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REVIEW ARTICLE

A systematic review and meta-analysis of studies comparing laparoscopic and open distal pancreatectomy

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Abstract

Objectives: Currently, laparoscopic distal pancreatectomy (LDP) is regarded as a safe and effective surgical approach for lesions in the body and tail of the pancreas. This review compares outcomes of the laparoscopic technique with those of open distal pancreatectomy (ODP) and assesses the efficacy, safety and feasibility of each type of procedure.

Methods: Comparative studies published between January 1996 and April 2012 were included. Studies were selected based on specific inclusion and exclusion criteria. Evaluated endpoints were operative outcomes, postoperative recovery and postoperative complications.

Results: Fifteen non-randomized comparative studies that recruited a total of 1456 patients were analysed. Rates of conversion from LDP to open surgery ranged from 0% to 30%. Patients undergoing LDP had less intraoperative blood loss [weighted mean difference (WMD) –263.36.59 ml, 95% confidence interval (CI) –330.48 to –196.23 ml], fewer blood transfusions [odds ratio (OR) 0.28, 95% CI 0.11–0.76], shorter hospital stay (WMD –4.98 days, 95% CI –7.04 to –2.92 days), a higher rate of splenic preservation (OR 2.98, 95% CI 2.18–3.91), earlier oral intake (WMD –2.63 days, 95% CI –4.23 to 1.03 days) and fewer surgical site infections (OR 0.37, 95% CI 0.18–0.75). However, there were no differences between the two approaches with regard to operation time, time to first flatus and the occurrence of pancreatic fistula and other postoperative complications.

Conclusions: Laparoscopic resection results in improved operative and postoperative outcomes compared with open surgery according to the results of the present meta-analyses. It may be a safe and feasible option for patients with lesions in the body and tail of the pancreas. However, randomized controlled trials should be undertaken to confirm the relevance of these early findings.

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Introduction

Laparoscopic surgery is now widely accepted and recognized as a standard technique in many surgical procedures.[1,2] Initially, the laparoscopic approach was not commonly used in pancreatic resection; however, increasing experience means laparoscopic distal pancreatectomy (LDP) is now performed more frequently in the surgical management of benign, non-invasive and even malignant lesions in the body and tail of the pancreas.[3] Some studies have reported LDP to be associated with decreased intraoperative blood loss, a higher rate of splenic conservation, shorter hospital stay and less morbidity compared with open distal pancreatectomy (ODP).[4–6] By contrast, other studies report findings in favour of ODP.[7,8] Because these various reports indicate a discrepancy in the published literature, the present authors considered it necessary to summarize and analyse the published data to provide evidence to determine whether the literature supports the use of a laparoscopic approach as an alternative to open surgery in the resection of the distal pancreas.

*These authors contributed equally to this work.

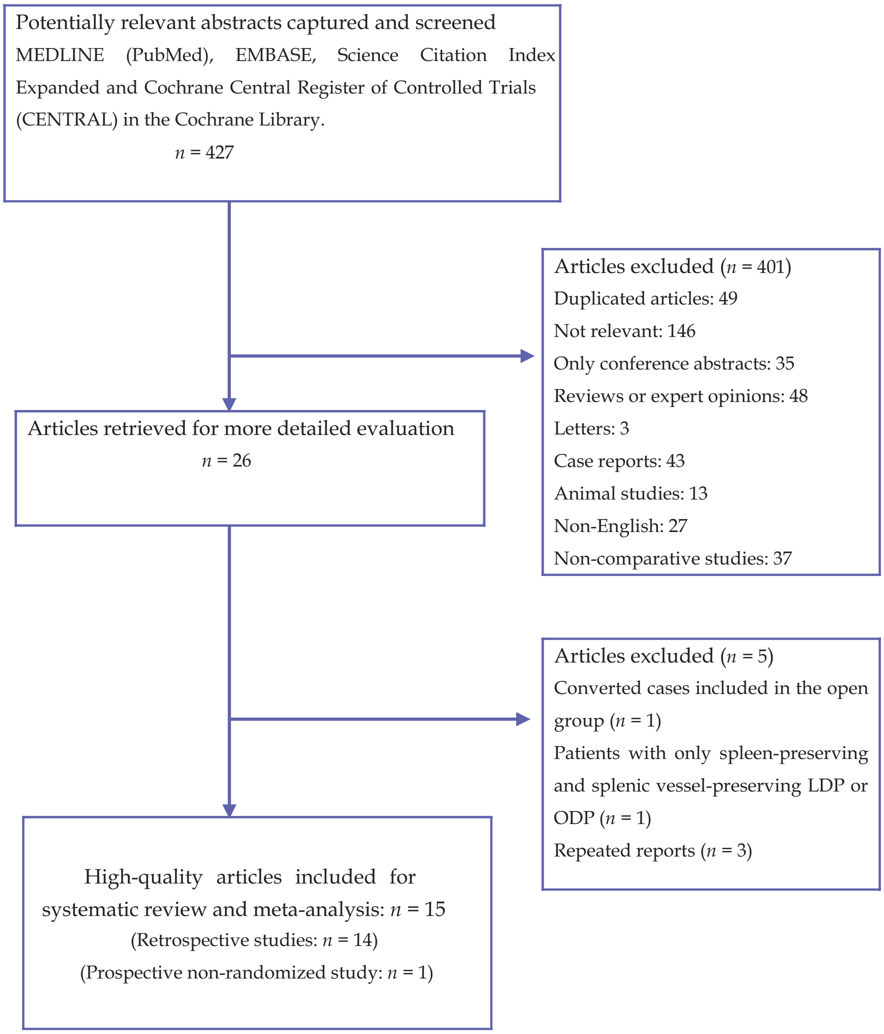


Figure 1 Flow diagram depicting the process of identifying and selecting studies for inclusion. LDP, laparoscopic distal pancreatectomy; OPD, open distal pancreatectomy

Materials and methods

Study selection

Major databases including PubMed (MEDLINE), EMBASE, the Science Citation Index Expanded and the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library were searched for studies comparing outcomes in LDP and ODP, published in English from January 1996 to April 2012 (the first LDP was described in 1996). The medical search headings (MeSH) 'laparoscopy', 'pancreatectomy', 'comparative study' and combinations of these were used, as were the keywords 'laparoscopic', 'open distal pancreatic resection', 'left pancreatic resection', 'pancreatic surgery', 'distal pancreatectomy' and 'minimally invasive surgery'. The reference lists of articles identified were examined to find relevant studies that had not been identified by the database searches. Only comparative clinical trials with full-text descriptions were included. The final inclusion of articles was determined by consensus between authors TJ and KA; when this failed, a third author (JJX) adjudicated.

Inclusion and exclusion criteria

Two authors (TJ and KA) identified and screened the search findings for potentially eligible studies. Inclusion criteria required the studies to: (i) be written in English and published in peer-reviewed journals; (ii) be human studies; (iii) examine at least one of the predetermined outcomes, and (iv) provide clear documentation of the operative techniques as 'laparoscopic' or 'open'. In contexts in which multiple studies were published from the same institution and/or by the same authors, either the higher-quality study or the most recent publication was included in the analysis.

Exclusion criteria excluded: (i) abstracts, letters, editorials, expert opinions, case reports, reviews and studies lacking control groups; (ii) studies that included only patients undergoing spleen-

Table 1 Characteristics of included studies

Author(s)	Year	Country	Study design	LDP, *n*	ODP, *n*	Inclusion/exclusion criteria	Matching/ comparable factors[a]	Study quality[b] (point scoring scale)
Velanovich[4]	2006	USA	Retro	15	15	Not specified	2, 4	*******
Teh *et al.*[5]	2007	USA	Retro	12	16	Benign pancreatic disease (I)	1, 2, 3, 4	******
Matsumoto *et al.*[6]	2008	Japan	Retro	14	19	Benign or borderline malignant pancreatic tumour (I)	1, 2, 3	*********
Kim *et al.*[26]	2008	Korea	Retro	93	35	Benign pancreatic disease (I)	2, 3, 4	*******
Kooby *et al.*[18]	2008	USA	Retro	23	189	Ductal adenocarcinoma (I)	1, 2, 3	******
						Background IPMN/cystadenocarcinoma (E)		
Baker *et al.*[21]	2009	USA	PNR	27	85	Not specified	1, 3, 4	******
Jayaraman *et al.*[27]	2010	USA	Retro	100	100	Additional organ resection (E)	None	*******
DiNorcia *et al.*[28]	2010	USA	Retro	71	168	Laparoscopic-assisted DP (E)	1	******
						DP as part of a completion pancreatectomy (E)		
						Concomitant portomesenteric venous resection and reconstruction (E)		
						DP secondary to debridement for necrotizing pancreatitis (E)		
						Non-pancreatic primary neoplasms or pancreatic injury (E)		
Casadei *et al.*[29]	2010	Italy	Retro	22	22	Endocrine and cystic pancreatic tumours (I)	1, 2	*******
						Ductal adenocarcinoma (E)		
Waters *et al.*[30]	2010	USA	Retro	18	22	Urgent surgery (E) Concurrent major surgery an indication for surgery of acute or chronic pancreatitis (E)	1, 4	******
Mehta *et al.*[31]	2012	France	Retro	30	30	DP for non-pancreatic pathologies (E)	2, 3, 4	******
						Resections amounting to less than a DP or total pancreatectomy (E)		
Butturini *et al.*[32]	2012	Italy	Retro	43	73	Benign and borderline neoplasms (I)	2, 3	********
						Ductal cancer or other malignant tumours (E)		
Abu *et al.*[38]	2011	UK	Retro	35	16	Additional organ resections (E)	3, 4	*****
Fox *et al.*[33]	2012	Canada	Retro	42	76	Additional organ resection (E)	1, 3, 4	*****
Limongelli *et al.*[34]	2012	Italy	Retro	16	29	Only tumour enucleation was accomplished (E)	1, 2, 4	******
						Additional organ resection (E)		

[a]Matching/comparable factors are: 1, American Society of Anesthesiologists (ASA) status; 2, type of pancreatic pathology; 3, mean size of tumour, and 4, presence of chronic pancreatitis.
[b]Based on Newcastle–Ottawa Scale with maximum of **** for selection, ** for comparability, and ** for outcome.
LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy; Retro, retrospective; PNR, prospective non-randomized; I, inclusion criteria; E, exclusion criteria; IPMN, intraductal papillary mucinous neoplasm; DP, distal pancreatectomy.

preserving LDP or ODP, and (iii) studies in which patients converted to open surgery were included in the ODP group.

Outcomes of interest and definitions of complications

The following outcomes were used to compare patients undergoing LDP with those undergoing ODP. Operative outcomes included operative time, intraoperative blood loss, blood transfusion and splenic preservation. Postoperative recovery comprised time to oral intake, time to first flatus and duration of postoperative hospital stay. Postoperative complications included pancreatic fistula, clinically significant fistula [International Study Group on Pancreatic Fistula (ISGPF) grades B and C[9]], mortality, surgical site infection, intra-abdominal abscess, intra-abdominal fluid collection, postoperative haemorrhage, reoperation and readmission.

Data extraction and quality assessment

Data were extracted by two independent observers (WH and MAJ) using standardized forms. Data recorded included patient and study characteristics, pathological characteristics of resected specimens, and operative and postoperative outcomes. The

Table 2 Operative and postoperative outcomes of included comparative studies

Author	Conversion n (%)	Spleen preservation n (%)		Operation time, min, mean/median (range)		Hospital stay, days, mean/median (range)		PF/clinically significant PF n (%)		Mortality n (%)	
		LDP	ODP	LDP	ODP	LDP	ODP	LDP	ODP	LDP	ODP
Velanovich[4]	3 (20)	NA	NA	NA	NA	5 (3–9)	8 (6–23)	2 (13)	2 (13)	NA	NA
Teh *et al.*[5]	2 (16.7)	NA	NA	212 (60–360)	278 (180–420)	6.2 (3–16)	10.6 (7–19)	1 (8.3)	1 (6.2)	0	0
Matsumoto *et al.*[6]	1 (7.1)	NA	NA	290.7 ± 53.2[a]	213.8 ± 84.6[a]	12.9 ± 4.8[a]	23.8 ± 11.8[a]	0	2 (10.5)	0	0
Kim *et al.*[26]	NA	38 (40.8)	2 (5.7)	195 (82–453)	190 (88–482)	10 (5–36)	16 (8–65)	8 (8.6)	5 (14.3)	0	0
Kooby *et al.*[18]	20 (12.6)	43 (30)	24 (12)	230 ± 97[a]	216 ± 100[a]	5.9 ± 3.8[a]	9.0 ± 6.0[a]	37 (26)/16 (11)	64 (32)/36 (18)	0	1 (1)
Baker *et al.*[21]	1 (3.7)	NA	NA	236 ± 82[a]	253.2 ± 292.3[a]	4.0 ± 0.3[a]	8.6 ± 0.7[a]	6 (22)/4 (14.8)	12 (14)/12 (14.1)	0	1 (1.2)
Jayaraman *et al.*[27]	32 (30)	14 (42.4)	33 (14.0)	195	160	5	6	8 (10.8)	13 (5.5)	0	2 (0.8)
DiNorcia *et al.*[28]	24 (25.3)	11 (15.5)	26 (15.8)	191 (163–214)	192 (157–236)	5 (4–6)	6 (5–8)	8 (11.3)	25 (14.9)	0	1 (0.6)
Casadei *et al.*[29]	0	4 (18.2)	4 (18.2)	225 ± 83[b]	145 ± 49[b]	8.0 ± 1.3[b]	11.0 ± 3.0[b]	2 (9.1)	4 (18.2)	0	0
Waters *et al.*[30]	2 (11)	5 (28)	3 (14)	224 (100–346)	234 (136–437)	6 (3–34)	8 (3–25)	2 (11.1)	4 (18.2)	0	0
Mehta *et al.*[31]	0	21 (70)	9 (30)	188 ± 72[a]	226 ± 87[a]	8.7 ± 4.2[a]	12.6 ± 8.7[a]	5 (16.7)/5 (16.7)	4 (13.3)/4 (13.3)	0	1 (3.3)
Butturini *et al.*[32]	0	19 (44.2)	8 (11)	180	180	8	9	12 (27.9)	10 (13.7)	0	0
Abu *et al.*[38]	0	14 (40)	3 (19)	200 (120–420)	225 (120–460)	7 (3–25)	11 (5–46)	10 (29)	7 (44)	NA	NA
Fox *et al.*[33]	5 (11.91)	15 (35.7)	17 (22.4)	304 (265–348)	281 (247–333)	5 (4–6)	7 (6–9)	12 (28.6)/0 (0)	10 (13.2)/4 (5.3)	NA	NA
Limongelli *et al.*[34]	1 (6)	5 (31)	3 (14)	204 ± 31[a]	160 ± 35[a]	6.4 ± 2.3[a]	8.6 ± 1.7[a]	3 (18)/1 (6)	6 (20)/5 (17.2)	0 (0)	1 (3)

[a]Mean ± standard deviation.
[b]Median ± standard deviation.
PF, pancreatic fistula; LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy; NA, not available.

Table 3 Definitions of postoperative pancreatic fistula in the included studies

Author	Definition of postoperative pancreatic fistula
Velanovich[4]	Amylase-rich fluid after PoD 3
Teh *et al.*[5]	Amylase >1000 after PoD 3
Matsumoto *et al.*[6]	Fluid amylase >5000 U/l after PoD 7
Kim *et al.*[26]	Drainage of >30 ml with amylase level >5-fold more than serum level ≥5 days after surgery
Kooby *et al.*[18]	Fluid amylase >350 mg/dl or need for postoperative percutaneous fluid collection
Baker *et al.*[21]	ISGPF definition
Jayaraman *et al.*[27]	ISGPF definition
DiNorcia *et al.*[28]	ISGPF definition
Casadei *et al.*[29]	ISGPF definition
Waters *et al.*[30]	Not defined
Mehta *et al.*[31]	ISGPF (grades B and C)
Butturini *et al.*[32]	ISGPF definition
Abu *et al.*[38]	ISGPF definition
Fox *et al.*[33]	ISGPF definition
Limongelli *et al.*[34]	ISGPF definition

PoD, postoperative day; ISGPF, International Study Group on Pancreatic Fistula.

quality of studies was assessed using the modified Newcastle–Ottawa Scale, modified to reflect the needs of this study.[10] The maximum numbers of points awarded in the selection, comparability and outcome categories were three, four and two, respectively. Studies achieving six or more points were considered to be of high quality.[11] Only these studies were included in the final analyses. Subgroup analyses included all studies (high and low quality) in order to obtain a cumulative result.

Statistical analysis

Meta-analysis was performed using Review Manager Version 5.0 (Cochrane Collaboration, Oxford, UK). For continuous variables, treatment effects were expressed as the weighted mean difference (WMD) with the corresponding 95% confidence interval (CI). For categorical variables, treatment effects were expressed as the odds ratio (OR) with the corresponding 95% CI. Heterogeneity was evaluated using the chi-squared test and a P-value of <0.1 was considered to indicate statistical significance.[12] The fixed-effects model was initially calculated for all outcomes,[13] but if the test rejected the assumption of homogeneity of studies, random-effects analysis was performed.[14] If data in the included studies were considered to be inappropriate for meta-analysis, some outcomes were presented descriptively. Sensitivity analyses were performed by removing individual studies from the dataset and analysing the effect on the overall results to identify sources of significant heterogeneity. Subgroup analyses were undertaken by including high-quality studies to present cumulative evidence.

Table 4 Results of meta-analysis comparing outcomes in laparoscopic and open distal pancreatectomy in high-quality studies

Outcome of interest	Studies, *n*	Patients, *n*	OR/WMD	95% CI	*P*-value*
Operative outcomes					
Operation time, min	5	343	19.71	–10.01 to 49.44	0.19
Intraoperative blood loss, ml	5	343	–263.36	–330.48 to –196.23	<0.00001
Blood transfused	5	375	0.28	0.11–0.76	0.01
Splenic preservation	10	1148	2.98	2.18–4.06	<0.00001
Postoperative recovery					
Time to oral intake, days	2	161	–2.63	–4.23 to –1.03	0.001
Time to first flatus, days	2	161	–1.80	–2.14 to –1.47	<0.00001
Hospital stay, days	5	343	–4.98	–7.04 to –2.92	<0.00001
Postoperative complications					
Clinically significant fistula	4	335	0.67	0.41–1.09	0.11
Postoperative haemorrhage	4	329	1.87	0.59–5.95	0.29
Intra-abdominal abscess	6	331	0.78	0.25–2.45	0.67
Intra-abdominal fluid collections	3	304	1.47	0.67–3.22	0.34
Surgical site infection	5	264	0.37	0.18–0.75	0.006
Mortality	11	1155	0.61	0.16–2.27	0.46
Reoperation	8	683	0.90	0.43–1.84	0.76
Readmission	5	772	0.70	0.41–1.21	0.20

WMD, weighted mean difference; OR, odds ratio; 95% CI, 95% confidence interval.

Funnel plots were constructed to evaluate potential publication bias[15] based on the major complication of pancreatic fistula.

Results

Description of trials included in the meta-analysis

The search strategy initially generated 427 relevant clinical reports. Finally, 26 full-text articles[4–6,16–38] were identified for further investigation. Of these, two studies[16,17] were excluded for various reasons: one study included patients in whom LDP had been converted to open surgery in the ODP group,[16] and the other included patients who had undergone only spleen-preserving and splenic vessel-preserving LDP or ODP.[17] Three studies[18–20] reported from the same institution described overlapping patient populations. According to the inclusion criteria, the highest-quality study[18] was included in the present meta-analysis. Similarly, of two studies published by Baker *et al.*,[21,22] the higher-quality study[21] was included. Six studies were low-quality studies, which should be excluded. Finally, 15 high-quality studies were identified for inclusion; these included one prospective non-randomized study and 14 retrospective studies. Figure 1 shows the process by which comparative studies were selected for inclusion in the present meta-analysis.

Study and patient characteristics

The study characteristics, quality and comparability assessments are shown in Table 1. Details of outcome measures are listed in Table 2. Definitions of pancreatic fistula are shown in Table 3. A total of 1456 patients were included; this number included 561 and 895 patients in the LDP and ODP groups, respectively. Five studies[5,6,26,29,32] looked at benign tumours only. The remaining 10 studies[4,19,21,27,28,30,31,33,34,38] looked at both benign and malignant lesions. Most of the studies conducted a matched comparative analysis. The results of the analyses are summarized in Table 4.

Operative outcomes

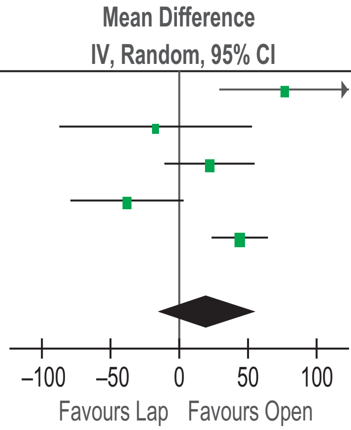
Five studies[6,19,21,31,34] reported operation time. The present analysis showed no statistically significant difference between the two groups (WMD 19.71 min, 95% CI –10.01 to 49.44; P = 0.19). Similarly, findings in five studies[6,19,21,31,34] were pooled to provide an estimation of mean blood loss in each of the LDP and ODP groups. Intraoperative blood loss was significantly lower in the LDP group than in the ODP group (WMD –263.36 ml, 95% CI –330.48 to –196.23; P < 0.00001). Additionally, fewer patients required blood transfusions in the LDP group (OR 0.28, 95% CI 0.11–0.76; P = 0.01). The rate of splenic preservation was identified as significantly higher in the LDP group than in the ODP group (OR 2.98, 95% CI 2.18–3.91; P < 0.00001). Forest plots are shown in Fig. 2.

Postoperative recovery

Patients in the LDP group had a shorter postoperative hospital stay (WMD –4.98 days, 95% CI –7.04 to –2.92; P < 0.00001) and were able to resume flatus earlier (WMD –1.80 days, 95% CI –2.14 to –1.47; P < 0.000001) than their counterparts in the ODP group (Fig. 3). However, there was no significant difference between the groups in time to oral intake (WMD –2.63 days, 95% CI –4.23 to 1.03; P = 0.001).

Study or Subgroup	Lap Mean	Lap SD	Lap Total	Open Mean	Open SD	Open Total	Weight	Mean Difference IV, Random, 95% CI	Year
Matsumoto et al. 2008	290.7	53.2	14	213.8	84.6	19	18.6%	76.90 (29.74, 124.06)	2008
Baker *et al.* 2009	236	82	27	253.2	292.3	85	13.5%	–17.20 (–86.61, 52.21)	2009
Kooby *et al.* 2010	238	68	23	216	69	70	22.4%	22.00 (–10.15, 54.15)	2010
Mehta *et al.* 2012	188	72	30	226	87	30	20.3%	–38.00 (–78.41, 2.41)	2011
Limongelli *et al.* 2012	204	31	16	160	35	29	25.2%	44.00 (24.18, 63.82)	2012
Total (95% CI)			**110**			**233**	**100.0%**	**20.27 (–15.60, 56.14)**	

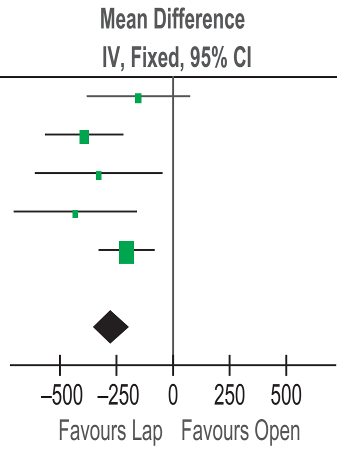
Heterogeneity: Tau² = 1225.38; Chi² = 18.60, d.f. = 4 (P = 0.0009); I^2 = 78%
Test for overall effect: Z = 1.11 (P = 0.27)



(a)

Study or Subgroup	Lap Mean	Lap SD	Lap Total	Open Mean	Open SD	Open Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Matsumoto *et al.* 2008	247.1	227.4	14	400.3	423.5	19	13.1%	–153.20 (–377.81, 71.41)	2008
Baker *et al.* 2009	219.4	159	27	612.6	744.02	85	23.1%	–393.20 (–562.36, –224.04)	2009
Kooby *et al.* 2010	422	473	23	751	853	70	8.5%	–329.00 (–607.02, –50.98)	2010
Mehta *et al.* 2012	294	245	30	726	709	30	9.2%	–432.00 (–700.43, –163.57)	2011
Limongelli *et al.* 2012	160	185	16	365	215	29	46.1%	–205.00 (–324.75, –85.25)	2012
Total (95% CI)			**110**			**233**	**100.0%**	**–273.10 (–354.39, –191.81)**	

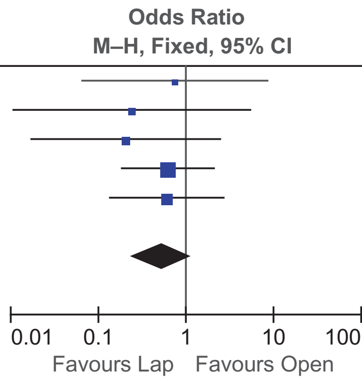
Heterogeneity: Chi² = 5.77, d.f. = 4 (P = 0.22); I^2 = 31%
Test for overall effect: Z = 6.58 (P < 0.00001)



(b)

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M–H, Fixed, 95% CI	Year
Kim *et al.* 2008	2	93	1	35	8.0%	0.75 (0.07, 8.51)	2008
Matsumoto *et al.* 2008	0	14	2	19	11.6%	0.24 (0.01, 5.44)	2008
Abu *et al.* 2011	1	35	2	16	14.9%	0.21 (0.02, 2.46)	2011
Fox *et al.* 2012	4	42	11	76	39.7%	0.62 (0.19, 2.09)	2011
Limongelli et al. 2012	3	16	8	29	25.9%	0.61 (0.14, 2.71)	2012
Total (95% CI)		**200**		**175**	**100.0%**	**0.52 (0.24, 1.15)**	
Total events	10		24				

Heterogeneity: Chi² = 0.98, d.f. = 4 (P = 0.91); I^2 = 0%
Test for overall effect: Z = 1.61 (P = 0.11)

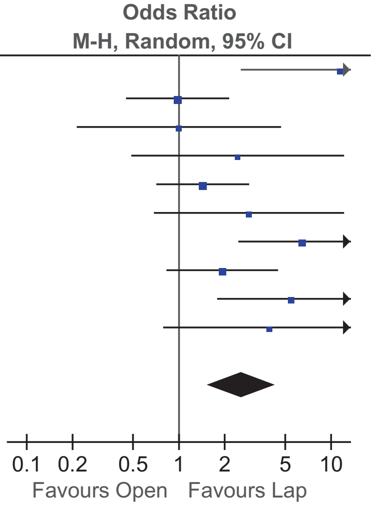


(c)

Figure 2 Forest plots illustrating the results of a meta-analysis comparing operative outcomes in laparoscopic and open distal pancreatectomy. Pooled odds ratios (ORs) or weighted mean differences (WMDs) with 95% confidence intervals (CIs) were calculated using the fixed-effects model or the random-effects model. (a) Operation time. (b) Intraoperative blood loss. (c) Blood transfusions. (d) Splenic preservation. SD, standard deviation

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Kim *et al.* 2008	38	93	2	35	7.5%	11.40 (2.58, 50.38)	2008
DiNorcia *et al.* 2010	11	71	26	165	13.8%	0.98 (0.46, 2.11)	2010
Casadei *et al.* 2010	4	22	4	22	7.2%	1.00 (0.22, 4.63)	2010
Waters *et al.* 2010	5	18	3	22	6.8%	2.44 (0.49, 12.01)	2010
Jayaraman *et al.* 2010	14	74	33	236	14.6%	1.44 (0.72, 2.86)	2010
Abu *et al.* 2011	14	35	3	16	7.9%	2.89 (0.69, 12.02)	2011
Butturini *et al.* 2012	19	43	8	73	11.8%	6.43 (2.49, 16.62)	2011
Fox *et al.* 2012	15	42	17	76	13.1%	1.93 (0.84, 4.42)	2011
Mehta *et al.* 2012	21	30	9	30	10.4%	5.44 (1.80, 16.43)	2011
Limongelli *et al.* 2012	5	16	3	29	6.9%	3.94 (0.80, 19.43)	2012
Total (95% CI)		**444**		**704**	**100.0%**	**2.59 (1.55, 4.35)**	
Total events	146		108				

Heterogeneity: Tau² = 0.35; Chi² = 19.86, d.f. = 9 (P = 0.02); I^2 = 55%
Test for overall effect: Z = 3.62 (P = 0.0003)



(d)

Figure 2 *Continued*

Postoperative complications

There was no difference in rates of clinically significant fistula (OR 0.67, 95% CI 0.41–1.09; $P = 0.11$) and mortality (OR 0.61, 95% CI 0.16–2.27; $P = 0.46$) between the two techniques. The LDP group experienced fewer surgical site infections (OR 0.37, 95% CI 0.18–0.75; $P = 0.006$), but other postoperative complications, such as intra-abdominal abscesses (OR 0.78, 95% CI 0.25–2.45; $P = 0.67$), intra-abdominal fluid collections (OR 1.47, 95% CI 0.67–3.22; $P = 0.34$) and postoperative haemorrhage (OR 1.87, 95% CI 0.59–5.95; $P = 0.29$), were found to occur at similar frequencies in both groups. In addition, rates of reoperation (OR 0.90, 95% CI 0.43–1.84; $P = 0.76$) and readmission (OR 0.70, 95% CI 0.41–1.21; $P = 0.20$) did not differ between the groups (Fig. 4).

Sensitivity and subgroup analysis

Sensitivity analyses were carried out by excluding each study from the analysis of each outcome measure. These exclusions did not alter the results obtained in cumulative analyses. In addition, subgroup analyses were undertaken for all outcome measures by including only high-quality studies. Analysis of the high-quality studies showed time to first flatus to be significantly shorter (WMD −1.80 days, 95% CI −2.14 to −1.47; $P < 0.00001$). However, the analyses for other outcomes did not change in comparison with previous analyses. These are summarized in Table 4.

Publication bias

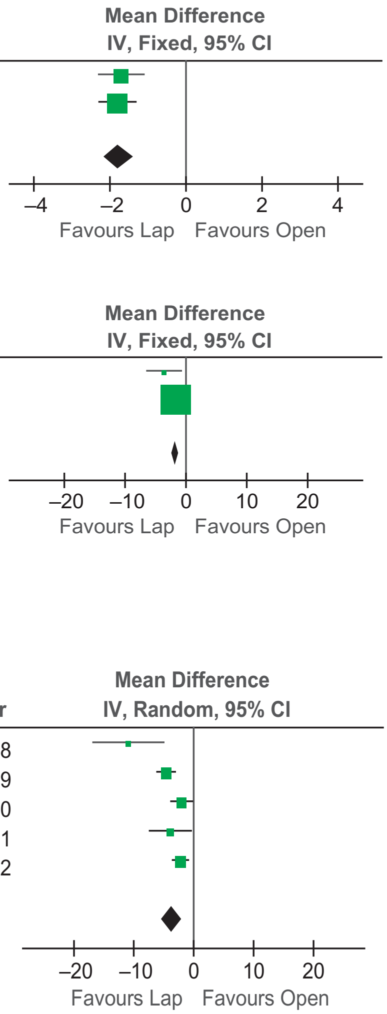
A funnel plot based on the incidence of pancreatic fistula is shown in Fig. 5. None of the studies lies outside the limits of the 95% CI and hence there is no evidence of publication bias.

Discussion

Gagner and Pomp[39] are considered to have pioneered the introduction of laparoscopy in pancreatic surgery for chronic pancreatitis and published the first description of an LDP. Initially, laparoscopy was mainly used for diagnostic purposes in pancreatology. However, laparoscopic pancreatic resections are gaining in popularity as a result of improvements in technology and increasing laparoscopic surgical experience. Distal pancreatectomy, which involves the resection of the pancreas to the left of the superior mesenteric vessels, is regarded as the standard procedure in chronic pancreatitis or benign and malignant tumours in the body or tail of the pancreas.[40] The increased use of LDP represents a paradigm shift from the practice of ODP and the former is now recognized as providing feasible, safe and effective treatment for some conditions of the pancreas.[3]

The results of the present meta-analysis favour the laparoscopic approach with regard to intraoperative blood loss and blood transfusion rate. Interestingly, there was no difference in operating time between the laparoscopic and open interventions, although the pooled estimate tends to favour the ODP group. This may reflect the fact that the current data were not stratified according to surgical experience, although stage on the learning curve has been shown to affect intraoperative blood loss, operation time and other intraoperative parameters.[4] Moreover, patient-specific factors, such as localized fibrosis, inflammatory changes caused by the tumour and tumour infiltration can also prolong the duration of surgery.[5]

En bloc splenectomy is usually performed during conventional ODP. Some studies have advocated splenic preservation whenever possible as it has been found to be associated with a reduced incidence of perioperative infectious complications and severe complications, and a shorter hospital stay.[41–44] The present results illustrate that LDP favours splenic preservation. These findings are consistent with the higher rates of splenic preservation, of up to 85% in some series, reported after LDP,[45] which may be attributable to the improved vision afforded by the laparoscopic approach, which, in turn, facilitates the more accurate



(a)

Study or Subgroup	Lap Mean	Lap SD	Lap Total	Open Mean	Open SD	Open Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Kim *et al.* 2008	2.8	1.3	93	4.5	1.6	35	39.6%	–1.70 (–2.29, –1.11)	2008
Matsumoto *et al.* 2008	2.5	0.9	14	4.3	0.2	19	60.4%	–1.80 (–2.28, –1.32)	2008
Total (95% CI)			**107**			**54**	**100.0%**	**–1.76 (–2.13, –1.39)**	

Heterogeneity: Chi² = 0.07, d.f. = 1 (*P* = 0.80); *I*² = 0%
Test for overall effect: *Z* = 9.25 (*P* < 0.00001)

(b)

Study or Subgroup	Lap Mean	Lap SD	Lap Total	Open Mean	Open SD	Open Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Matsumoto *et al.* 2008	3.5	1.5	14	7.1	6	19	4.3%	–3.60 (–6.41, –0.79)	2008
Kim *et al.* 2008	2.8	1.3	93	4.5	1.6	35	95.7%	–1.70 (–2.29, –1.11)	2008
Total (95% CI)			**107**			**54**	**100.0%**	**–1.78 (–2.36, –1.20)**	

Heterogeneity: Chi² = 1.68, d.f. = 1 (*P* = 0.19); *I*² = 41%
Test for overall effect: *Z* = 6.02 (*P* < 0.00001)

(c)

Study or Subgroup	Lap Mean	Lap SD	Lap Total	Open Mean	Open SD	Open Total	Weight	Mean Difference IV, Random, 95% CI	Year
Matsumoto *et al.* 2008	12.9	4.8	14	23.8	11.8	19	7.2%	–10.90 (–16.77, –5.03)	2008
Baker *et al.* 2009	4	1.56	27	8.6	6.45	85	26.3%	–4.60 (–6.09, –3.11)	2009
Kooby *et al.* 2010	7.4	3.4	23	9.4	4.7	70	24.4%	–2.00 (–3.77, –0.23)	2010
Mehta *et al.* 2012	8.7	4.2	30	12.6	8.7	30	14.6%	–3.90 (–7.36, –0.44)	2011
Limongelli *et al.* 2012	6.4	2.3	16	8.6	1.7	29	27.6%	–2.20 (–3.49, –0.91)	2012
Total (95% CI)			**110**			**233**	**100.0%**	**–3.65 (–5.44, –1.87)**	

Heterogeneity: Tau² = 2.58; Chi² = 14.22, d.f. = 4 (*P* = 0.007); *I*² = 72%
Test for overall effect: *Z* = 4.01 (*P* < 0.0001)

Figure 3 Forest plots illustrating the results of a meta-analysis comparing postoperative recovery outcomes in laparoscopic and open distal pancreatectomy. Pooled weighted mean differences (WMDs) with 95% confidence intervals (CIs) were calculated using the random-effects model. (a) Time to first flatus. (b) Time to oral intake. (c) Length of hospital stay. SD, standard deviation

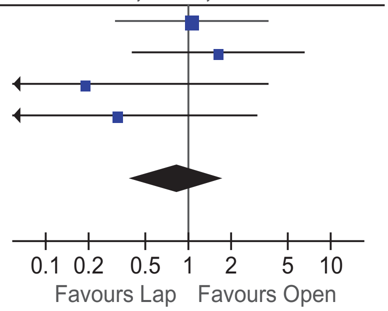
dissection of the pancreas from the splenic vessels and the splenic hilum.[31,32]

Margin-negative resection is the only way of curing pancreatic cancer.[46] The success of any oncological operation is determined by the achievement of tumour-free margins and lymph node yield. Some studies in the past have suggested that pancreatic adenocarcinoma is a contraindication to laparoscopic resection[47,48] because the role and oncologic safety of laparoscopic resection in pancreatic cancer remain unknown. Recent studies[49,50] have shown that the laparoscopic approach to malignant pancreatic tumours is feasible and results in similar rates of morbidity and mortality as it does in benign tumours. Of the studies included in the present analyses, only a few studies[21,30] with small sample sizes reported this outcome and thus the available data are not sufficient to make a cumulative analysis. Furthermore, none of the studies provide data on longterm oncologic follow-up and therefore additional well-designed studies are needed to provide convincing evidence.

Laparoscopic surgery has the advantage of requiring smaller incisions and less bowel manipulation than does open surgery and thereby reduces pain and analgesic requirements, and facilitates the earlier recovery of bowel function and ambulation.[5,6] The results of this present meta-analysis were found to be consistent with published data in terms of indicating a shorter time to oral intake and shorter hospital stay in LDP patients than in ODP patients. When only high-quality studies were included in the analysis, time to first flatus was found to be greatly reduced in the LDP group. Additionally, a low rate of conversion to open surgery was observed, which highlights the feasibility of the laparoscopic approach.

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Baker *et al.* 2009	4	27	12	85	33.6%	1.06 (0.31, 3.60)	2009
Mehta *et al.* 2012	6	30	4	30	21.8%	1.63 (0.41, 6.47)	2011
Fox *et al.* 2012	0	42	4	76	21.8%	0.19 (0.01, 3.61)	2011
Limongelli *et al.* 2012	1	16	5	29	22.8%	0.32 (0.03, 3.01)	2012
Total (95% CI)		**115**		**220**	**100.0%**	**0.82 (0.38, 1.78)**	
Total events	11		25				

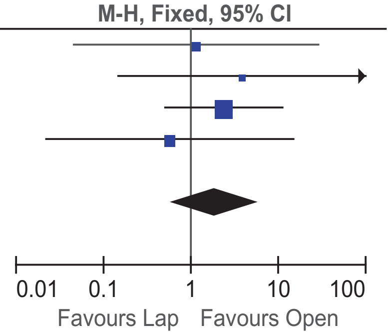
Heterogeneity: Chi² = 2.73, d.f. = 3 (*P* = 0.44); *I*² = 0%
Test for overall effect: *Z* = 0.49 (*P* = 0.62)



(a)

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Kim *et al.* 2008	1	93	0	35	16.9%	1.15 (0.05, 28.93)	2008
Waters *et al.* 2010	1	18	0	22	9.9%	3.86 (0.15, 100.58)	2010
Butturini *et al.* 2012	4	43	3	73	48.0%	2.39 (0.51, 11.25)	2011
Limongelli *et al.* 2012	0	16	1	29	25.1%	0.58 (0.02, 14.96)	2012
Total (95% CI)		**170**		**159**	**100.0%**	**1.87 (0.59, 5.95)**	
Total events	6		4				

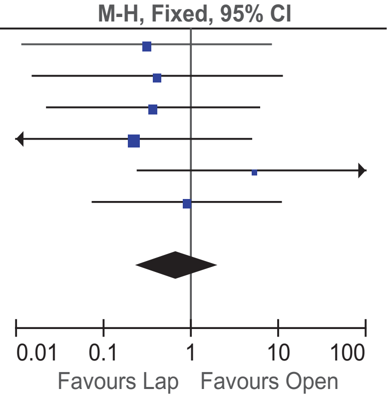
Heterogeneity: Chi² = 0.88, d.f. = 3 (*P* = 0.83); *I*² = 0%v
Test for overall effect: *Z* = 1.06 (*P* = 0.29)



(b)

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Velanovich 2006	0	15	1	15	17.9%	0.31 (0.01, 8.28)	2006
Teh *et al.* 2007	0	12	1	16	15.4%	0.41 (0.02, 11.05)	2007
Kim *et al.* 2008	1	93	1	35	17.7%	0.37 (0.02, 6.07)	2008
Waters *et al.* 2010	0	18	2	22	27.1%	0.22 (0.01, 4.92)	2010
Mehta *et al.* 2012	2	30	0	30	5.6%	5.35 (0.25, 116.31)	2011
Limongelli *et al.* 2012	1	16	2	29	16.4%	0.90 (0.08, 10.77)	2012
Total (95% CI)		**184**		**147**	**100.0%**	**0.69 (0.24, 2.03)**	
Total events	4		7				

Heterogeneity: Chi² = 2.77, d.f. = 5 (*P* = 0.74); *I*² = 0%
Test for overall effect: *Z* = 0.67 (*P* = 0.51)

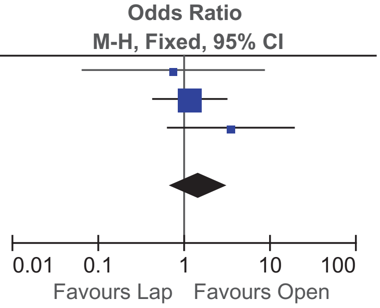


(c)

Figure 4 Forest plots illustrating the results of a meta-analysis comparing postoperative complications in laparoscopic and open distal pancreatectomy. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using the fixed-effects model. (a) Clinically significant fistula. (b) Postoperative haemorrhage. (c) Intra-abdominal abscess. (d) Intra-abdominal fluid collections. (e) Surgical site infection. (f) Mortality. (g) Reoperation. (h) Readmission

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Kim *et al.* 2008	2	93	1	35	13.9%	0.75 (0.07, 8.51)	2008
Butturini *et al.* 2012	8	43	12	73	70.6%	1.16 (0.43, 3.12)	2011
Mehta *et al.* 2012	6	30	2	30	15.6%	3.50 (0.65, 18.98)	2011
Total (95% CI)		**166**		**138**	**100.0%**	**1.47 (0.67, 3.22)**	
Total events	16		15				

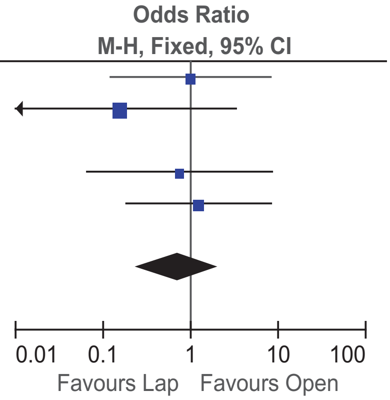
Heterogeneity: Chi² = 1.53, d.f. = 2 (P = 0.47); I^2 = 0%
Test for overall effect: Z = 0.96 (P = 0.34)



(d)

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Velanovich 2006	2	15	2	15	21.8%	1.00 (0.12, 8.21)	2006
Teh *et al.* 2007	0	12	3	16	36.7%	0.15 (0.01, 3.30)	2007
Matsumoto *et al.* 2008	0	14	0	19		Not estimable	2008
Kim *et al.* 2008	2	93	1	35	17.9%	0.75 (0.07, 8.51)	2008
Limongelli *et al.* 2012	2	16	3	29	23.5%	1.24 (0.18, 8.31)	2012
Total (95% CI)		**150**		**114**	**100.0%**	**0.70 (0.24, 2.07)**	
Total events	6		9				

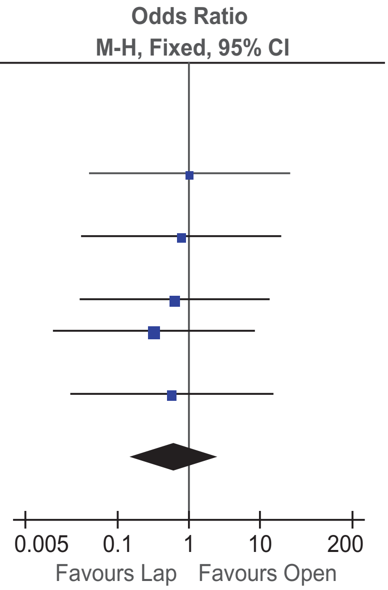
Heterogeneity: Chi² = 1.40, d.f. = 3 (P = 0.71); I^2 = 0%
Test for overall effect: Z = 0.65 (P = 0.52)



(e)

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Teh *et al.* 2007	0	12	0	16		Not estimable	2007
Kim *et al.* 2008	0	93	0	35		Not estimable	2008
Matsumoto *et al.* 2008	0	14	0	19		Not estimable	2008
Baker *et al.* 2009	0	27	1	85	13.6%	1.02 (0.04, 25.88)	2009
Casadei *et al.* 2010	0	22	0	22		Not estimable	2010
DiNorcia *et al.* 2010	0	71	1	168	16.7%	0.78 (0.03, 19.40)	2010
Waters *et al.* 2010	0	18	0	22		Not estimable	2010
Jayaraman *et al.* 2010	0	74	2	236	22.4%	0.63 (0.03, 13.26)	2010
Mehta *et al.* 2012	0	30	1	30	27.7%	0.32 (0.01, 8.24)	2011
Butturini *et al.* 2012	0	43	0	73		Not estimable	2011
Limongelli *et al.* 2012	0	16	1	29	19.7%	0.58 (0.02, 14.96)	2012
Total (95% CI)		**420**		**735**	**100.0%**	**0.61 (0.15, 2.55)**	
Total events	0		6				

Heterogeneity: Chi² = 0.27, d.f. = 4 (P = 0.99); I^2 = 0%
Test for overall effect: Z = 0.67 (P = 0.50)



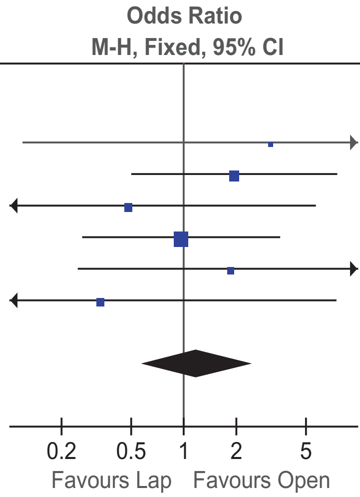
(f)

Figure 4 *Continued*

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Teh *et al.* 2007	0	12	0	16		Not estimable	2007
Matsumoto *et al.* 2008	0	14	0	19		Not estimable	2008
Casadei *et al.* 2010	1	22	0	22	3.6%	3.14 (0.12, 81.35)	2010
DiNorcia *et al.* 2010	4	71	5	168	21.5%	1.95 (0.51, 7.47)	2010
Mehta *et al.* 2012	1	30	2	30	14.8%	0.48 (0.04, 5.63)	2011
Butturini *et al.* 2012	4	43	7	73	36.1%	0.97 (0.27, 3.52)	2011
Fox *et al.* 2012	2	42	2	76	10.4%	1.85 (0.25, 13.63)	2011
Limongelli *et al.* 2012	0	16	2	29	13.5%	0.33 (0.02, 7.38)	2012
Total (95% CI)		**250**		**433**	**100.0%**	**1.19 (0.57, 2.47)**	
Total events	12		18				

Heterogeneity: $\text{Chi}^2 = 2.31$, d.f. = 5 ($P = 0.81$); $I^2 = 0\%$

Test for overall effect: $Z = 0.47$ ($P = 0.64$)

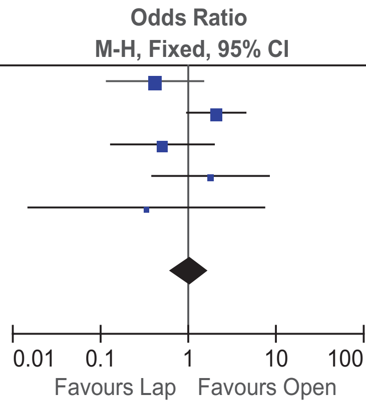


(g)

Study or Subgroup	Lap Events	Lap Total	Open Events	Open Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
DiNorcia *et al.* 2010	3	71	16	168	32.6%	0.42 (0.12, 1.49)	2010
Jayaraman *et al.* 2010	12	74	20	236	28.6%	2.09 (0.97, 4.51)	2010
Fox *et al.* 2012	3	42	10	76	23.6%	0.51 (0.13, 1.96)	2011
Mehta *et al.* 2012	5	30	3	30	8.9%	1.80 (0.39, 8.32)	2011
Limongelli *et al.* 2012	0	16	2	29	6.3%	0.33 (0.02, 7.38)	2012
Total (95% CI)		**233**		**539**	**100.0%**	**1.04 (0.62, 1.74)**	
Total events	23		51				

Heterogeneity: $\text{Chi}^2 = 7.25$, d.f. = 4 ($P = 0.12$); $I^2 = 45\%$

Test for overall effect: $Z = 0.13$ ($P = 0.89$)



(h)

Figure 4 *Continued*

The present analysis found that surgical site infections occurred less frequently in the LDP group compared with the ODP group. This may reflect the association between laparoscopic surgery and reduced surgical trauma, which results in a less acute phase response compared with open surgery, and the fact that local (peritoneal) immune function is affected by carbon dioxide as a result of pneumoperitoneum.[51] The present analyses failed to demonstrate any differences between the LDP and ODP groups with regard to postoperative mortality, haemorrhage, reoperation rate, readmission rate, intra-abdominal fluid collections and intra-abdominal abscesses. It is of note that the sample sizes for reporting these complications were small; studies with larger sample sizes are needed to facilitate an accurate summary. It was not possible to undertake cumulative analyses to assess overall morbidity, as reported in many studies, because the criteria used to define such complications varied among the studies. Criteria for assessing morbidity included the DeOliveira scoring system, the Martin scoring system, the National Cancer Institute's common toxicity criteria and the Clavien classification system; it is inappropriate to pool results obtained using such varied systems in order to make a cumulative analysis.

Pancreatic fistula remains the most challenging complication in pancreatic surgery as it can lead to intra-abdominal abscess, delayed gastric emptying, haemorrhage, sepsis and electrolyte imbalances.[52] Reported rates of pancreatic fistula in distal pancreatectomy vary between 23% and 26%.[53,54] In the present analysis, the pooled results show no significant difference in the rate of pancreatic fistula between the LDP (17%) and ODP (18%) groups and no difference in the rate of clinically significant fistula. It is important to note that although the majority of the reports included in the present analysis used the ISGPF definition of pancreatic fistula, variation exists in this regard and therefore, in order to achieve homogeneity and increase the reliability of the present results, only studies that used the ISGPF definition were included in the analysis.

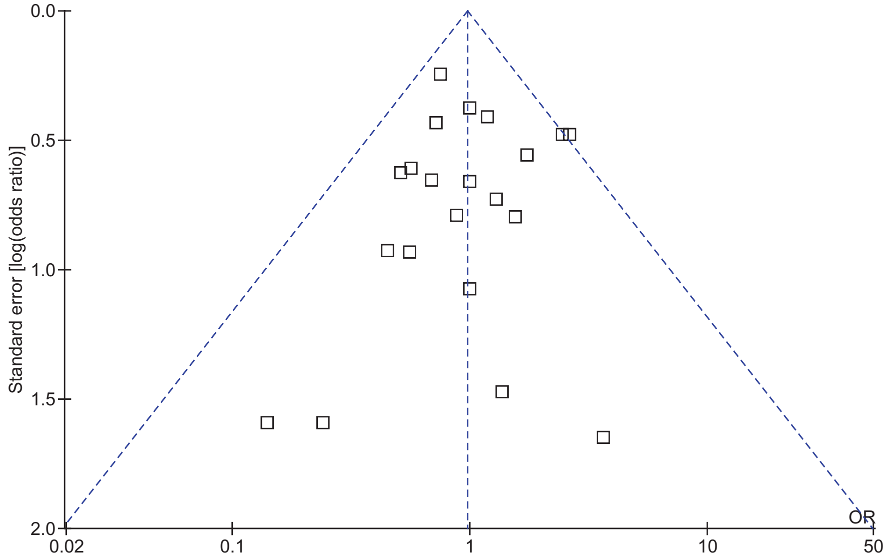


Figure 5 Funnel plot based on incidences of pancreatic fistula. The funnel plot revealed no publication bias

This meta-analysis of non-randomized studies may have several limitations, which must be taken into account when considering the results. Firstly, all of the studies included were non-randomized in nature and therefore the results provide only a possible estimate. This remains the biggest limitation of this study and results in a weak level of evidence. However, the present study made a strong attempt to select the best evidence available by selecting high-quality studies and pooling their findings. This does not resolve the problem, but it does improve the quality of the synthesized data and adds reliability to the results. It also highlights the need for better designed randomized studies that are able to resolve all of the relevant questions. It is hoped that this will also provide guidelines for the design of future trials on the subject. Secondly, it is important to note that the results were not stratified according to whether the underlying pathology was benign or malignant in nature as the studies included patients with different types of pancreatic disease. This may have an effect on the outcome measures. Thirdly, significant heterogeneity was seen among the included studies for some outcome measures. This may well reflect differences in adjuvant treatment measures and medical insurance systems. However, investigation of this heterogeneity through meta-regression was not possible because of the small number of studies and the unavailability of relevant data. Additionally, it will be of crucial importance to ascertain the financial implications of these procedures in order to make recommendations for their specific indications.

Conclusions

In conclusion, this is the most comprehensive review to date to compare outcomes of LDP and ODP. The present results indicate that LDP is a safe and feasible technique in comparison with ODP. The current findings are reliable and the pooled estimates enable the resolution of some of the discrepancies in data among individual studies in the literature. However, these results need to be validated in large, well-designed randomized controlled trials.

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Conflicts of interest

None declared.

References

1. Sain AH. (1996) Laparoscopic cholecystectomy is the current ‘gold standard’ for the treatment of gallstone disease. *Ann Surg* 224:689–690.
2. Smith CD, Weber CJ, Amerson JR. (1999) Laparoscopic adrenalectomy: new gold standard. *World J Surg* 23:389–396.
3. Song KB, Kim SC, Park JB, Kim YH, Jung YS, Kim MH *et al*. (2011) Single-centre experience of laparoscopic left pancreatic resection in 359 consecutive patients: changing the surgical paradigm of left pancreatic resection. *Surg Endosc* 25:3364–3372.
4. Velanovich V. (2006) Case–control comparison of laparoscopic versus open distal pancreatectomy. *J Gastrointest Surg* 10:95–98.
5. Teh SH, Tseng D, Sheppard BC. (2007) Laparoscopic and open distal pancreatic resection for benign pancreatic disease. *J Gastrointest Surg* 11:1120–1125.
6. Matsumoto T, Shibata K, Ohta M, Iwaki K, Uchida H, Yada K *et al*. (2008) Laparoscopic distal pancreatectomy and open distal pancreatectomy: a non-randomized comparative study. *Surg Laparosc Endosc Percutan Tech* 18:340–343.
7. Stutchfield BM, Joseph S, Duckworth AD, Garden OJ, Parks RW. (2009) Distal pancreatectomy: what is the standard for laparoscopic surgery? *HPB* 11:210–214.

8. Tseng WH, Canter RJ, Bold RJ. (2011) Perioperative outcomes for open distal pancreatectomy: current benchmarks for comparison. *J Gastrointest Surg* 15:2053–2058.
9. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J *et al*. (2005) Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 138:8–13.
10. Athanasiou T, Al-Ruzzeh S, Kumar P, Crossman MC, Amrani M, Pepper JR *et al*. (2004) Off-pump myocardial revascularization is associated with less incidence of stroke in elderly patients. *Ann Thorac Surg* 77:745–753.
11. Simillis C, Constantinides VA, Tekkis PP, Darzi A, Lovegrove R, Jiao L *et al*. (2007) Laparoscopic versus open hepatic resections for benign and malignant neoplasms – a meta-analysis. *Surgery* 141:203–211.
12. Higgins JP, Thompson SG, Deeks JJ, Altman DG. (2003) Measuring inconsistency in meta-analyses. *BMJ* 327:557–560.
13. Demets DL. (1987) Methods for combining randomized clinical trials: strengths and limitations. *Stat Med* 6:341–350.
14. DerSimonian R, Laird N. (1986) Meta-analysis in clinical trials. *Control Clin Trials* 7:177–188.
15. Sterne JA, Egger M, Smith GD. (2001) Systematic reviews in health care: investigating and dealing with publication and other biases in meta-analysis. *BMJ* 323:101–105.
16. Finan KR, Cannon EE, Kim EJ, Wesley MM, Arnoletti PJ, Heslin MJ *et al*. (2009) Laparoscopic and open distal pancreatectomy: a comparison of outcomes. *Am Surg* 75:671–679.
17. Bruzoni M, Sasson AR. (2008) Open and laparoscopic spleen-preserving, splenic vessel-preserving distal pancreatectomy: indications and outcomes. *J Gastrointest Surg* 12:1202–1206.
18. Kooby DA, Gillespie T, Bentrem D, Nakeeb A, Schmidt MC, Merchant NB *et al*. (2008) Left-sided pancreatectomy: a multicentre comparison of laparoscopic and open approaches. *Ann Surg* 248:438–446.
19. Kooby DA, Hawkins WG, Schmidt CM, Weber SM, Bentrem DJ, Gillespie TW *et al*. (2010) A multicentre analysis of distal pancreatectomy for adenocarcinoma: is laparoscopic resection appropriate? *J Am Coll Surg* 210:779–785.
20. Cho CS, Kooby DA, Schmidt CM, Nakeeb A, Bentrem DJ, Merchant NB *et al*. (2011) Laparoscopic versus open left pancreatectomy: can preoperative factors indicate the safer technique? *Ann Surg* 253:975–980.
21. Baker MS, Bentrem DJ, Ujiki MB, Stocker S, Talamonti MS. (2009) A prospective single institution comparison of perioperative outcomes for laparoscopic and open distal pancreatectomy. *Surgery* 146:635–643; discussion 643–645.
22. Baker MS, Bentrem DJ, Ujiki MB, Stocker S, Talamonti MS. (2011) Adding days spent in readmission to the initial postoperative length of stay limits the perceived benefit of laparoscopic distal pancreatectomy when compared with open distal pancreatectomy. *Am J Surg* 201:295–299; discussion 299–300.
23. Tang CN, Tsui KK, Ha JP, Wong DC, Li MK. (2007) Laparoscopic distal pancreatectomy: a comparative study. *Hepatogastroenterology* 54:265–271.
24. Nakamura Y, Uchida E, Aimoto T, Matsumoto S, Yoshida H, Tajiri T. (2009) Clinical outcome of laparoscopic distal pancreatectomy. *J Hepatobiliary Pancreat Surg* 16:35–41.
25. Shimura T, Suehiro T, Mochida Y, Hashimoto S, Okada K, Asao T *et al*. (2006) Laparoscopy-assisted distal pancreatectomy with mobilization of the distal pancreas and the spleen outside the abdominal cavity. *Surg Laparosc Endosc Percutan Tech* 16:387–389.
26. Kim SC, Park KT, Hwang JW, Shin HC, Lee SS, Seo DW *et al*. (2008) Comparative analysis of clinical outcomes for laparoscopic distal pancreatic resection and open distal pancreatic resection at a single institution. *Surg Endosc* 22:2261–2268.
27. Jayaraman S, Gonen M, Brennan MF, D'Angelica MI, DeMatteo RP, Fong Y *et al*. (2010) Laparoscopic distal pancreatectomy: evolution of a technique at a single institution. *J Am Coll Surg* 211:503–509.
28. DiNorcia J, Schrope BA, Lee MK, Reavey PL, Rosen SJ, Lee JA *et al*. (2010) Laparoscopic distal pancreatectomy offers shorter hospital stays with fewer complications. *J Gastrointest Surg* 14:1804–1812.
29. Casadei R, Ricci C, D'Ambra M, Marrano N, Alagna V, Rega D *et al*. (2010) Laparoscopic versus open distal pancreatectomy in pancreatic tumours: a case–control study. *Updat Surg* 62:171–174.
30. Waters JA, Canal DF, Wiebke EA, Dumas RP, Beane JD, Aguilar-Saavedra JR *et al*. (2010) Robotic distal pancreatectomy: cost-effective? *Surgery* 148:814–823.
31. Mehta SS, Doumane G, Mura T, Nocca D, Fabre JM. (2012) Laparoscopic versus open distal pancreatectomy: a single-institution case–control study. *Surg Endosc* 26:402–407.
32. Butturini G, Inama M, Malleo G, Manfredi R, Melotti GL, Piccoli M *et al*. (2012) Perioperative and longterm results of laparoscopic spleen-preserving distal pancreatectomy with or without splenic vessels conservation: a retrospective analysis. *J Surg Oncol* 105:387–392.
33. Fox AM, Pitzul K, Bhojani F, Kaplan M, Moulton CA, Wei AC *et al*. (2012) Comparison of outcomes and costs between laparoscopic distal pancreatectomy and open resection at a single centre. *Surg Endosc* 26:1220–1230.
34. Limongelli P, Belli A, Russo G, Cioffi L, D'Agostino A, Fantini C *et al*. (2012) Laparoscopic and open surgical treatment of left-sided pancreatic lesions: clinical outcomes and cost-effectiveness analysis. *Surg Endosc* 26:1830–1836.
35. Eom BW, Jang JY, Lee SE, Han HS, Yoon YS, Kim SW. (2008) Clinical outcomes compared between laparoscopic and open distal pancreatectomy. *Surg Endosc* 22:1334–1338.
36. Aly MY, Tsutsumi K, Nakamura M, Sato N, Takahata S, Ueda J *et al*. (2010) Comparative study of laparoscopic and open distal pancreatectomy. *J Laparoendosc Adv Surg Tech A* 20:435–440.
37. Vijan SS, Ahmed KA, Harmsen WS, Que FG, Reid-Lombardo KM, Nagorney DM *et al*. (2010) Laparoscopic vs. open distal pancreatectomy: a single-institution comparative study. *Arch Surg* 145:616–621.
38. Abu Hilal M, Hamdan M, Di Fabio F, Pearce NW, Johnson CD. (2011) Laparoscopic versus open distal pancreatectomy: a clinical and cost-effectiveness study. *Surg Endosc* 26:1670–1674.
39. Gagner M, Pomp A. (1994) Laparoscopic pylorus-preserving pancreatoduodenectomy. *Surg Endosc* 8:408–410.
40. Andren-Sandberg A, Wagner M, Tihanyi T, Lofgren P, Friess H. (1999) Technical aspects of left-sided pancreatic resection for cancer. *Dig Surg* 16:305–312.
41. Shoup M, Brennan MF, McWhite K, Leung DH, Klimstra D, Conlon KC. (2002) The value of splenic preservation with distal pancreatectomy. *Arch Surg* 137:164–168.
42. Mekeel KL, Moss AA, Reddy KS, Mulligan DC, Harold KL. (2011) Laparoscopic distal pancreatectomy: does splenic preservation affect outcomes? *Surg Laparosc Endosc Percutan Tech* 21:362–365.
43. Aldridge MC, Williamson RC. (1991) Distal pancreatectomy with and without splenectomy. *Br J Surg* 78:976–979.

44. Fernandez-Cruz L, Blanco L, Cosa R, Rendon H. (2008) Is laparoscopic resection adequate in patients with neuroendocrine pancreatic tumours? *World J Surg* 32:904–917.
45. Taylor C, O'Rourke N, Nathanson L, Martin I, Hopkins G, Layani L *et al*. (2008) Laparoscopic distal pancreatectomy: the Brisbane experience of forty-six cases. *HPB* 10:38–42.
46. Chang DK, Johns AL, Merrett ND, Gill AJ, Colvin EK, Scarlett CJ *et al*. (2009) Margin clearance and outcome in resected pancreatic cancer. *J Clin Oncol* 27:2855–2862.
47. Kang CM, Kim DH, Lee WJ. (2010) Ten years of experience with resection of left-sided pancreatic ductal adenocarcinoma: evolution and initial experience to a laparoscopic approach. *Surg Endosc* 24:1533–1541.
48. Patterson EJ, Gagner M, Salky B, Inabnet WB, Brower S, Edye M *et al*. (2001) Laparoscopic pancreatic resection: single-institution experience of 19 patients. *J Am Coll Surg* 193:281–287.
49. Fernandez-Cruz L, Cosa R, Blanco L, Levi S, Lopez-Boado MA, Navarro S. (2007) Curative laparoscopic resection for pancreatic neoplasms: a critical analysis from a single institution. *J Gastrointest Surg* 11:1607–1621; discussion 1621–1622.
50. Gumbs AA, Chouillard EK. (2012) Laparoscopic distal pancreatectomy and splenectomy for malignant tumours. *J Gastrointest Cancer* 43:83–86.
51. Targarona EM, Balague C, Knook MM, Trias M. (2000) Laparoscopic surgery and surgical infection. *Br J Surg* 87:536–544.
52. Knaebel HP, Diener MK, Wente MN, Buchler MW, Seiler CM. (2005) Systematic review and meta-analysis of technique for closure of the pancreatic remnant after distal pancreatectomy. *Br J Surg* 92:539–546.
53. Fahy BN, Frey CF, Ho HS, Beckett L, Bold RJ. (2002) Morbidity, mortality, and technical factors of distal pancreatectomy. *Am J Surg* 183:237–241.
54. Pannegeon V, Pessaux P, Sauvanet A, Vullierme MP, Kianmanesh R, Belghiti J. (2006) Pancreatic fistula after distal pancreatectomy: predictive risk factors and value of conservative treatment. *Arch Surg* 141:1071–1076.