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PANCREATIC BODY AND TAIL CANCER: IS LAPAROSCOPIC SURGERY AN EFFECTIVE METHOD?

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ABSTRACT

Background: Laparoscopic treatment of pancreas body and tail cancers is still a matter of debate. The aim of this study is to evaluate the safety and feasibility of laparoscopic distal pancreatectomy (LDP) in pancreas cancer patients. **Material & Methods:** The data of 108 patients who underwent distal pancreatectomy for pancreatic cancer were evaluated. Patients were categorized into two groups by operation method: laparoscopic distal pancreatectomy [LDP; 35 cases] and open distal pancreatectomy [ODP; 73 cases]. Patient characteristics, surgical findings, short- and long-term results were compared. **Results:** The operation time was significantly shorter in ODP (p<0.001). The blood loss (100 ml [min-max: 50-800]) of the LDP was significantly lower than ODP (200 [min-max: 100-800]) (p<0.001). There was no significant difference between the groups in terms of postoperative complications. The median hospital stay (6 [min-max: 4-32]) was found to be significantly higher in ODP (p=0.024). Oncological findings (tumor size; harvested lymph node; metastatic lymph node; perineural invasion; lymphovascular invasion) of patients with pancreatic adenocarcinoma were similar. There was no significant difference in the overall survival rates of the two groups (Log-rank=0.066; p=0.798). **Conclusion:** Although the preference of LDP in pancreatic cancer patients prolongs the operation time, it reduces hospital stay and blodd loss. Overall complication rates and oncologic outcomes appear to be similar. In conclusion, LDP is a feasible and safe method in pancreatic cancer patients.

Keywords: laparoscopic approach, pancreatic neoplasms, pancreas cancer, pancreatectomy, pancreas surgery

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INTRODUCTION

Laparoscopic distal pancreatectomy (LDP) has been performed by surgeons since 1994 [1]. Some advantages of this method have been reported based on the experience gained from laparoscopic surgeries for other diseases. Examples of these include minimal blood loss, shorter hospital stay, early onset of intestinal motility, and better cosmetic results [2]. Conditions such as pancreatic body and tail tumors (benign, borderline or malignant), pancreatic injury, and pseudocyst located in this localization are indications for both open distal pancreatectomy (ODP) and LDP [3]. Presence of distant metastases, invasion of adjacent organs or major vascular structures are contraindications for LDP [4]. In some studies, it has been stated that the long-term oncological outcomes of LDP are comparable to the open method [5,6]. LDP can be performed in a limited number of centers due to anatomical features such as the difficulty of the laparoscopic technique and

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the close proximity of the pancreas to the main vascular structures. Applicability of the laparoscopic method for pancreatic surgery lags behind colorectal diseases. There are few studies comparing the results of LDP and ODP in the literature.
The aim of this study is to compare the short and long term results of LDP and ODP for pancreatic body and tail cancers, and to discuss the reliability and feasibility of the laparoscopic method.

MATERIALS & METHODS

This retrospective study has ethics committee approval (decision dated 23.11.2021 and numbered 2021/145). A total of 108 patients who underwent distal pancreatectomy for pancreatic body and tail ductal adenocarcinoma between January 2015 and January 2021 were included in the study. Patient data were retrospectively scanned. Patients were divided into two groups according to the operation technique: laparoscopic distal pancreatectomy [LDP; 35 cases] and open distal pancreatectomy [ODP; 73 cases]. Inclusion criteria were distal pancreatectomy for pancreatic body and tail cancer, complete patient data records, and absence of distant metastases. Patients with missing data records and distant metastases were excluded from the study.
Patient characteristics, operative outcomes, and short- and long-term results were included in the parameters examined. Age, gender, body mass index (BMI), ASA score and tumor localization were evaluated in terms of patient characteristics. Additional organ resection status, conversion to open operation, operation time (min), and blood loss (ml) were evaluated as surgical findings. Postoperative morbidity, mortality, and hospital stay and intensive care unit (ICU) stay within 30 days of surgery were evaluated as short-term outcomes. Complications were evaluated separately according to their types, such as surgical, cardiovascular, pulmonary complications, acut kidney failure (AKF) and other complications. Surgical complications included pancreatic fistula, intra-abdominal abscess, bleeding (hematoma), chylous fistula, abscess and colon perforation. Pancreatic fistula types (biochemical fistula (BL), grade B and grade C) were evaluated separately according to the current classification of the International Study Group of Pancreatic Fistula (ISGPF). Tumor size, havested total lymph node, metastatic lymph node, perineural invasion and lymphovascular invasion were evaluated as. Overall survival (OS) was evaluated as a long-term outcome. Finally, the results were compared between groups.

Surgical Procedure

The operations were performed by 3 surgeons who were highly specialized in both open and laparoscopic surgery in the pancreatobiliary system. All open cases were performed in the supine position with a midline incision. Some of the laparoscopic cases were performed in the supine position (11 cases), while the other part was performed in the right lateral decubitus position (24 cases). All patients were taken to the operating room after 8 hours of fasting and prophylactic single dose antibiotherapy (IV 1 g cefazolin sodium) was administered. In laparoscopic cases performed in the supine position, the laparoscopy tower was placed at the left shoulder. The patient's legs were opened wide enough for the surgeon to enter and both arms were kept closed. In laparoscopic cases where the right lateral decubitus position is preferred, the surgical team was placed on the right side of the patient and the laparoscopy system was positioned behind the patient. A 30 degree camera and 4 trocars was used in LDP. In cases performed in the supine position, dissection was performed from medial to lateral, giving priority to pancreatic dissection. In laparoscopic cases performed in the lateral decubitus position, lateral to medial (starting from the splenocolic, gatrosplenic and splenophrenic ligaments) were dissected. In all LDP cases, the splenic artery and vein were clipped with a hem-o-lok clip and the pancreas was transected with a vascular stapler.

Statistical analysis

Continuous variables were reported as mean±standard deviation (SD) or median (min-max) depending on the distribution of data and were analyzed with Mann-Whitney U test and Independent t-test, as appropriate. Categorical variables were presented with frequency (n) and percentage (%) and analyzed with Pearson chi-square and Fisher's Exact test. Survival curves were generated by the Kaplan-Meier method and the log-rank test was performed to compare OS between the laparoscopic and open operation groups. Statistical analysis was made using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). Two-sided p-value less than 0.05 was considered statistically significant.

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RESULTS

Thirty-five (32.4%) of 108 patients were operated laparoscopically and 73 (67.6%) were operated with open method. The mean age of the patients was 58.13±14.99 (min-max: 18-90) years. Forty-seven (43.5%) patients were male. No significant difference was found in terms of the mean age and gender distribution of the patients (respectively, p=0.433; p=0.750). There was no significant difference in terms of ASA scores (p=0.086) and BMI averages (p=0.899) of the patients. There was no significant difference in terms of tumor localization (p=0.620) (**Table 1**).

Table 1. Patient characteristics

Variables	ODP (n=73)	LDP (n=35)	p
Age (year)	58.92±14.82	56.49±15.43	0.433
Gender			
Male	31(42.5)	16(45.7)	0.750
Female	42(57.5)	19(54.3)	
Tumor localization			
Body	29(39.7)	15(42.8)	0.620
Tail	44(60.2)	20(57.1)	
BMI	25.11±2.88	25.03±3.02	0.899
ASA			
1	33(45.2)	22(62.9)	0.086
2	35(47.9)	9(25.7)	
3	5(6.8)	4(11.4)	

Values are expressed as mean – standard deviation, or n (%). Independent t-test, Pearson chi-square test. ASA, American Society of Anesthesiologists; BMI, body mass index.

The median operation time was 130 (min-max: 90-230) in patients operated with open method and 150 (min-max: 110-230) minutes in patients operated on laparoscopically, and the operation time was significantly shorter in ODP (p<0.001). The median blood loss amount (100 ml [min-max: 50-800]) of the patients who were operated with the laparoscopic method was significantly lower than those who had open operation (200 [min-max: 100-800]) (p<0.001). Conversion to open surgery was performed in 3 (8.5%) patients. Additional organ resection (due to adjacent organ invasion; such as stomach, colon) rates (p=0.557) of the two groups were statistically similar (**Table 2**).

Table 2. Postoperative short-term outcomes

Variables	ODP (n=73)	LDP (n=35)	p
Postoperative complications	15(20,5)	8(22,9)	0,784
Surgical complications			
Biyo leak (BL)	3(4,1)	3(8,6)	0,387
Pancreatic fistula grade B	1(1,4)	1(2,9)	0,545
Pancreatic fistula grade C	1(1,4)	0(0)	0,999
Chylous fistula	1(1,4)	0(0)	0,999
Bleeding	1(1,4)	0(0)	0,999
Colon perforation	0(0)	2(5,7)	0,103
Abscess	0(0)	2(5,7)	0,103
Cardiovascular complications			
MI	0(0)	1(2,9)	0,324
AF	1(1,4)	0(0)	0,999
Pulmonary complications			
Atelectasis	2(2,7)	0(0)	0,999
Pneumonia	0(0)	1(2,9)	0,324
Pleural effusion	1(1,4)	0(0)	0,999
AKF	2(2,7)	0(0)	0,999
Other			
Cerebrovascular event	1(1,4)	0(0)	0,999
Clavien-Dindo ≥ 3	5(6,8)	3(8,6)	0,712
Reoperation	2(2,7)	2(5,7)	0,594
Inhospital mortality	2(2,7)	0(0)	0,999
Hospital stay (day)	6(4-32)	5(3-21)	**0,024**
ICU stay (day)	1(1-7)	1(1-5)	0,342

Values are expressed as mean – standard deviation, or n (%). Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test. MI, myocardial infarction; AF, trial fibrillation; AKF, acut kidney failure.

The postoperative complication rates of the groups were similar (p=0.784). When complications were evaluated separately according to their types, such as surgery, cardiovascular, pulmonary complications, acut kidney failure (AKF) and other complications, there was no statistically significant difference between the two groups (p>0.05). There was no significant difference in the rates of Clavien-Dindo ≥ 3 complications (p=0.712), reoperation (p=0.594) and in-hospital mortality (p=0.999). A total of four patients were reoperated. The reasons for reoperation are Grade C fistula (ODP group; 1 case), bleeding (ODP group; 1 case) and colon perforation (LDP group; 2 cases).

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Mortality developed in 2 patients in the ODP group due to Grade C fistula-related sepsis and cerebrovascular event. While no significant difference was observed between the groups in terms of ICU stay (p=0.342), the median hospital stay (6 [min-max: 4-32]) was found to be significantly higher in ODP (p=0.024) (**Table 3**).

Table 3. Postoperative short-term outcomes

Variables	ODP (n=73)	LDP (n=35)	p
Postoperative complications	15(20,5)	8(22,9)	0,784
Surgical complications			
Biyo leak (BL)	3(4,1)	3(8,6)	0,387
Pancreatic fistula grade B	1(1,4)	1(2,9)	0,545
Pancreatic fistula grade C	1(1,4)	0(0)	0,999
Chylous fistula	1(1,4)	0(0)	0,999
Bleeding	1(1,4)	0(0)	0,999
Colon perforation	0(0)	2(5,7)	0,103
Abscess	0(0)	2(5,7)	0,103
Cardiovascular complications			
MI	0(0)	1(2,9)	0,324
AF	1(1,4)	0(0)	0,999
Pulmonary complications			
Atelectasis	2(2,7)	0(0)	0,999
Pneumonia	0(0)	1(2,9)	0,324
Pleural effusion	1(1,4)	0(0)	0,999
AKF	2(2,7)	0(0)	0,999
Other			
Cerebrovascular event	1 (1,4)	0(0)	0,999
Clavien-Dindo ≥ 3	5 (6,8)	3(8,6)	0,712
Reoperation	2 (2,7)	2(5,7)	0,594
Inhospital mortality	2 (2,7)	0(0)	0,999
Hospital stay (day)	6 (4-32)	5(3-21)	**0,024**
ICU stay (day)	1 (1-7)	1(1-5)	0,342

Values are expressed as mean – standard deviation, or n (%). Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test. MI, myocardial infarction; AF, trial fibrillation; AKF, acut kidney failure.

There was no significant difference between the groups in terms of tumor size (p=0.139), total lymph node number (p=0.350), metastatic lymph node number (p=0.455), perineural invasion (p=0.520) and lymphovascular invasion (p=0.694) rates in patients (**Table 4**).

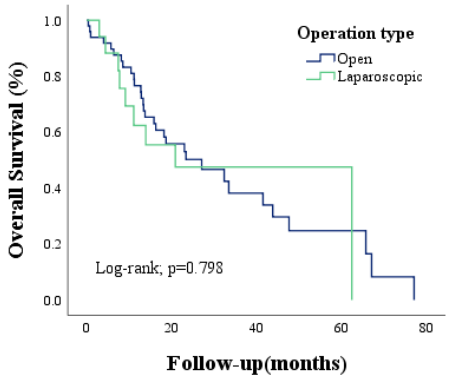
Table 4. Oncological findings of patients

Variables	ODP (n:73)	LDP (n:35)	p
Tumor size (cm)	4(1-13)	3,5(1-8)	0,139
Harvested total lymph node	5(1-27)	4(2-20)	0,350
Metastatic lymph node	0(0-7)	1(0-8)	0,455
Perineural invasion	17(23.2)	8(22,9)	0,520
Lymphovascular invasion	30(41,1)	13(37,1)	0,694

Values are expressed as mean – standard deviation, or n (%). Mann-Whitney U test, Pearson chi-square test.

The median survival time of the patients was 23,4 (%95 CI: 8,4-38,3) months. The OS time of patients who underwent open surgery was 27,1 (%95 CI: 11,2-42,9) months and 20,9 (%95 CI: 0-43,4) months for those who were operated on laparoscopically. The OS rates of 1, 3, and 5 years of open surgery were, respectively; were %76.6, %38.2 and %24.7. The 1-year survival rate of the patients who were operated laparoscopically was % 62.4 and the 3-year and 5-year survival rate was 47.5%. There was no significant difference in the overall survival rates of the two groups (Log-rank=0,066; p=0,798) (**Figure 1**).

Figure 1. Comparison of survival between odp and ldp



DISCUSSION

Diseases of the body and tail of the pancreas are usually treated with open distal pancreatectomy. The rapid development of medical technology in the last 30 years has led surgeons to tend to minimally invasive surgery. Laparoscopic surgery is increasingly being used in malignant diseases as well as in benign diseases of the digestive system. This trend has also shown its effect on pancreatic surgery. Cusciheri performed the first LDP in 1994, leading a new era in pancreatic surgery [1]. Although LDP has been accepted by surgeons since then, it has not yet become as routine as a

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laparoscopic colorectal surgery or laparoscopic cholecystectomy. This can be related to the difficult anatomical location of the pancreas and the long learning curve of laparoscopic surgery. In a French study, the rate of surgeons using LDP was 12% [7]. It was stated that the LDP preference rate was 40% in the UK in 2006-2016, and 60% in Norway in 2012-2016 [8-10]. Some studies have reported that surgeons in Europe believe ODP is superior in tumor surgery [7,11]. That's why the LDP versus ODP debate is still going on.

Consistent with other studies, patient characteristics of the groups were similar [5,12]. In this study, the operation time of the LDP was significantly longer ($p<0,001$). This can be reletead to the long learning curve of LDP and the difficulty of the laparoscopic technique. In the study by Jarufe et al., although the operation time of LDP was long, this difference was not significant [5]. In other studies in the literature, no difference was found in terms of operation time [12,13]. In this study, the median blood loss of the LDP group was significantly lower than those who had open surgery ($p<0.001$). Similar results were found in the meta-analysis conducted by Gavriilidis et al [13]. In a meta-analysis by Lyu et al., blood loss of LDP was significantly less in all 12 studies [14]. In a Dutch multicenter study, patients who underwent LDP had significantly less intraoperative blood loss and a significantly longer operative time [15]. The laparoscopic method is being modified day by day to improve the perioperative results of LDP. One of the effective techniques made in recent years is the modified lasso technique defined by Kawasaki et al. [16]. The aim of this approach is to reduce blood loss and operative time by transecting the splenic vessels and pancreas simultaneously.

In the present study, conversion to open surgery was performed in 3 patients (8.5%) due to bleeding and excessive intra-abdominal adhesions. In the study conducted by Jarufe et al., conversion to open operation was performed in three out of 57 patients [5]. In the literature, it was stated that conversion from laparoscopy to open ranged from 0 to 34% [17]. The most common causes are bleeding and adhesions. In this study, both the overall postoperative morbidity rates ($p=0.784$) and the Clavien-Dindo ≥ 3 complication rates ($p=0.712$) of the groups were similar. Postoperative pancreatic fistula (POPF) is one of the leading complications after distal pancreatectomy, and its incidence varies between 4% and 69% [18]. According to the current definition of the ISGPF, there are 3 grades of POPF: biochemical fistula (BL), grade B and grade C. Consistent with previous studies, no significant difference was found between the groups in terms of either BL or grade B and grade C pancreatic fistula (respectively, $p=0.387$; $p=0.545$, $p=0.999$). BL is not a significant threat to the patient. However, grade B and especially grade C pancreatic fistulas can lead to dangerous results such as intra-abdominal abscess and related sepsis, bleeding and ileus. In the meta-analysis by Lyu et al., it was determined that ODP and LDP had similar results in terms of POPF [14]. Similar results were obtained in another review article by Fingerhut et al. [19]. In contrast with this, Venkat et al. meta-analysis showed that less POPF developed in the LDP group [20]. POPF development is associated with many factors such as age, gender, pancreatic tissue characteristics, surgical technique, pancreatic stump closure technique, and surgeon's experience [21]. In our series, after the pancreatic tissue was transected with a linear stapler in the ODP group, the stump was closed by hand-sewn with a non-absorbable suture. In cases performed with the laparoscopic method, the pancreas was transected with an Endo-GIA vascular stapler and the stump was not sutured. Different methods did not affect the risk of POPF in our study. Consistent with this, it has been shown in the literature that there is no difference between hand-sewn closure and stapler closure [22]. Many methods have been proposed by surgeons to prevent the development of POPF. Suzuki et al. stated that the use of ultrasonic dissector reduces the risk of pancreatic fistula development [23]. Some authors claim that performing stapled transection line reinforcment reduces the risk of fistula [24]. There are also surgeons who use fibrin glue and sealant patches for this purpose [25,26]. Although different methods have been tried to reduce the development of POPF, there is no proven common method in this regard. In this study, the duration of hospital stay was significantly shorter in individuals who underwent laparoscopic surgery ($p=0.024$). In consistent with our study, Mehrabi et al. reported that LDP significantly shortened the length of hospital stay [27]. Along with single-center studies supporting this result, there are also multi-centre studies such as LEOPARD [28,29].

In present study, no difference was found between the groups in terms of harvested total lymph node, metastatic lymph node, tumor size and other histological features (lymphovascular and perineural invasion) of patients. A meta-analysis by Gavrilidis et al. revealed similar results [13]. Similar results are also found in some single-center studies [5,29]. In contrast with this, Pan-European property score matched study showed that, LDP was related to the lower number of harvested lymph nodes [30]. In addition, Lee et al. claim that ODP is more efficient in terms of harvested lymph node [19].

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In our study, the overall survival time of patients who underwent open surgery was 27.1 months, and those who underwent laparoscopic surgery was 20.9 months, and there was no difference between the groups (p=0.798). These results confirm previous single-center study and meta-analysis results (5,6]. A Propensity Score Matched Analysis by Shin et al. stated a median survival of 33.4 months in laparoscopic group vs. 29.1 months in open group (P=0.025) [29]. In another multicenter study examining distal pancreatectomy for pancreatic cancer, it was reported that there was no difference between the groups in terms of overall survival, and the overall survival was low (16 months) in both groups [31].

The strength of our study is the comparison of both short-term and long-term oncological outcomes. Complications in particular have been studied in great detail. The limitations of this study are that this study was retrospective, the sample size was small, and the surgeries were not performed by a single surgeon.

CONCLUSION

Compared to the open method, the preference for the laparoscopic method for distal pancreatectomy prolongs the operation time. However, the laparoscopic method has important advantages such as less blood loss and shorter hospital stay. The fact that postoperative morbidity and oncological results are similar to the open method shows that LDP can be performed safely in cancer patients. In conclusion, LDP is a reliable and feasible method for pancreatic body and tail neoplasms. Although our study sheds light on this issue, further prospective randomized studies are needed.

CONFLICTS OF INTEREST

The authors declared that there is no conflict of interest.

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