Laparoscopic versus open distal pancreatectomy: A meta-analysis

Cheng-Jun Sui, Bin Li, Jia-Mei Yang, Shuang-Jia Wang, Yan-Ming Zhou

Objective: Laparoscopic distal pancreatectomy (LDP) is a minimally invasive surgical technique. The aim of the present study was to evaluate the currently available literature and compare the short-term clinical outcomes of patients who underwent LDP for left-sided pancreatic pathology with patients who underwent traditional open surgery.

Methods: A literature search was performed to identify and compare studies that reported the clinical outcomes of both LDP and open distal pancreatectomy (ODP). Pooled odds ratios (OR) and weighted mean differences (WMD) with 95% confidence intervals (95% CI) were calculated using either fixed-effects or random-effects models.

Results: Nineteen nonrandomized controlled studies were identified that matched the selection criteria and reported the clinical outcomes of 1935 patients, of whom 805 underwent LDP and 1130 underwent ODP. Compared with open surgery, reports on laparoscopic resection indicate potentially favorable outcomes in terms of operative blood loss (WMD: -273.11; 95% CI: -404.61 to -141.61), the requirement of a blood transfusion (OR: 0.28; 95% CI: 0.11 to 0.71), postoperative time until oral intake (WMD: -1.19; 95% CI: -1.87 to -0.50), time to first flatus (WMD: -1.03, 95% CI: -1.93 to -0.12), length of hospital stay (WMD: -3.87, 95% CI: -5.06 to -2.68), and overall morbidity (OR: 0.70, 95% CI: 0.56 to 0.87). There were no differences in terms of the extent of oncologic clearance and postoperative mortality.

Conclusion: LDP results in a faster postoperative recovery and a comparable oncologic clearance in comparison with open surgery. Additional large trials are required to delineate the
1. Introduction

Since the introduction of laparoscopic cholecystectomy in 1987, the laparoscopic approach has been applied to the entire spectrum of abdominal procedures. However, the development of laparoscopic pancreatic surgery has been relatively slow because of the retroperitoneal position of the pancreas and the complex anatomical relationship between the pancreas and the surrounding vessels. Laparoscopic distal pancreatectomy (LDP) has recently been adopted by many centers due to the more straightforward nature of the resection and the lack of pancreatic ductal anastomosis, but current supporting evidence for this approach exists only in retrospective case series and a few case-control studies.

To improve the level of evidence available regarding LDP, we undertook this meta-analysis to compare this approach and open distal pancreatectomy (ODP) with regard to the short-term clinical outcomes.

2. Methods

2.1. Study selection

The MEDLINE, EMBASE, OVID, and Cochrane database were all searched for clinical studies published through 2010 to compare the clinical outcomes following the use of LDP and ODP to treat pancreatic diseases. The following Mesh search headings were used: “laparoscopic distal pancreatectomy” and “laparoscopic left pancreatectomy.” Reference lists of all the retrieved articles were manually searched for additional studies.

2.2. Data extraction

Two reviewers (BL and CJS) independently extracted the following data from each study: first author, year of publication, characteristics of the study population, study design, inclusion and exclusion criteria, number of subjects that underwent each procedure, male:female ratio, and conversion rate. All relevant text, tables, and figures were reviewed for data extraction. Discrepancies between the two reviewers were resolved by discussion and consensus.

2.3. Criteria for inclusion and exclusion

For inclusion in this meta-analysis, a study had to fulfill the following criteria: 1) compare the laparoscopic and open approaches among patients who underwent distal pancreatectomy for benign or malignant diseases; 2) report on at least one of the clinical outcome measures mentioned below and provide the standard deviation of the mean for the continuous outcomes of interest (or provide enough data to calculate the standard deviation); 3) clearly report the indications for surgery for the laparoscopic and open groups; 4) regarding dual (or multiple) studies that were reported by the same institution and/or authors, either the study of higher quality or the most recent publication was included in the analysis. Abstracts, letters, editorials, expert opinions, reviews without original data, case reports, and studies without control groups were excluded.

2.4. Outcomes of interest

The following outcomes were used to compare the two operative techniques: operative outcomes (which included operative time, operative blood loss, number of patients requiring blood transfusion, and oncologic clearance in terms of pathological resection margins) and postoperative outcomes (including time required until oral intake, time to first flatus, hospital stay, morbidity, and mortality).

2.5. Statistical methods

This meta-analysis was performed using the Review Manager (RevMan) software, version 4.2.7. We analyzed the dichotomous variables by estimating the odds ratios (OR) with a 95% confidence interval (95% CI), and continuous variables were analyzed using weighted mean difference (WMD) with a 95% CI. The pooled effect was calculated using either fixed-effects or random-effects models. Heterogeneity was evaluated using either $\chi^2$ or $I^2$, which can be interpreted as the percentage of the total variation between studies that can be attributable to heterogeneity rather than chance. We considered heterogeneity to be present if the $I^2$ statistic was > 50%. A $p$ value < 0.05 was considered significant.

3. Results

The literature search identified 19 studies that were published between 2006 and 2010 that matched the selection criteria and were therefore included. These 19 studies included a total of 1935 patients: 805 in the LDP group and 1130 in the ODP group. Ten studies were conducted in the United States, four in Japan, two in Korea, one in Hong Kong, one in Italy, and one in China. The sample size of each study varied from 11 to 342 patients. The study characteristics and patient demographics are summarized in Table 1.

In these 19 studies, the patients in the two groups were matched according to age, gender, body mass index, preoperative comorbidities, and tumor size.
The conversion rate ranged from 0–30%. The total of 102 conversions from laparoscopic to open laparotomy were reported in 12 studies.9,11,14,17,19-24,26,27

### 3.1. Meta-analysis of the operative outcomes

The results of the overall meta-analysis are outlined in Table 2.9-27 The pooled analysis of the 10 studies that provided data shows that operative time was significantly increased in the LDP group in comparison with the ODP group with a WMD of 27.91 (95% CI: -40.61 to -141.61) with significant heterogeneity between studies (I² = 85.3%; Fig. 1).

Eight studies reported operative blood loss, which was found to be significantly lower in the LDP group versus the ODP group (WMD: -273.11, 95% CI: -404.61 to -141.61) with significant heterogeneity between the studies (I² = 95%; Fig. 2). Accordingly, patients in the LDP group demonstrated a lower rate of blood transfusion (6 trials reported these data; OR: 0.28; 95% CI: 0.11 to 0.71). Seven studies reported the adequacy of oncological clearance in terms of pathologic resection margins, and no significant differences were noted between the two groups (Fig. 3).

### 3.2. Meta-analysis of the postoperative outcomes

All measures of postoperative recovery were significantly better in the LDP group: specifically, time to oral intake (6 trials reported these data; WMD: -1.19; 95% CI: -1.87 to -0.50), time to first flatus (4 trials reported these data; WMD: -1.84; 95% CI: -4.28 to 0.61), and time to full flatus (4 trials reported these data; WMD: -2.46; 95% CI: -5.73 to 0.81) with significant heterogeneity between studies (I² = 85.3%, 74.6%, and 83.8%, respectively; Figs. 4 and 5).
WMD: -1.03; 95% CI: -1.93 to -0.12), and length of hospital stay (11 trials reported these data; WMD: -3.87; 95% CI: -5.06 to -0.26). However, significant heterogeneity was found among the studies that reported these outcomes ($I^2 > 50%$; Figs. 4e-6).

Overall, morbidity was indicated in 28.4% of patients treated with LDP and in 37.8% of those treated with ODP, with the difference being statistically significant and favorable to LDP (17 trials reported these data; OR: 0.70; 95% CI: 0.56 to 0.87; Fig. 7). Wound infection was found to be significantly lower in the LDP group (7 trials reported these data; OR: 0.37; 95% CI: 0.20 to 0.68). In contrast, the incidence of pancreatic fistula (LDP, 14.5%; ODP, 17.9%; $p = 0.29$), pulmonary complications (LDP, 3.2%; ODP, 7.8%; $p = 0.18$), and reoperation (LDP, 4.0%; ODP, 3.0%; $p = 0.41$) were similar between the two groups. Other complications such as intra-abdominal abscess, urinary tract infection, fluid collection, atrial fibrillation, incisional hernia, paralytic ileus, and deep venous thrombosis were only reported in one or two studies. Therefore, we did not analyze these data.

Postoperative mortality was similar between the two groups (17 trials reported these data; OR: 0.75; 95% CI: 0.25 to 2.28). Three and nine deaths were reported in the LDP and ODP groups, respectively, yielding an overall mortality rate of 0.4% and 1.0%, respectively.

4. Discussion

This meta-analysis revealed that LDP requires a longer operating time than ODP. The longer operating time for LDP may in part reflect the early learning curve because this is a relatively new procedure that requires extensive experience in open pancreatic surgery in combination with a high level of laparoscopic skill. This effect can be minimized by adopting a team approach, allowing the consolidation of skills and expertise. The decrease in blood loss and the low transfusion requirement rate in the LDP group may be related to the less invasive nature of the operation.

The pooled data showed a shorter hospital stay for the LDP group in comparison with the ODP group. The earlier

### Table 2

<table>
<thead>
<tr>
<th>Outcome of interest</th>
<th>No. of studies</th>
<th>No. of patients</th>
<th>OR/WMD</th>
<th>95% CI</th>
<th>$p$</th>
<th>$I^2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operative outcomes</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Operative time</td>
<td>1010–12, 17, 18, 20, 21, 24, 25, 27</td>
<td>LDP = 354, ODP = 559</td>
<td>27.91</td>
<td>4.01, 51.94</td>
<td>0.02</td>
<td>85.3</td>
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<tr>
<td>Blood loss</td>
<td>811, 12, 17, 18, 20, 21, 24, 27</td>
<td>LDP = 301, ODP = 475</td>
<td>273.11</td>
<td>404.61, 141.61</td>
<td>&lt;0.001</td>
<td>95</td>
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<tr>
<td>Blood transfusion required</td>
<td>610, 13, 16, 17, 20, 27</td>
<td>LDP = 197, ODP = 179</td>
<td>0.28</td>
<td>0.11, 0.71</td>
<td>0.007</td>
<td>6.7</td>
</tr>
<tr>
<td>Positive resection margin</td>
<td>711, 13, 22–24, 26, 27</td>
<td>LDP = 475, ODP = 709</td>
<td>0.61</td>
<td>0.36, 1.05</td>
<td>0.07</td>
<td>26.2</td>
</tr>
<tr>
<td><strong>Postoperative outcomes</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Time to oral intake (d)</td>
<td>616, 17, 20, 21, 25, 27</td>
<td>LDP = 219, ODP = 169</td>
<td>-1.19</td>
<td>-1.87, -0.50</td>
<td>&lt;0.001</td>
<td>7.78</td>
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<td>Time to first flatus (d)</td>
<td>417, 20, 21, 27</td>
<td>LDP = 104, ODP = 112</td>
<td>-1.03</td>
<td>-1.93, -0.12</td>
<td>0.03</td>
<td>92.7</td>
</tr>
<tr>
<td>Hospital stay (day)</td>
<td>1111–12, 18–21, 24–27</td>
<td>LDP = 484, ODP = 744</td>
<td>-3.87</td>
<td>-5.06, -2.68</td>
<td>&lt;0.001</td>
<td>90.9</td>
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<td>Overall morbidity</td>
<td>1717–19, 20–22, 25–27</td>
<td>LDP = 738, ODP = 959</td>
<td>0.70</td>
<td>0.56, 0.87</td>
<td>0.001</td>
<td>23.8</td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>1619–21, 13–16, 22, 23–25, 27</td>
<td>LDP = 770, ODP = 1048</td>
<td>0.86</td>
<td>0.66, 1.13</td>
<td>0.29</td>
<td>0</td>
</tr>
<tr>
<td>Wound infection</td>
<td>717, 11, 14, 19, 21, 26, 27</td>
<td>LDP = 383, ODP = 512</td>
<td>0.37</td>
<td>0.20, 0.68</td>
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<td>Pulmonary complications</td>
<td>719, 10, 14, 17, 19, 21, 27</td>
<td>LDP = 186, ODP = 293</td>
<td>0.59</td>
<td>0.27, 1.28</td>
<td>0.18</td>
<td>0</td>
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<tr>
<td>Reoperation</td>
<td>418, 17, 22, 25</td>
<td>LDP = 249, ODP = 262</td>
<td>1.55</td>
<td>0.55, 4.40</td>
<td>0.41</td>
<td>0</td>
</tr>
<tr>
<td>Mortality</td>
<td>1719–22, 25–27</td>
<td>LDP = 682, OLR = 960</td>
<td>0.75</td>
<td>0.25, 2.28</td>
<td>0.61</td>
<td>0</td>
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LDP = laparoscopic distal pancreatectomy; ODP = open distal pancreatectomy; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval.

Figure 1 Results of the meta-analysis regarding operating time.
recovery of bowel function, shorter time required to tolerate oral intake, and reduced postoperative stress after LDP versus ODP are probably responsible for this benefit. Furthermore, ODP usually requires an extensive abdominal incision. Wound pain in association with the long incision would prevent an early return to normal activities.

Patients in the LDP group developed fewer overall complications than those in the ODP group. This may be due to the more rapid postoperative recovery of the LDP group. The shorter incision that is needed to perform LDP is believed to contribute to its lower rate of wound infection. The incidence of postoperative pancreatic leak, the most serious complication after distal pancreatectomy, was similar in both groups. The method of pancreatic transection varied between the LDP and ODP groups. In the LDP group, the pancreas was usually transected using a harmonic scalpel, LigaSure, bipolar cautery, or an Endo GIA stapler, whereas in the ODP group pancreatic transection was usually performed using an electrocautery blade or Endo GIA stapler.10,26,27 Teh et al14 stated it is likely that pancreatic leak will develop, regardless of the approach and the method used to close the pancreatic stump. Recently, a Japanese group described a peri-firing compression method in which the pancreas is compressed directly using Echelon. After the first compression, compression is maintained on the pancreas for another 3 minutes and then the stapler is fired. After firing, the pancreas is kept compressed for a further 2 minutes. No pancreatic leakage was observed in a consecutive series of 17 patients who underwent LDP,28 but this must be confirmed by further studies by other centers.

Some authors have suggested that malignant pancreatic neoplasms are a contraindication to laparoscopic resection because of concerns regarding the radicality of the resection.30 The present study shows there are no significant differences in terms of the proportion of patients with positive radial margins between the two groups. Another concern about the laparoscopic resection of malignancies is the potential risk of trocar site metastases, wound recurrence, peritoneal carcinomatosis, and the promotion of neoplastic growth by pneumoperitoneum.31–33 However, there is no definitive evidence in the literature that the use of the laparoscopic technique increases the risk of...
neoplastic dissemination,34 and none of the patients followed in the current study developed any trocar site or peritoneal metastasis. More recently, a large multicenter study reported that patients with pancreatic ductal adenocarcinoma (an aggressive malignancy) who underwent LDP demonstrated similar median survival in comparison with those who underwent ODP in a matched cohort analysis (16 months vs. 16 months).24 Taken together, these results suggest that LDP does not compromise oncological principles.

The results of this meta-analysis should be interpreted with caution because of several limitations. First, all of data in the present study were reported in nonrandomized controlled trials. Meta-analysis of such data leads to less powerful results than those based purely on randomized patients. However, we should take into account that it is difficult to conduct a prospective randomized study because of poor patient compliance. Second, it was impossible to match the patient characteristics across all of these studies, which could have caused the heterogeneity between the groups. We applied a random-effect model in order to take between-study variation into consideration. This does not necessarily rule out the effect of heterogeneity between studies, but one may expect a very limited influence. Finally, the effects on the long-term clinical outcomes of patients diagnosed with malignant neoplasms of the pancreas were not well evaluated due to insufficient data. Further investigations regarding these outcomes are warranted.

The present meta-analysis included a total of 1935 patients who were treated with distal pancreatectomy for pancreatic diseases, representing the largest body of information currently available for the comparison of LDP

Figure 4  Results of the meta-analysis regarding time required until oral intake.

Figure 5  Results of the meta-analysis regarding time to first flatus.

Figure 6  Results of the meta-analysis regarding length of hospital stay.
and ODP. This study demonstrates that LDP is a feasible and safe alternative to the open technique. Patients undergoing LDP may benefit from less blood loss, faster postoperative recovery, and reduced overall morbidity and wound infection without compromising oncologic clearance. These results suggest some of the advantages of LDP. Further large trials are required to delineate the long-term clinical outcomes of patients diagnosed with malignant neoplasms.

Competing interests

The authors declare that they have no financial interests related to the materials presented in this article.

References


