

## Laparoscopic versus open distal pancreatectomy for pancreatic ductal adenocarcinoma: a single-center experience<sup>\*</sup>

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**Abstract:** Objective: The aim of this study was to compare complications and oncologic outcomes of patients undergoing laparoscopic distal pancreatectomy (LDP) and open distal pancreatectomy (ODP) at a single center. Methods: Distal pancreatectomies performed for pancreatic ductal adenocarcinoma during a 4-year period were included in this study. A retrospective analysis of a database of this cohort was conducted. Results: Twenty-two patients underwent LDP for pancreatic ductal adenocarcinoma, in comparison to seventy-six patients with comparable tumor characteristics treated by ODP. No patients with locally advanced lesions were included in this study. Comparing LDP group to ODP group, there were no significant differences in operation time ( $P=0.06$ ) or blood loss ( $P=0.24$ ). Complications (pancreatic fistula,  $P=0.62$ ; intra-abdominal abscess,  $P=0.44$ ; postpancreatectomy hemorrhage,  $P=0.34$ ) were similar. There were no significant differences in the number of lymph nodes harvested ( $11.2\pm4.6$  in LDP group vs.  $14.4\pm5.5$  in ODP group,  $P=0.44$ ) nor the rate of patients with positive lymph nodes (36% in LDP group vs. 41% in ODP group,  $P=0.71$ ). Incidence of positive margins was similar (9% in LDP group vs. 13% in ODP group,  $P=0.61$ ). The mean overall survival time was ( $29.6\pm3.7$ ) months for the LDP group and ( $27.6\pm2.1$ ) months for ODP group. There was no difference in overall survival between the two groups ( $P=0.34$ ). Conclusions: LDP is a safe and effective treatment for selected patients with pancreatic ductal adenocarcinoma. A slow-compression of pancreas tissue with the GIA stapler is effective in preventing postoperative pancreatic fistula. The oncologic outcome is comparable with the conventional open approach. Laparoscopic radical antegrade modular pancreatectomy contributed to oncological clearance.

**Key words:** Laparoscopic distal pancreatectomy; Open distal pancreatectomy; Pancreatic neoplasm; Pancreatic fistula  
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### 1 Introduction

Surgical resection currently remains the only treatment option with the curative potential for long-term survival of pancreatic cancer (Riviere *et al.*, 2016). Distal pancreatectomy is provided as a standard surgical procedure for cancers of the body or tail of the pancreas (Strasberg *et al.*, 2007; de Rooij *et al.*, 2016). It can be performed using either a laparoscopic

or an open approach. Laparoscopic distal pancreatectomy (LDP) is a relatively new procedure, in contrast to the well-established role of the conventional open approach. Several studies have demonstrated the safety of LDP with regards to intraoperative blood loss and postoperative complications (Teh *et al.*, 2007; Nigri *et al.*, 2011; Jusoh and Ammori, 2012; Pericleous *et al.*, 2012). However, concerns remain about the efficacy of LDP in achieving oncological clearance and long-term survival. In this study, we aim to compare the oncologic outcomes of LDP with those of the conventional open approach. Pancreatic fistula was simultaneously analyzed as the most serious complication after distal pancreatectomy determining the safety of LDP.

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## 2 Materials and methods

### 2.1 Patients

This study is retrospectively designed. Patients' data were collected from an electronic medical database that records all the perioperative and postoperative information.

From January 2010 to August 2014, 367 patients were diagnosed with tumors of the pancreas body and tail and received distal pancreatectomy at the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China. Twenty-six patients underwent LDP with a final histopathologic diagnosis of ductal adenocarcinoma, of whom 4 were excluded because of the involvement of adjacent vasculature or organs, leaving a total of 22 patients (13 females and 9 males) included in the study. Seventy-six patients (46 females and 30 males) with comparable tumor characteristics underwent open distal pancreatectomy (OPD) in the same period. This group of patients was included for comparison.

Patients' characteristics were collected including operation details, mortality, morbidity, final pathology diagnosis, and survival. Postoperative mortality was defined as the number of deaths that occurred within 30 d after surgery. Morbidity was defined as major complications including pancreatic fistula, intra-abdominal abscess, and postpancreatectomy hemorrhage following the operation until the day of discharge. Pancreatic fistula, intra-abdominal abscess, and postpancreatectomy hemorrhage were defined according to the criteria of the International Study Group of Pancreatic Surgery (Bassi *et al.*, 2005; Wente *et al.*, 2007). Oncologic outcomes were analyzed for all patients including tumor size, number of harvested lymph nodes, and number of patients with a positive finding in lymph nodes, margin status, and overall survival.

### 2.2 Surgical procedure

As commonly accepted (Velanovich, 2006), distal pancreatectomy was defined as the resection of the pancreas reaching the left side of the superior mesenteric vein. All patients underwent splenectomy at the same time owing to the malignant characteristic of the disease. LDP was performed by experienced pancreatic surgeons. Briefly, the gastrocolic ligament was dissected and the pancreas was accessed. Laparoscopic ultrasonography was utilized to identify the pancreatic tumor and its relationship to adjacent splenic vessels. A tunnel along the superior mesenteric vein was created between the neck of the pancreas and the underlying splenic vessels. Then the pancreas was transected at the left side of the superior mesenteric vein with an endoscopic gastrointestinal anastomosis (endo-GIA) stapler (Ethicon Endo-Surgery, Cincinnati, OH, USA). The handle of the endo-GIA instrument was closed slowly over 2–3 min to compress the pancreas tissue reliably. The compression was sustained for another 2–3 min and then the stapler was fired. Splenic vessels were clipped separately. The dissection was performed from right to left and a concurrent lymphadenectomy was performed. After a celiac node dissection and superior mesenteric artery node dissection were completed, the dissection runs posteriorly along the planes of the superior mesenteric artery and celiac trunk till at the level of the aorta and then laterally to the adrenal. The specimen was removed with an endo-bag through a circumumbilical incision. Closed drainages were placed at the pancreatic bed and the left subdiaphragmatic area. OPD was performed with similar steps to the laparoscopic approach. In the open procedure, the pancreas was transected with a harmonic scalpel or electrocautery blade. Pancreatic ductules were ligated when the main ductules of the pancreas were found in 64 cases. The transected pancreas stump was sutured with a non-absorbable polypropylene (Prolene Ethicon, Johnson & Johnson, Somerville, NJ, USA).

Endoscopic ultrasonography was utilized to identify the pancreatic tumor and its relationship to adjacent splenic vessels. A tunnel along the superior mesenteric vein was created between the neck of the pancreas and the underlying splenic vessels. Then the pancreas was transected at the left side of the superior mesenteric vein with an endoscopic gastrointestinal anastomosis (endo-GIA) stapler (Ethicon Endo-Surgery, Cincinnati, OH, USA). The handle of the endo-GIA instrument was closed slowly over 2–3 min to compress the pancreas tissue reliably. The compression was sustained for another 2–3 min and then the stapler was fired. Splenic vessels were clipped separately. The dissection was performed from right to left and a concurrent lymphadenectomy was performed. After a celiac node dissection and superior mesenteric artery node dissection were completed, the dissection runs posteriorly along the planes of the superior mesenteric artery and celiac trunk till at the level of the aorta and then laterally to the adrenal. The specimen was removed with an endo-bag through a circumumbilical incision. Closed drainages were placed at the pancreatic bed and the left subdiaphragmatic area. OPD was performed with similar steps to the laparoscopic approach. In the open procedure, the pancreas was transected with a harmonic scalpel or electrocautery blade. Pancreatic ductules were ligated when the main ductules of the pancreas were found in 64 cases. The transected pancreas stump was sutured with a non-absorbable polypropylene (Prolene Ethicon, Johnson & Johnson, Somerville, NJ, USA).

### 2.3 Adjuvant chemotherapy and follow-up

We recommend adjuvant chemotherapy for all patients according to the pathological staging of resected pancreatic cancer either in LDP or in OPD group. This recommendation is consistent with guidelines from the American Society of Clinical Oncology (ASCO) (Khorana *et al.*, 2016). Adjuvant chemotherapy is typically initiated within four to six weeks after surgical resection and continued for a total of six months. Chemotherapy was managed by one physician team.

Patient follow-up was implemented with a standardized protocol. Routine physical examination and lab tests were performed monthly in the first quarter and then every three months in a year if there was no sign of recurrence. Patients received a computed

tomography (CT) scan one month after the operation and quarterly in the first year and then twice a year subsequently.

## 2.4 Statistical analysis

The continuous variables were expressed in mean and standard deviation (SD) and were analyzed with the Student's *t*-test or Mann-Whitney *U* test appropriately. Categorical variables were compared using the Chi-squared test. Survival analysis was performed using the Kaplan-Meier estimated survival. Statistical significance was defined as  $P<0.05$ . All statistical calculations were made with the SPSS computer software (SPSS Statistics 21.0, SPSS Inc., Chicago, IL, USA).

## 3 Results

### 3.1 Patient details

Twenty-two patients underwent LDP with a final histopathology of ductal adenocarcinoma of the pancreas body and tail. Contemporarily, 76 patients who had similar tumor characteristics underwent ODP. Table 1 shows patient details consisting of age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status classification, and the preoperative biochemistry value of the two groups. No significant differences existed between the groups in any of these parameters.

### 3.2 Operative details and complications

Table 2 demonstrates the operation details and postoperative complications of the patients in the two groups. Operation time in the LDP group was  $(188\pm39)$  min compared to  $(160\pm35)$  min in the ODP group. No significant differences were found between the two groups ( $P=0.06$ ). The LDP group had a mean blood loss of  $(210\pm130)$  ml while the ODP group had  $(240\pm120)$  ml, though there were still no significant differences ( $P=0.24$ ).

Incidence of pancreatic fistula was 36% (8/22) in the LDP group and 25% (19/76) in the ODP group. No significant difference favors either group ( $P=0.62$ ). However, it is noted that two patients complicated with grade C pancreatic fistula were reported in the ODP group, while no grade C pancreatic fistula was reported in the LDP group. Incidences of intra-abdominal abscess ( $P=0.44$ ) and postpancreatectomy hemorrhage ( $P=0.34$ ) were not significantly different between LDP and ODP groups. No perioperation mortality was recorded in either group.

### 3.3 Oncologic outcomes

In the LDP group, the tumor size was  $(3.6\pm1.3)$  cm. In the ODP group, the tumor size was  $(4.4\pm1.4)$  cm. Tumor size did not vary significantly between the LDP and ODP groups ( $P=0.89$ ). The number of harvested lymph nodes was  $11.2\pm4.6$  in the LDP group and  $14.4\pm5.5$  in the ODP group. No significant

**Table 1 Clinical details of patients undergoing LDP and ODP**

Group	Age (year)	Gender (female/male)	ASA score		BMI (kg/m <sup>2</sup> )	Hemoglobin (g/L)	Albumin (g/L)
			1–2	3–4			
LDP ( <i>n</i> =22)	55.2±13.1	13/9	20	2	23.9±2.7	11.8±2.2	31.4±4.7
ODP ( <i>n</i> =76)	59.8±9.0	46/30	70	6	23.7±3.3	11.1±2.2	33.5±3.7
<i>P</i> -value	0.15	0.10		0.36	0.68	0.68	0.32

LDP: laparoscopic distal pancreatectomy; ODP: open distal pancreatectomy; ASA: American Society of Anesthesiologists; BMI: body mass index. Data are expressed as mean±SD or count

**Table 2 Operation details and complications of patients undergoing LDP and ODP**

Group	Operation time (min)	Blood loss (ml)	Pancreatic fistula			Intra-abdominal abscess	Postpancreatectomy hemorrhage
			A	B	C		
LDP ( <i>n</i> =22)	188±39	210±130	6	2	0	0	0
ODP ( <i>n</i> =76)	160±35	240±120	12	5	2	2	3
<i>P</i> -value	0.06	0.24		0.62		0.44	0.34

LDP: laparoscopic distal pancreatectomy; ODP: open distal pancreatectomy. Data are expressed as mean±SD or count

difference was detected between the two groups ( $P=0.44$ ). In the LDP group, 36% (8/22) of patients had at least one positive lymph node on pathological examination, while 41% (31/76) of patients had positive lymph nodes in the ODP group. No significant difference was detected between the two groups ( $P=0.71$ ). Two patients (9%) in the LDP group had a positive microscopic margin on pathological examination. Ten patients (13%) in the ODP group had a positive microscopic margin. There was no significant difference between the two groups ( $P=0.61$ ) (Table 3).

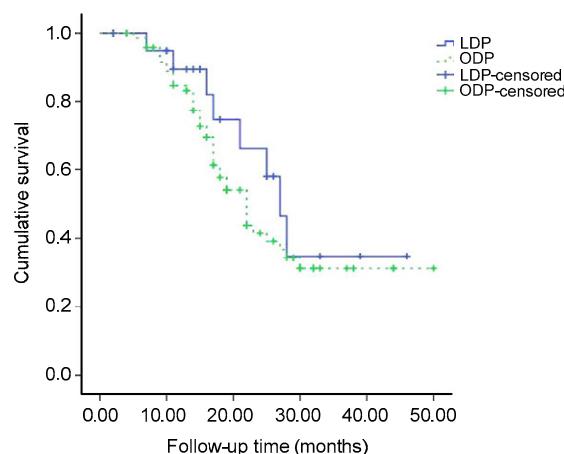
The mean overall survival was  $(29.6\pm3.7)$  months for the LDP group and  $(27.6\pm2.1)$  months for ODP group. There was no difference in overall survival between the two groups ( $P=0.34$ ; Fig. 1).

#### 4 Discussion

The evolution of laparoscopic techniques represents one of the great leaps in the field of surgery during the past decades. It has been reported that the

LDP is associated with a reduction in postoperative morbidity and shorter hospital stays in comparison with the open approach (Kooby *et al.*, 2008; Baker *et al.*, 2009; Briggs *et al.*, 2009; Yan *et al.*, 2015). In this study, patients in the LDP group experienced a similar overall morbidity as those in the ODP group. The method of pancreatic transection varied between the LDP and ODP groups in this study. In the LDP group, the pancreas was usually transected with an endo-GIA stapler, whereas in the ODP group the pancreas was transected with a harmonic scalpel or an electrocautery blade, and a continuous suture along the transected pancreatic surface with non-absorbable polypropylene was performed. Sugiyama *et al.* (2001) propose that the transection of pancreatic ductules on the cut surface of the pancreas is one of the risk factors leading to pancreatic fistula in distal pancreatectomy. From this point of view, the conventional method of ligating the main pancreatic duct should be advantageous to prevent pancreatic fistula. Nakamura *et al.* (2011) reported a prolonged compression maneuver when using a linear stapler in LDP. It was reported that incidence of pancreatic fistula was significantly decreased compared with the method without prolonged compression. In our series, a similar maneuver was applied when firing a linear stapler. In our experience, after the tunnel along the superior mesenteric vein was created, the endo-GIA instrument was closed slowly over 2–3 min to compress the pancreas tissue reliably. The compression was kept for another 2–3 min and then the stapler was fired. The two groups had a similar incidence of postoperative pancreatic fistula, regardless of the methods used to close the pancreas stump. It suggests that the stapling method is competent to seal pancreatic ductules when a slow compression maneuver is applied.

Our study was further concerned with oncological clearance as a short- and long-term outcome of LDP. LDP is commonly performed for benign or low



**Fig. 1** Overall survival of patients undergoing LDP and ODP

**Table 3** Pathological variables of the tumor of patients undergoing LDP and ODP

Group	Tumor size (cm)	AJCC stage				Number of harvested lymph nodes	Number of patients with positive lymph node	Resection margin status	
		I	II	III	IV			R0	R1
LDP (n=22)	$3.6\pm1.3$	8 (36%)	14 (64%)	0	0	11.2±4.6	8 (36%)	20 (91%)	2 (9%)
ODP (n=76)	$4.4\pm1.4$	23 (30%)	51 (70%)	0	0	14.4±5.5	31 (41%)	66 (87%)	10 (13%)
<i>P</i> -value	0.89		0.59			0.44	0.71		0.61

LDP: laparoscopic distal pancreatectomy; ODP: open distal pancreatectomy; AJCC: American Joint Committee on Cancer. Data are expressed as mean±SD or count (percentage)

malignant potential pancreatic lesions, such as well circumferential cystadenomas and low-grade neuroendocrine tumors (Soh *et al.*, 2012). Pancreatic ductal adenocarcinoma (PDAC) is a highly invasive malignancy with a troublesome recurrence rate even after aggressive resection. There were some studies claiming that more radical surgical approaches such as radical antegrade modular pancreateosplenectomy (RAMPS) may improve the surgical margin clearance and node harvest (Strasberg *et al.*, 2007). The efficacy of LPD for PDAC for oncological clearance is still controversial. Malignant pancreatic cancers were historically considered to be contraindicated with laparoscopic resection due to concerns about compromising the radicality of the resection (Patterson *et al.*, 2001). Recently, several authors have reported positive results regarding the radicality of the LPD. Kooby *et al.* (2010) reported on a series of 212 patients undergoing distal pancreatectomy for PDAC, of which 23 (11%) were performed laparoscopically. This report described a rate of positive margins as 26% in the whole series. The mean number of harvested nodes was 12.6 and 114 (54%) patients were found to have positive nodes. There was no difference regarding the rate of positive margins or the number of harvested lymph nodes between their LDP and ODP groups. Fernández-Cruz *et al.* (2007) described 13 cases with 90% of patients achieving R0 resection by LPD. A mean lymph node count of 14.5 and an overall survival time of 14 months were reported in their series. In the present study, the mean number of harvested lymph nodes was 11.2 in the LDP group and 14.4 in the ODP group. There is no significant difference in the number of harvested lymph node between the two groups. Node dissection is thought to mainly depend on three variables: patient factors such as BMI, surgical technique, and thoroughness of pathologic node assessment (Adsay *et al.*, 2009). Some authors stated that at least 12 lymph nodes should be assessed histologically for detecting metastatic disease in order to adequately stage patients with PDAC (Slidell *et al.*, 2008). From this point of view, the laparoscopic approach is reasonable for PDAC. At the same time, we also assessed the oncologic outcome of the laparoscopic approach in terms of margin clearance. Our report documented a rate of positive radial margins as low as 9% in the

LPD group. The incidence of positive margins was similar between LDP and ODP cases. We noted that the rate of positive margins in our series was markedly lower than the rate reported by Kooby *et al.* (2010). Margin status may vary with resection techniques and pathologic assessment methods. The difference of the rate of positive margins between different institutes may partly be due to the method of pathologic assessment. We are convinced that our improvement of the surgical procedure, by utilizing some aspects of RAMPS, contributed to this result.

Currently the rate of patient survival after resection for distal PDAC remains poor, which may be attributed to the late presentation of the disease as compared with right-sided pancreatic tumors (Shoup *et al.*, 2003). A median survival time ranging from 16 to 31 months has been documented (Kooby *et al.*, 2010; Sahakyan *et al.*, 2016; Stauffer *et al.*, 2016). Here we reported a mean survival of 29.6 months in the LDP group and 27.6 months in the ODP group. The mean survival in our study reaches the average benchmark in the literature. The patients in the LDP group in our study had similar oncological outcomes to the ODP group. Although limited by non-randomized data, the results do suggest that the laparoscopic approach does not adversely affect overall survival in patients with PDAC.

In conclusion, LDP is a safe and effective treatment approach for distal pancreatectomy for selected patients with PDAC. The slow-compression maneuver of pancreas tissue with the GIA stapler can achieve a comparable incidence of postoperative pancreatic fistula. Moreover, the oncologic outcome of LDP at least should not be inferior to conventional open approach, by taking advantage of laparoscopic RAMPS. Taking into account the minimally invasive nature of laparoscopic techniques, LDP could be a favorable surgical option for patients with PDAC.

### Compliance with ethics guidelines

Ai-bin ZHANG, Ye WANG, Chen HU, Yan SHEN, and Shu-sen ZHENG declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study.

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## 中文摘要

**题 目:** 腹腔镜与开腹胰体尾切除术对胰腺导管腺癌的治疗经验

**目 的:** 评估腹腔镜(LDP)与开腹胰体尾切除术(ODP)的并发症发生率和肿瘤清除效果。

**创新点:** 本组病例的腹腔镜手术组采用 endo-GIA 缓慢压榨方法处理胰腺残端，并采用根治性顺行模块化

胰脾切除术，获得了较低的术后胰漏发生率和良好的手术清除效果。

**方 法:** 收集4年间实施胰体尾切除手术的胰腺导管腺癌病例资料，进行回顾性分析。

**结 论:** 22例胰腺导管腺癌进行了LDP手术，76例病人进行了ODP手术。比较LDP和ODP组，两组在胰漏( $P=0.62$ )、腹腔内脓肿( $P=0.44$ )和术后出血( $P=0.34$ )发生率无显著性差异。LDP组和ODP组术中获取的淋巴结数量( $11.2\pm4.6$  vs.  $14.4\pm5.5$ ,  $P=0.44$ )和淋巴结阳性病例数(36% vs. 41%,  $P=0.71$ )无显著性差异。切缘阳性发生率(9% vs. 13%,  $P=0.61$ )也无显著性差异。LDP组平均生存期( $29.6\pm3.7$ )月，ODP组为( $27.6\pm2.1$ )月，无显著性差异( $P=0.35$ )。综上所述，腹腔镜胰体尾切除术对早期的胰腺导管癌是安全有效的。采用endo-GIA缓慢压榨方法可以预防术后胰漏发生，腹腔镜下根治性顺行模块化胰腺切除有利于肿瘤清除。腹腔镜手术可以达到和传统开腹手术相似的肿瘤清除效果。

**关键词:** 腹腔镜胰体尾切除术；开腹胰体尾切除术；胰腺肿瘤；胰漏