verify the effectiveness and oncologic safety of LAPD compared with the open procedure, well designed clinical trials should be performed in the future.

References

1. Whipple AO, Parsons WB, Mullins CR (1935) TREATMENT OF CARCINOMA OF THE AMPULLA OF VATER. *Annals of Surgery* 102:763–779.
2. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ, Büchler MW (2007) Delayed gastric emptying (DGE) after pancreatic surgery: A suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 142:761–768.
3. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Yeo CJ, Büchler MW (2007) Postpancreatectomy hemorrhage (PPH)?An International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery* 142:20–25.
4. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernández-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouma DJ, Hackert T, Izbicki J, Lillemoe KD, Neoptolemos JP, Olah A, Schulick R, Shrikhande SV, Takada T, Takaori K, Traverso W, Vollmer CR, Wolfgang CL, Yeo CJ, Salvia R, Buchler M, International Study Group on Pancreatic Surgery (ISGPS) (2017) The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery* 161:584–591.
5. Cuschieri A (1994) Laparoscopic surgery of the pancreas. *J R Coll Surg Edinb* 39:178–184.
6. Gagner M, Pomp A (1994) Laparoscopic pylorus-preserving pancreatoduodenectomy. *Surg Endosc* 8:408–410.
7. Braga M, Pecorelli N, Ferrari D, Balzano G, Zuliani W, Castoldi R (2015) Results of 100 consecutive laparoscopic distal pancreatectomies: postoperative outcome, cost-benefit analysis, and quality of life assessment. *Surg Endosc* 29:1871–1878.

8. Edwin B, Sahakyan MA, Abu Hilal M, Besselink MG, Braga M, Fabre J-M, Fernández-Cruz L, Gayet B, Kim SC, Khatkov IE, EAES Consensus Conference Study Group (2017) Laparoscopic surgery for pancreatic neoplasms: the European association for endoscopic surgery clinical consensus conference. *Surg Endosc* 31:2023–2041.
9. Shin SH, Kim SC, Song KB, Hwang DW, Lee JH, Park K-M, Lee Y-J (2016) Appraisal of Laparoscopic Distal Pancreatectomy for Left-Sided Pancreatic Cancer: A Large Volume Cohort Study of 152 Consecutive Patients. *PLoS ONE* 11:e0163266.
10. Melotti G, Cavallini A, Butturini G, Piccoli M, Delvecchio A, Salvi C, Pederzoli P (2007) Laparoscopic distal pancreatectomy in children: case report and review of the literature. *Ann Surg Oncol* 14:1065–1069.
11. Kendrick ML, Cusati D (2010) Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. *Arch Surg* 145:19–23.
12. Gumbs AA, Gayet B, Hoffman JP (2011) Video: laparoscopic Whipple procedure with a two-layered pancreatojejunostomy. *Surg Endosc* 25:3446–3447.
13. Asbun HJ, Stauffer JA (2012) Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. *Journal of the American College of Surgeons* 215:810–819.
14. Kim SC, Song KB, Jung YS, Kim YH, Park DH, Lee SS, Seo DW, Lee SK, Kim MH, Park KM, Lee YJ (2013) Short-term clinical outcomes for 100 consecutive cases of laparoscopic pylorus-preserving pancreatoduodenectomy: improvement with surgical experience. *Surg Endosc* 27:95–103.
15. Sánchez-Cabús S, Pittau G, Gelli M, Memeo R, Schwarz L, Sa Cunha A (2015) Laparoscopic pancreaticoduodenectomy: hybrid surgical technique. *Journal of the American College of Surgeons* 220:e7–11.
16. Keck T, Kuesters S, Wellner U, Hopt UT, Karcz WK (2011) Laparoscopic pylorus-preserving pancreatic head resection and hybrid open reconstruction via pancreatogastrostomy. *J*

Gastrointest Surg 15:373–377.

17. Cho A, Yamamoto H, Nagata M, Takiguchi N, Shimada H, Kainuma O, Souda H, Gunji H, Miyazaki A, Ikeda A, Tohma T, Matsumoto I (2009) Comparison of laparoscopy-assisted and open pylorus-preserving pancreaticoduodenectomy for periampullary disease. *Am J Surg* 198:445–449.
18. Lee JS, Han JH, Na GH, Choi HJ, Hong TH, You YK, Kim DG (2013) Laparoscopic pancreaticoduodenectomy assisted by mini-laparotomy. *Surg Laparosc Endosc Percutan Tech* 23:e98–102.
19. Mendoza AS, Han H-S, Yoon Y-S, Cho JY, Choi Y (2015) Laparoscopy-assisted pancreaticoduodenectomy as minimally invasive surgery for periampullary tumors: a comparison of short-term clinical outcomes of laparoscopy-assisted pancreaticoduodenectomy and open pancreaticoduodenectomy. *J Hepatobiliary Pancreat Sci* 22:819–824.
20. Dindo D, Demartines N, Clavien P-A (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals of Surgery* 240:205–213.
21. Kim J, Han H-S, Yoon Y-S, Cho JY, Ahn KS, Kwon Y (2012) Outcomes of the patients who were postoperatively diagnosed as malignancy after laparoscopic distal pancreatectomy. *Surg Laparosc Endosc Percutan Tech* 22:467–470.
22. Mendoza AS, Han H-S, Ahn S, Yoon Y-S, Cho JY, Choi Y (2016) Predictive factors associated with postoperative pancreatic fistula after laparoscopic distal pancreatectomy: a 10-year single-institution experience. *Surg Endosc* 30:649–656.
23. Pierce RA, Spitler JA, Hawkins WG, Strasberg SM, Linehan DC, Halpin VJ, Eagon JC, Brunt LM, Frisella MM, Matthews BD (2007) Outcomes analysis of laparoscopic resection of pancreatic neoplasms. *Surg Endosc* 21:579–586.
24. Dulucq JL, Wintringer P, Mahajna A (2006) Laparoscopic pancreaticoduodenectomy for benign and malignant diseases. *Surg Endosc* 20:1045–1050.

25. Palanivelu C, Jani K, Senthilnathan P, Parthasarathi R, Rajapandian S, Madhankumar MV (2007) Laparoscopic pancreaticoduodenectomy: technique and outcomes. *Journal of the American College of Surgeons* 205:222–230.
26. Zureikat AH, Breaux JA, Steel JL, Hughes SJ (2011) Can laparoscopic pancreaticoduodenectomy be safely implemented? *J Gastrointest Surg* 15:1151–1157.
27. de Rooij T, Lu MZ, Steen MW, Gerhards MF, Dijkgraaf MG, Busch OR, Lips DJ, Festen S, Besselink MG, Dutch Pancreatic Cancer Group (2016) Minimally Invasive Versus Open Pancreatoduodenectomy: Systematic Review and Meta-analysis of Comparative Cohort and Registry Studies. *Annals of Surgery* 264:257–267.
28. Correa-Gallego C, Dinkelspiel HE, Sulimanoff I, Fisher S, Viñuela EF, Kingham TP, Fong Y, DeMatteo RP, D'Angelica MI, Jarnagin WR, Allen PJ (2014) Minimally-invasive vs open pancreaticoduodenectomy: systematic review and meta-analysis. *Journal of the American College of Surgeons* 218:129–139.
29. Langan RC, Graham JA, Chin AB, Rubinstein AJ, Oza K, Nusbaum JA, Smirniotopoulos J, Kayser R, Jha R, Haddad N, Al-Kawas F, Carroll J, Hanna J, Parker A, Al-Refaie WB, Johnson LB (2014) Laparoscopic-assisted versus open pancreaticoduodenectomy: early favorable physical quality-of-life measures. *Surgery* 156:379–384.
30. Wellner UF, Küsters S, Sick O, Busch C, Bausch D, Bronsert P, Hopt UT, Karcz KW, Keck T (2014) Hybrid laparoscopic versus open pylorus-preserving pancreatoduodenectomy: retrospective matched case comparison in 80 patients. *Langenbecks Arch Surg* 399:849–856.
31. Wang Y, Bergman S, Piedimonte S, Vanounou T (2014) Bridging the gap between open and minimally invasive pancreaticoduodenectomy: the hybrid approach. *Can J Surg* 57:263–270.
32. Speicher PJ, Nussbaum DP, White RR, Zani S, Mosca PJ, Blazer DG, Clary BM, Pappas TN, Tyler DS, Perez A (2014) Defining the learning curve for team-based laparoscopic

pancreaticoduodenectomy. *Ann Surg Oncol* 21:4014–4019.

33. Wang M, Meng L, Cai Y, Li Y, Wang X, Zhang Z, Peng B (2016) Learning Curve for Laparoscopic Pancreaticoduodenectomy: a CUSUM Analysis. *J Gastrointest Surg* 20:924–935.

초 록

복강경 보조하 췌십이지장 절제술 : 90례의 사례 분석과 학습 곡선 분석

서 론 : 최소 침습 수술의 발전에 따라 복강경하 췌장 수술에 대한 관심이 높아지고 있다. 좌측 췌장 병변에 대한 복강경하 췌미부 절제술은 보편적인 술기로 인식되고 있다. 반면에, 복강경하 문합술의 기술적 어려움으로 인해 췌십이지장 절제술은 췌미부 절제술에 비하여 복강경 술식이 제한적으로 적용되어지고 있다. 이에 복강경을 이용한 절제술 후 작은 절개창을 가하여 개복하 문합술을 시행하는 복강경 보조하 췌십이지장 절제술이 최소 침습 췌장 수술의 한 술기로 도입되었다. 본 연구에서는 단일 기관에서 시행된 복강경 보조하 췌십이지장 절제술의 사례와 학습 곡선을 분석하였다.

방 법 : 2003 년 3 월 부터 2017 년 5월까지 단일 기관에서 복강경 보조하 췌십이지장 절제술을 시행받은 90 명의 환자들의 데이터를 후향적으로 분석하였다. 누적 합산 방법 (CUSUM) 과 위험도 보정 누적 합산 방법 (Risk Adjusted - CUSUM) 을 이용하여 학습 곡선을 분석하였다.

결 과 : 조직학적 결과, 췌관선암 (27 례, 30.0%) 이 가장 많은 수술의 적응증이었으며 이 후 바터 팽대부암 (16례, 17.8%), 담관암 (14례, 15.6%), 췌관내 유두상 점액종 (13례, 14.4%) 의 순서였다. 평균 수술 시간은 556 분 (범위 300 - 865 분) 이었으며 평균 수술 중 출혈량은 546 ml (범위 50 - 2000 ml)

였다. 환자들의 평균 재원 기간은 21.4 일 이었으며 수술 후 합병증은 33명 (36.7%) 에서 발생하였다. 이들 중 12명 (13.2%) 의 환자에게서는 임상적으로 유의한 채장루가 발생하였다. 학습 곡선의 경우 누적 흡산 방법과 위험도 보정 누적 흡산 방법을 종합하였을 때 3 그룹으로 분류되었다. 이들 그룹 중 그룹1 과 그룹2에서 수술 적응증의 차이가 확인되었다. ($p=0.001$)

결 론 : 복강경과 개복술의 장점을 모두 가지는 복강경 보조하 채십이지장 절제술은 선택된 환자들에게 시행시 기술적으로 안전한 술식이며, 개복술에서 전복강경 채십이지장 절제술로의 전환 과정에서 중요한 술식이다.

주요어 : 복강경, 채십이지장절제술, 학습곡선
Student Number : 2016-22224