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REVIEW ARTICLE

Comparison of surgical outcomes of robot-assisted laparoscopic distal pancreatectomy versus laparoscopic and open resections: A systematic review and meta-analysis

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Robotics;
Laparoscopy;
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Summary Robot-assisted distal pancreatectomy (RADP) has been developed with the aim of improving surgical quality and overcoming the limitations of laparoscopic distal pancreatectomy (LDP) and open distal pancreatectomy (ODP) for pancreatic resections. A systematic search was performed in the PubMed, EMBASE, Cochrane Library, Web of Science, and China Biology Medicine databases up to December 2016 for studies that compared the surgical outcomes of RADP vs. LDP or ODP for pancreatic resections. The weighted mean differences, odds ratios and 95% confidence intervals were calculated, and the data were combined using the random-effects model. The GRADE system was used to interpret the primary outcomes of this meta-analysis. A total of seventeen non-randomized observational clinical studies involving 2133 patients satisfied the eligibility criteria. Compared with LDP, RADP was associated with a longer operative time ($P = 0.018$), a shorter hospital length of stay ($P = 0.030$), and a higher rate of spleen preservation ($P = 0.022$). Moreover, RADP was associated with a shorter hospital LOS ($P = 0.014$) and a lower total complication rate ($P = 0.034$) than ODP. We found no statistically significant differences between the techniques in the mean estimated blood loss, severe complication rate, incidence of total pancreatic fistulas or incidence of severe pancreatic

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fistulas. The overall quality of evidence was poor for all outcomes. This meta-analysis indicates that RADP may be safe and comparable in terms of surgical results to LDP and ODP. Further RCTs are needed to confirm the outcomes of this meta-analysis.

1. Introduction

The development of minimally invasive approaches for pancreatic surgery represents one of the most recent and challenging fields in abdominal surgery[1] because of the retroperitoneal location of the pancreas and its proximity to major vasculature.[2,3] There are three types of surgeries that are performed for pancreatic disease. The type of surgery (e.g., the Whipple procedure, distal pancreatectomy and total pancreatectomy) a patient receives depends on where the lesion is located in the pancreas.[4,5] Since the first laparoscopic distal pancreatectomy (LDP) was performed in 1994,[6] LDP has been widely adopted for pancreatic disease because of the shorter hospital stay, reduced analgesic requirement, and reduced wound infection incidence compared with open distal pancreatectomy (ODP).[7] The advantages of the conventional laparoscopic approach mainly include the minimal invasiveness and expedited postoperative recovery, with an effectiveness and safety profile that are comparable to those of the open procedure.[8,9] However, laparoscopic surgery still has several limitations, such as limited degrees of freedom for manipulation, 2D imaging adaptation, and a steep learning curve.[11] To overcome the technical limitations of laparoscopic surgery, robotic surgical systems that allow for motion scaling, 3D visualization and a high degree of freedom have been introduced.[11,12]

According to recent reports, robotic surgery may be a simpler method of expanding the indications of minimally invasive surgery compared with laparoscopic surgery for pancreatic lesions. The literature pertaining to the robotic approach to this procedure is increasing. However, the adoption of minimally invasive techniques for pancreatic surgery has lagged behind that of other surgical techniques.[13,14] Barriers to the implementation of minimally invasive pancreatic surgery include the retroperitoneal location of the pancreas and its proximity to vascular structures.[15] Indeed, robotic assistance has minimally expanded the range of the feasibility of laparoscopic operations, and improvements in patient outcomes that have been proposed for many operations have not yet been unambiguously demonstrated. Additionally, the single-institution designs and varying systems of complication appraisal have limited the abilities of these studies to provide conclusive objective results. To overcome these limitations, a meta-analysis was performed to evaluate the relative merits of robotic surgery for pancreatic resections compared with conventional laparoscopic and open approaches to pancreatectomy.[16–18]

In the present study, we aimed to systematically and objectively assess the value of RADP for pancreatic lesions. Additionally, we adopted the Grades of Recommendation, Assessment, Development, and Evaluation Working Group (GRADE)[19] to interpret the quality of evidence for major outcomes in this meta-analysis. GRADE has been used as a tool with which to rate the qualities of bodies of evidence of meta-analyses and other forms of evidence and has been received with great enthusiasm by many national and international organizations.

2. Materials and methods

2.1. Registration number

This systematic review has been registered in the international prospective register of systematic reviews (PROSPERO #CRD 42017054195; http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017054195).

2.2. Literature search

A systematic search was performed in PubMed, EMBASE, the Cochrane Library, the Web of Science, and the China Biology Medicine disc (CBMdisc) up to December 2016 for studies that compared the surgical results of RADP vs. LDP or ODP. The following search terms were used: Pancreatectomy OR Pancreatectomies OR Pancreas OR Pancreas AND Robotics OR Da Vinci Robot OR Robot assisted OR robotic OR Da Vinci Robot assisted OR Telerobotics OR Remote Operations OR Robot OR Robotics. All searches were performed with combinations of the medical subject heading terms (MeSH) and free words. The retrieval strategies were determined by performing multiple pre-retrievals. We included studies that compared RADP vs. LDP or ODP for pancreatic lesions in patients of any age and gender and set RADP as the intervention group and LDP and ODP as the control groups according to the PICO programme.

2.3. Study selection

Studies were included if they were controlled studies of RADP vs. LDP or ODP and reported at least one of the outcomes. Additionally, only the most recent study was included if the authors and/or institutions included overlap between two or more studies. Two authors (Niu XD and Ma SX) independently evaluated the included studies and resolved disagreements by discussion. The third author (Yao L) made the final decision regarding the eligibility of the studies. The following studies were excluded: abstracts, letters, editorials and expert opinions, reviews without original data, case reports, studies lacking control groups,

studies that did not provide sufficient data for the above-mentioned techniques, studies with unclear patient outcomes and parameters, studies with the same authors and institutions, and studies with Newcastle–Ottawa Scale (NOS) scores < 7.[20]

2.4. Definitions

Surgeries for lesions in the middle part (body) or narrow end (tail) of the pancreas were termed distal pancreatectomies.[5] The following three primary intraoperative outcomes were analysed: operative time (OT), mean estimated blood loss (EBL), and spleen-preservation (SP) rate. The following five primary postoperative outcomes were analysed: hospital length of stay (LOS), total complications (TCs), severe complications (SCs), total pancreatic fistulas (TPFs), and severe pancreatic fistulas (SPFs). Pancreatic fistulas were defined by a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content >3 times the serum amylase level and were classified according to the criteria of the International Study Group of Pancreatic Fistula (ISGPF).[21] Grade B and C fistulas were regarded as clinical PFs, i.e., severe pancreatic fistulas. Postoperative complications were categorized with the Clavien-Dindo grading system (grades I–II and III–IV) for intra-abdominal surgical complications, and complications of grade III or higher were regarded as severe complications.[22] Conversion was defined when a resection was attempted via the robotic or laparoscopic approach but required an open incision (regardless of the incision size) to complete the resection.

2.5. Data extraction and methodological quality appraisal

The following information, if available, was independently extracted by two authors (Niu XD and Ma SX) and summarized for each of the included studies: 1) general information (i.e., the first author's surname, publication date, district, and study design); 2) characteristics of the participants (i.e., size, gender, age, body mass index [BMI], tumour size, and pathological diagnosis); and 3) clinical outcomes (i.e., operative time, EBL, SP, LOS, TCs, SCs, TPFs, and SPFs). Because all of the included studies were case-control studies, the quality assessment was performed with the NOS (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). A score of 0–10 was assigned to each study. In general, studies were considered to be of high quality if they achieved a score ≥ 7. Disagreements were resolved by discussion and consultation with the senior investigator (Yao L).

2.6. Quality of the evidence

The five GRADE considerations (i.e., risk for bias, consistency of effect, imprecision, indirectness, and publication bias) were used to assess the qualities of the primary outcomes. We concluded our evaluation of the quality of evidence using the methods and recommendations described in Section 8.5, Chapter 12, of the Cochrane Handbook for Systematic Reviews of Interventions and using the GRADEpro software.

2.7. Statistical analysis

The meta-analysis was performed with Stata/SE 12.0 (Stata Corp, College Station, Texas 77845, USA). A random-effects model is recommended for medical decision-making contexts, especially when the events are rare. Continuous variables were pooled using the weighted mean difference (WMD), and dichotomous variables were pooled using the odds ratio (OR). The WMD and OR values are reported with the 95% confidence intervals (CIs). P values < 0.05 were considered statistically significant. If the studies documented the outcomes as medians and ranges, the means and standard deviations (SDs) were estimated according to the methods described by Hozo et al[23] Heterogeneity was evaluated using the Higgins I^2 value, and values < 25, 25 to 50, and >50 were defined as corresponding to low, moderate, and high heterogeneity, respectively.[24] Potential causes of high heterogeneity were explored by performing sensitivity analyses. The significance of the intercept was determined with the t-test as suggested by Egger ($P < 0.050$ was considered representative of statistically significant publication bias).

3. Results

3.1. Study selection

Our combined search strategy generated 1569 studies. After exclusion of the irrelevant articles and elimination of duplicates, eighteen articles were considered for review. Among them, two studies[10,25] that were published by the same team at different times were regarded as duplicate studies, and we thus selected the latest study.[10] In total, seventeen[1,3,10,26–39] articles with a total of 2133 patients were selected according to our inclusion and exclusion criteria. The selection process is illustrated in Fig. 1.

3.2. Study characteristics

The study characteristics of the seventeen selected articles are displayed in Table 1. The 2133 included patients comprised 409 RADP, 970 LDP, and 754 ODP cases. All of the studies had retrospective and prospective designs because randomized controlled trials on this topic are lacking. There was only one prospective non-randomized study, and the others were retrospective studies. The three groups were comparable in age, BMI, gender, and malignancy rate.

3.3. Methodological quality assessment

The qualities of the included studies were satisfactory; specifically, three studies received nine stars, seven received seven stars, and the remaining studies received eight stars. All the studies were of high quality according to the NOS. Tables 2 and 3 present summaries and ratings of the evidence qualities of the primary outcomes, which included operative time, SP, TCs, TPFs and LOS, and

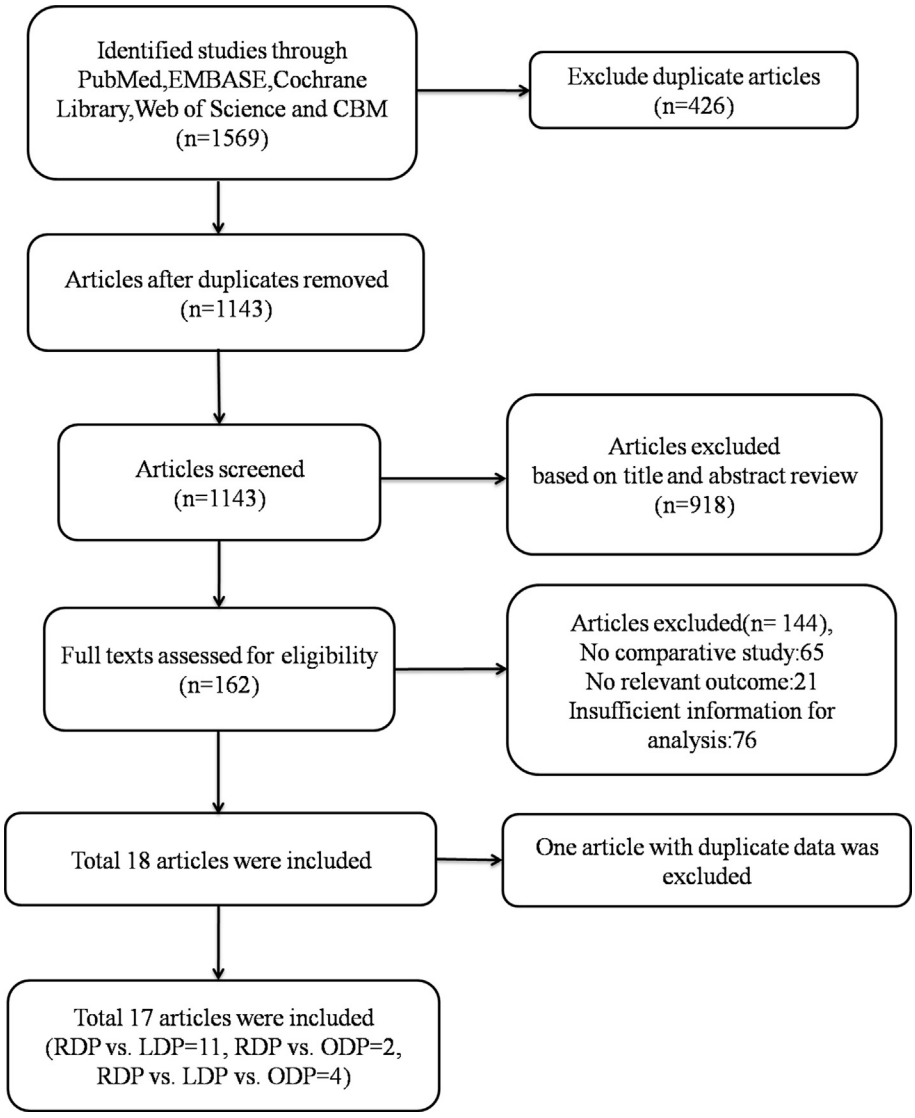

Figure 1 Flow chart of literature selection.

indicate that the total qualities of the evidence were low for the operative time, LOS, SP, and TPFs in the RADP vs. ODP and LDP comparisons. Additionally, the total quality of evidence was moderate for total complications in the RADP vs. ODP comparison.

3.4. Evidence from primary intraoperative outcomes

3.4.1. Operative time

Forest plots of the primary operative outcomes are presented in Figs. 2—4. All studies provided information on the operative time in addition to five articles.[1,3,30,32,35] The meta-analysis revealed significant heterogeneity between RADP and LDP or ODP (I^2 = 90.6%; P < 0.001 and I^2 = 87.8%; P < 0.001, respectively). The forest plots revealed that robotic surgery required a significantly longer operative time than LDP (WMD = 37.27 min, 95% CI, 6.34 to 68.21; P = 0.018; Fig. 2). However, the results of the meta-analysis of the six included studies revealed that the operative time was not different between RADP and ODP (WMD = 32.93 min, 95% CI, −13.43 to 79.29; P = 0.164; Fig. 2).

3.4.2. EBL

The EBL was reported in thirteen studies (Fig. 3). There was a wide variation in the EBL for RADP and LDP, and no significant difference was found between the groups (WMD = −14.94 ml, 95% CI, −125.97 to 96.10; P = 0.792). There was high heterogeneity among the studies (I^2 = 86.4%; P < 0.001). The EBL in ODP was comparable to that in RADP (WMD = −185.89 ml, 95% CI, −478.10 to 106.32; P = 0.212). There was no difference in EBL between the two groups (I^2 = 94.1%; P < 0.001).

3.4.3. SP

Twelve studies presented SP results (Fig. 4). The meta-analysis indicated that the SP was significantly higher for RADP than LDP (OR = 2.16, 95% CI, 1.12 to 4.17; P = 0.022), with high heterogeneity (I^2 = 53.6%;

Table 1 Summary of studies included in the meta-analysis.

Study	Year	District	Study group	Study design	Size	Gender(F)	Age (yr)	BMI	Malignant (%)	NOS (score)
Waters et al	2010	USA	RADP VS.LDP VS.ODP	prospective	17/18/22	65/50/55	64/59/59	NR	0/11/50	7
Kang et al	2011	Korea	RADP VS.LDP	retrospective	20/25	60/56	44.5 ± 15.9/ 56.5 ± 13.9	24.2 ± 2.9/23.4 ± 2.6	10/40	8
Daouadi et al	2013	USA	RADP VS.LDP	retrospective	30/94	67/65	59 ± 13/59 ± 16	27.9 ± 5.1/29.0 ± 7.1	43/15	7
Duran et al	2014	Spain	RADP VS.LDP VS.ODP	retrospective	16/18/13	44/50/53	61 ± 11/58.3 ± 10/ 63.8 ± 10	NR	56/44/46	7
Benizri et al	2014	France	RADP VS.LDP	retrospective	11/23	72.7/56.5	50.1 ± 21.1/ 52.3 ± 14.7	25.6 ± 5.8/26.5 ± 4.7	0/13	9
Boggi et al	2014	Italy	RADP VS.ODP	prospective	11/11	45.5/36.4	61.81(50—74)/ 68.45(49—78)	24.8(18.4—35.0)/ 25.0(17.9—30.8)	45.4/54.5	8
Butturini et al	2015	Italy	RADP VS.LDP	prospective	22/21	77.3/71.5	54(26—77)/55(20—71)	25.33/24.19	13.6/9.5	8
Chen et al	2015	China	RADP VS.LDP	retrospective	69/50	66.7/64.0	56.2 ± 13.3/ 56.5 ± 15.0	24.6 ± 2.8/24.6 ± 3.0	23.2/22.0	9
Lai et al	2015	Hong Kong SAR, China	RADP VS.LDP	retrospective	17/18	41.2/77.8	61.2 ± 10.4/ 63.2 ± 17.9	24.1 ± 2.3/25.7 ± 2.7	17.6/11.1	8
Lee S. Y	2015	USA	RADP VS.LDP VS.ODP	retrospective	37/131/637	73/56/55	58(11.1)/58(15.0)/ 63(13.5)	28.7/28.2/28.4	11/15/39	8
Ryan et al	2015	USA	RADP VS.LDP	prospective	18/16	50/38	68(67 ± 12.5)/ 58(60 ± 17.0)	28(29 ± 7.1)/ 25(25 ± 4.5)	22.2/18.8	7
Adam et al	2015	USA	RADP VS.LDP	retrospective	61/474	54/48	65 ± 14/64 ± 13	NR	NR	8
Deng et al	2015	China	RADP VS.LDP	retrospective	12/22	75/72.7	46.50 ± 16.08/ 48.50 ± 14.88	25.19 ± 3.47/ 23.63 ± 3.94	8.3/13.6	7
Lee et al	2016	Hong Kong	RADP VS.LDP VS.ODP	retrospective	18/6/46	50/50	58(39—80)/54.5(23 —80)/55.5(22—79)	NR	16.7/16.7/8.7	7
Eckhardt et al	2016	Germany	RADP VS.LDP	retrospective	11/23	66/59	48.5(29—76)/59(17 —85)	23(19.61—34.09)/ 26.99(19—36.4)	0/6	8
Goh et al	2016	Singapore	RADP VS.LDP	retrospective	8/31	75.0/41.9	57(21—68)/56(25—78)	27.6(21.5—30.7)/ 23.9(18.7—35.9)	0/12.9	9
Jin et al	2016	China	RADP VS.ODP	retrospective	31/25	64.5/52	51(40—63)/51(40—61)	23.8 ± 3.1/23.6 ± 4.3	25.8/16	7

Table 2 Robot-assisted compared to laparoscopy distal pancreatectomy.

Patient or population: patients with distal pancreatectomy						
Intervention: robot-assisted laparoscopic distal pancreatectomy						
Comparison: laparoscopic distal pancreatectomy						
Outcomes	Illustrative comparative risks[a] (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Laparoscopy	Robot				
Operative time		The mean operative time in the intervention groups was 37.27 higher (6.34 to 68.21 higher)		694 (12 studies)	⊕⊖⊖⊖ very low[b,c,d]	
Length of stay		The mean length of stay in the intervention groups was 1.33 lower (2.53 to 0.13 lower)		1286 (13 studies)	⊕⊕⊖⊖ low[b,c]	
Spleen-preservation rate	335 per 1000	568 per 1000 (361—678)	OR 2.61 (1.12—4.17)	612 (11 studies)	⊕⊕⊖⊖ low[b,c]	
Overall pancreatic fistula	289 per 1000	287 per 1000 (214—374)	OR 0.99 (0.67—1.47)	687 (11 studies)	⊕⊕⊖⊖ low[b,d]	
Overall complications	498 per 1000	517 per 1000 (423—609)	OR 1.08 (0.74—1.57)	656 (12 studies)	⊕⊕⊖⊖ low[b,d]	

CI: Confidence interval; OR: Odds ratio; GRADE Working Group grades of evidence.
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is a substantially different.
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low quality: We are very uncertain about the estimate We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
[a] The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
[b] Risk of bias was unclear or high in the study/studies.
[c] Heterogeneity >50.
[d] The confidence intervals were wide (overlapped clinically significant effects and no effect.

P < 0.017). Conversely, pooled analysis revealed no difference in SP between RADP and ODP (OR = 2.51, 95% CI, 0.73 to 8.63; P = 0.145).

3.5. Evidence from primary postoperative outcomes

3.5.1. Total complications

Forest plots of the primary postoperative outcomes are presented in Figs. 5—9. The short-term postoperative total complications were recorded in all but three studies that provided incomplete data.[3,28,29] The incidence of total postoperative complications was similar after RADP and LDP (OR = 1.08, 95% CI, 0.74 to 1.57; *P* = 0.686), without heterogeneity among studies (I^2 = 0%; P = 0.922); however, the TC rate was significantly lower after RADP than after ODP (OR = 0.55, 95% CI, 0.32 to 0.96; *P* = 0.034; Fig. 5). There was low heterogeneity between RADP and ODP (I^2 = 8.9%; P = 0.356).

3.5.2. Severe complications

SCs were recorded in nine studies. There was low heterogeneity for SCs, and the combined results (I^2 = 38.5%; P = 0.135 and I^2 = 38.8%; P = 0.162, respectively) in a fixed-effects model revealed no difference between RADP and LDP (OR = 1.39, 95% CI, 0.68 to 2.83; *P* = 0.366). Moreover, there was no statistically significant difference between RADP and ODP (OR = 0.91, 95% CI, 0.33 to 2.48; *P* = 0.853; Fig. 6).

3.5.3. Total pancreatic fistula

Twelve studies reported the incidence of TPFs. There was no difference in the incidence of TPFs between RADP and LDP (OR = 0.99, 95% CI, 0.67 to 1.47: *P* = 0.962), with no heterogeneity among studies (I^2 = 0%; P = 0.982). None of the five included studies revealed any significant difference in the pancreatic fistula rates of RADP and ODP, and the meta-analysis yielded a similar result (OR = 0.60, 95% CI, 0.29 to 1.24; *P* = 0.168), without heterogeneity among studies (I^2 = 0%; P = 0.843, Fig. 7).

Table 3 Robot-assisted compared to open distal pancreatectomy.

Patient or population: patients with distal pancreatectomy						
Intervention: robot-assisted laparoscopic distal pancreatectomy						
Comparison: open distal pancreatectomy						
Outcomes	Illustrative comparative risks[a] (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Open	Robotic				
Operative time		The mean operative time in the intervention groups was 32.93 higher (13.43 lower to 79.29 higher)		884 (6 studies)	⊕⊕⊖⊖ low[b,c]	
Length of stay		The mean length of stay in the intervention groups was 4.66 lower (8.38—0.93 lower)		884 (6 studies)	⊕⊕⊖⊖ low[b,c]	
Spleen-preservation rate	136 per 1000	283 per 1000 (103—576)	OR 2.51 (0.73—8.63)	828 (5 studies)	⊕⊕⊖⊖ low[b,c]	
Overall pancreatic fistula	145 per 1000	93 per 1000 (47—174)	OR 0.60 (0.29—1.24)	862 (5 studies)	⊕⊕⊖⊖ low[b,d]	
Overall complications	684 per 1000	544 per 1000 (409—675)	OR 0.55 (0.32—0.96)	855 (5 studies)	⊕⊕⊕⊖ moderate[b]	

CI: Confidence interval; OR: Odds ratio; GRADE Working Group grades of evidence.
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is a substantially different.
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low quality: We are very uncertain about the estimate. We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
[a] The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
[b] Risk of bias was unclear or high in the study/studies.
[c] Heterogeneity >50.
[d] The confidence intervals were wide (overlapped clinically significant effects and no effect).

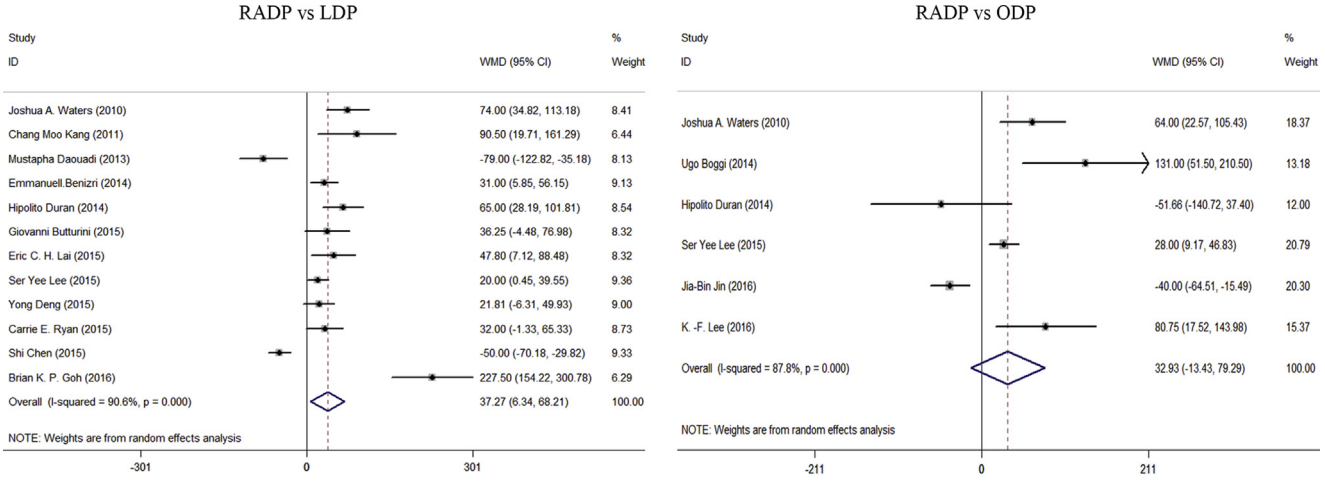

Figure 2 Forest plot comparing operative time for RADP versus LDP and ODP.

3.5.4. Severe pancreatic fistula

Eight studies reported the incidence of SPF. The analysis of SPF revealed homogeneity among the studies ($I^2 = 0$; $P = 0.864$). The meta-analysis of RADP and LDP revealed no statistically significant difference (OR = 1.36, 95% CI, 0.75 to 2.47; $P = 0.309$). Moreover, there was also no

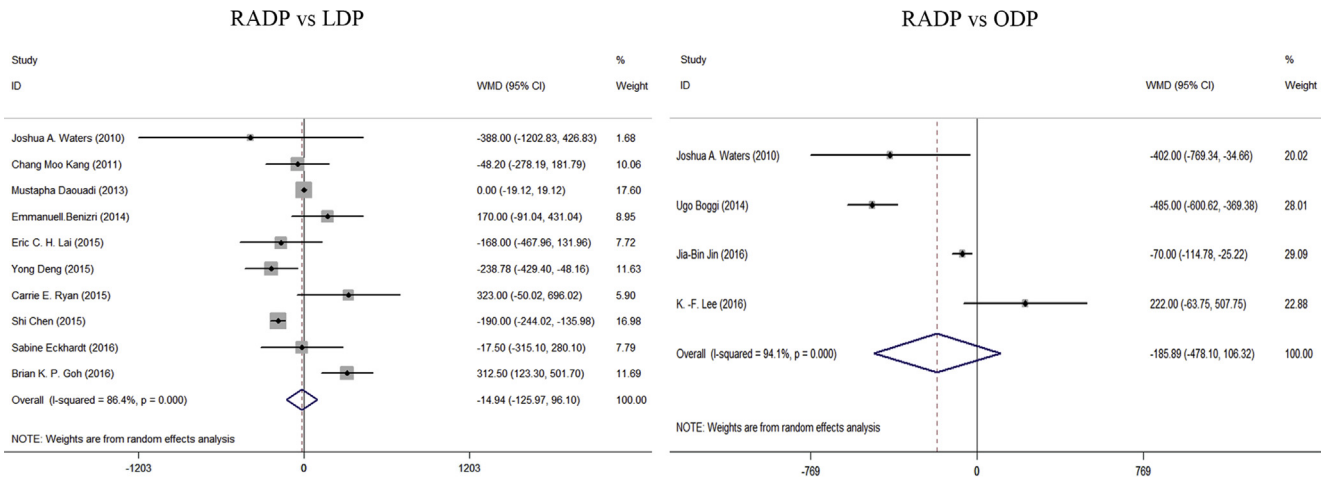

Figure 3 Forest plot comparing the mean amount of estimated blood loss for RADP versus LDP and ODP.

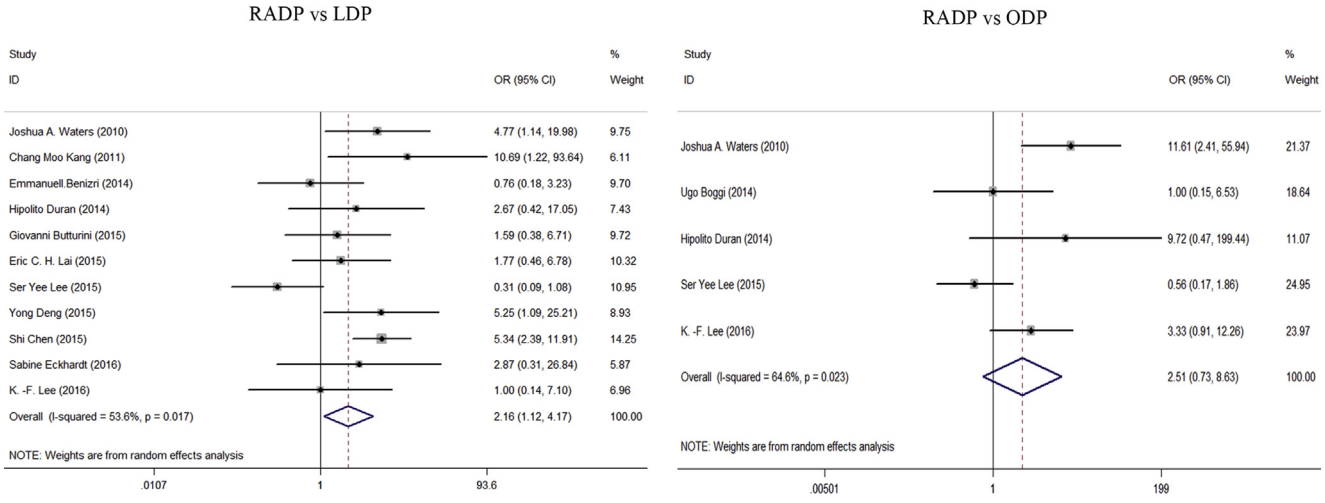

Figure 4 Forest plot comparing spleen-preservation rate for RADP versus LDP and ODP.

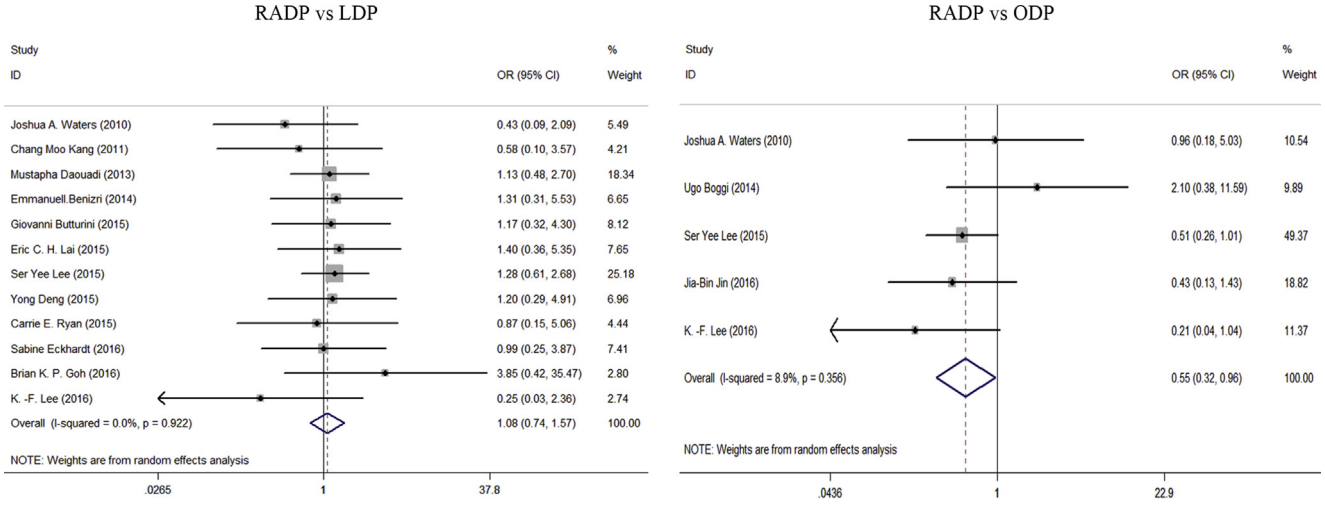

Figure 5 Forest plot comparing total complications for RADP versus LDP and ODP.

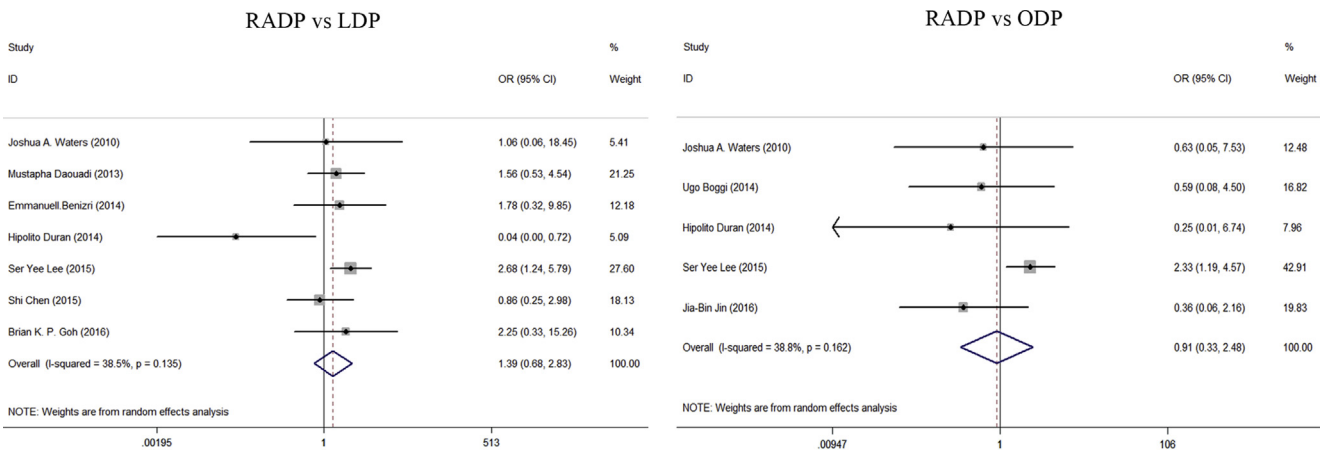

Figure 6 Forest plot comparing severe complications for RADP versus LDP and ODP.

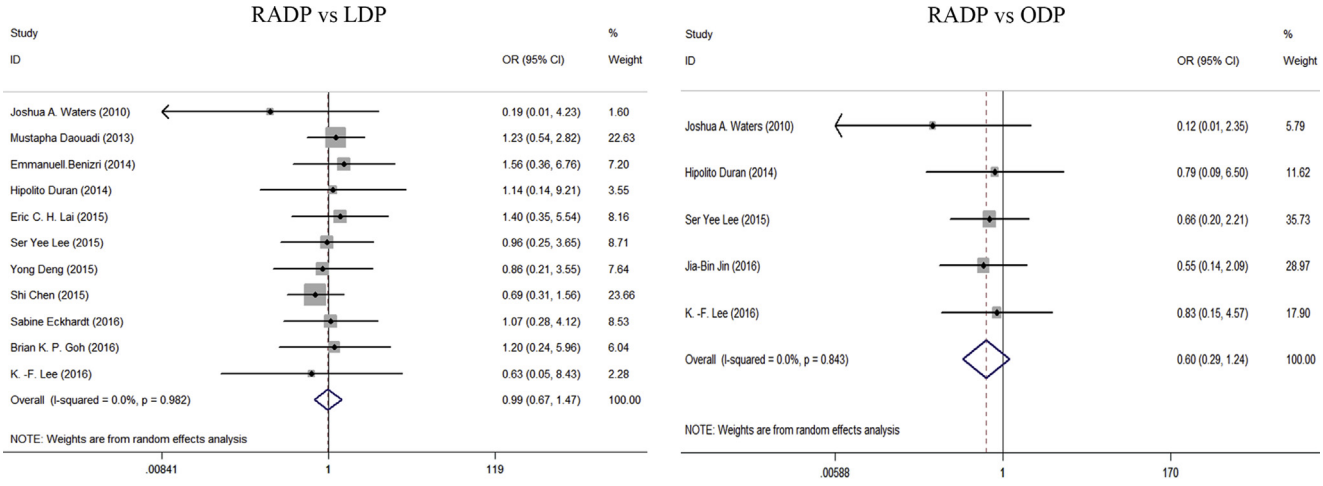

Figure 7 Forest plot comparing total pancreatic fistula for RADP versus LDP and ODP.

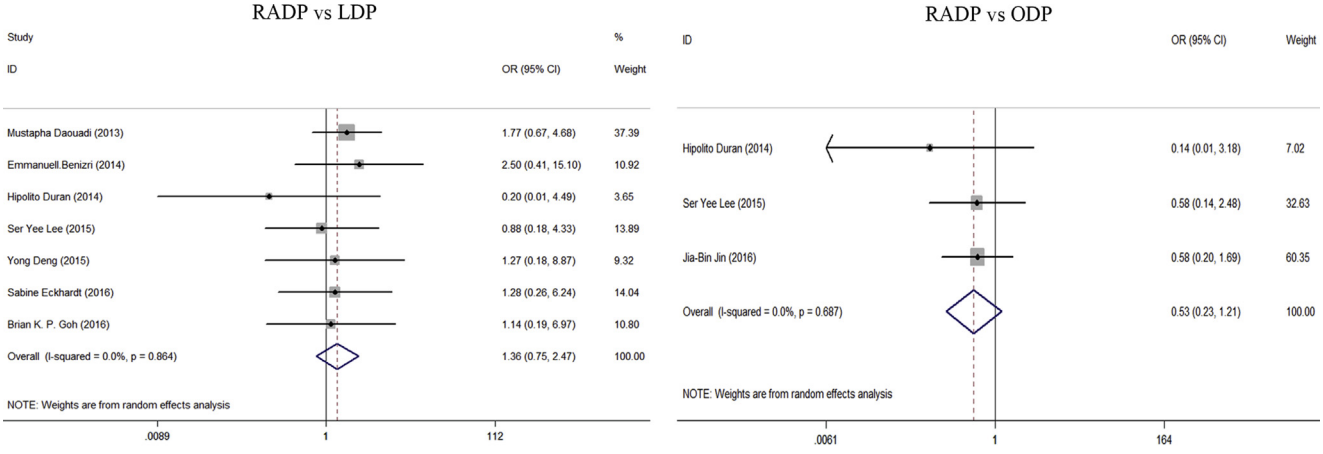

Figure 8 Forest plot comparing severe pancreatic fistula for RADP versus LDP and ODP.

statistically significant difference between RADP and ODP (OR = 0.53, 95% CI, 0.23 to 1.21; $P = 0.130$; Fig. 8).

3.5.5. LOS

LOS was reported in all but one study[3] (Fig. 9). The meta-analysis revealed significant heterogeneity between RADP and LDP or ODP ($I^2 = 71.0\%$; $P < 0.001$ and $I^2 = 82.8\%$; $P < 0.001$, respectively). The LOS was significantly shorter after RADP than LDP (WMD = −1.33 days, 95% CI, −2.53 to −0.13; $P = 0.030$). The patients who underwent RADP had a significantly shorter hospital stay than those who underwent ODP (WMD = −4.66 days, 95% CI, −8.38 to −0.93; $P = 0.014$).

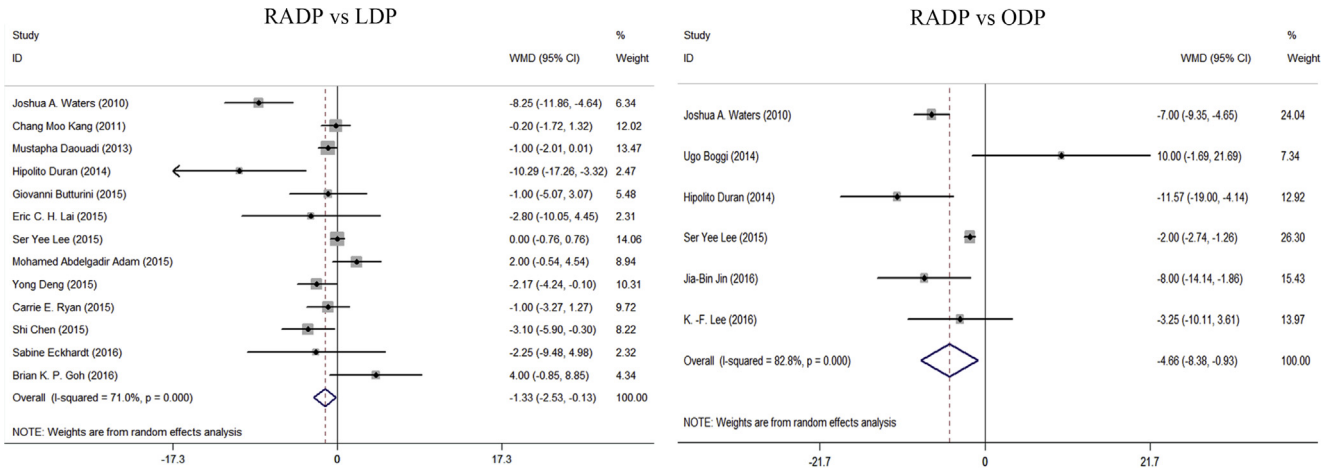

Figure 9 Forest plot comparing hospital length of stay for RADP versus LDP and ODP.

3.6. Sensitivity analysis

We performed a sensitivity analysis on the primary outcomes with high heterogeneity (i.e., operative time, EBL, SP, and LOS) to explore their potential sources and assess the robustness of these outcomes. After sequentially omitting each of the included studies for each outcome, we found that the study by Adam et al[26] may have been the source of heterogeneity for the length of hospital stay between RADP and LDP, and the heterogeneity of the pooled data analysis visibly decreased after the study was excluded (I^2 = 48.1%, P = 0.031). Similarly, the study by Lee et al[36] contributed to the high heterogeneity in the spleen preservation rate among RADP, LDP and ODP. This heterogeneity was low after the study was excluded (I^2 = 11.9%, P = 0.334; I^2 = 29.8%, P = 0.233, respectively). However, potential causes of the high heterogeneities for operative time and EBL could not be identified.

3.7. Publication bias

Egger tests were performed to assess publication bias and are presented in Table 4. The Egger tests did not indicate publication bias in any of the primary outcomes, i.e., operative time, mean amount of EBL, SP rate, hospital LOS, TCs, TPFs, or SPFs, with the exception of severe complications (P = 0.021).

4. Discussion

Although minimally invasive surgery improves quality of life, assurance that this technique does not increase morbidity and mortality is required.[24] With the development of the technique, minimally invasive surgery has become a revolutionary application in general surgery within the last century. According to most recent reports, robotic surgery has advantages over laparoscopy and open

Table 4 Results of Egger test for all outcomes: RADP versus LDP and ODP.

	Std_Eff	t		P>|t|	
		RADP VS. LDP	RADP VS. ODP	RADP VS. LDP	RADP VS. ODP
OT	slope	−1.61	−0.24	0.140	0.820
	bias	2.22	0.72	0.051	0.513
EBL	slope	−0.48	−0.39	0.647	0.732
	bias	−0.25	−0.51	0.806	0.661
LOS	slope	0.32	−1.64	0.756	0.176
	bias	−1.53	−0.98	0.154	0.382
SP	slope	1.19	−0.44	0.263	0.686
	bias	−0.46	0.81	0.659	0.479
TC	slope	1.27	−1.24	0.234	0.304
	bias	−1.13	0.51	0.284	0.648
SC	slope	2.62	5.10	0.047	0.015
	bias	−1.99	−4.42	0.103	0.021
TPF	slope	0.49	0.45	0.635	0.684
	bias	−0.56	−1.22	0.589	0.310
SPF	slope	2.58	0.71	0.049	0.606
	bias	−2.08	−2.81	0.092	0.217

surgery in gastric cancer and colorectal cancer.[40,41] However, the advantages of robotic surgery in colon cancer are not clear,[42] and for pancreatic resection, minimally invasive surgery has long been the subject of controversy focused on morbidity and mortality. Pancreatic resection has been regarded as a challenging surgical procedure that is associated with high morbidity and a mortality rate of up to 5%. NCCN experts recommend that surgery for pancreatic disease should only be performed in hospitals that perform more than 15 pancreatic surgeries each year. Hospitals that perform many pancreatic surgeries often produce better results.[5] With advances in techniques, instrumentation, and surgical experience, minimally invasive pancreatic resections are increasingly performed with satisfactory results. Distal pancreatectomy lends itself to an easier adoption of minimally invasive surgical techniques than pancreaticoduodenectomy because it does not require anastomotic reconstruction and intricate dissection. Distal pancreatectomy has been widely applied in open surgery as standard surgical treatment for pancreatic body and tail lesions.

Our study demonstrates the safety and feasibility of the robotic approach to distal pancreatectomy. Specifically, the results of our study show that RADP does not increase the rate of total complications, severe complications, is associated to higher rate of spleen preservation, reduces hospital length of stay and decreases total complications.

This meta-analysis revealed that the operative time was longer in patients undergoing RADP than those undergoing LDP but did not differ between RADP and ODP. In the present study, we found RADP to be associated with a longer operative time than LDP. This finding is consistent with those of most other studies in the literature.[43–46] There are several reasons that may account for the longer operative time associated with RADP. First, because this study represents most of the research regarding initial experiences with RADP, it includes the time required to adapt to a new technology and technique. It is likely that we are still in the learning phase for RADP, which may be attributable to the unavoidable surgical learning curve,[47] which, in turn, may be further compounded by the need to dock and undock the robot. Second, the prolonged time spent in the operative room for the robotic procedure is attributed to the additional setup procedures required for the robot, which include preparation and docking. The robotic setup often takes half an hour to complete. Third, most of the studies in the present analysis did not explicitly describe the surgeon's level of proficiency. It has been suggested that experienced laparoscopic surgeons reach a plateau in operative time after approximately 20 operations. To our surprise, the operative time was longer in the RADP group than in the ODP group, although the difference was not significant, even when accounting for the robot assembly and disassembly times. This fact is most likely due to the greater manoeuvrability provided by the robot, which increases the dexterity and range of motion,[6] and the shortened vascular dissection time in pancreatic surgeries. Additionally, extra time was required in the ODP group to open and close the abdomen, whereas the robotic docking and closure of the trocar could be completed in less than 30 min.

Spleen preservation is a critical measure of success in minimally invasive distal pancreatectomy. The preservation of the spleen, however, depends not only on technical factors but primarily on the indication for pancreatectomy. Appropriate indications for SP remain an open question. Some previous studies have reported a relatively higher morbidity rate for SP and have thus discouraged surgeons from performing LDP with SP.[18,19] Moreover, the preservation of the spleen during distal pancreatectomy can have a positive effect by increasing patients' immune system function and reducing the risk of postoperative bleeding.[48] Based on our data, we observed that RADP offers the possibility of improving the rate of spleen preservation during LDP. Conversely, the pooled analysis revealed no difference in the spleen preservation rate between RADP and ODP. Robotic-assisted surgery is a more recent development in minimally invasive pancreatic resections. This development theoretically retains the advantages of laparoscopic techniques in terms of smaller surgical scars and faster recovery and adds stable articulated instruments coupled with a magnified 3D high-definition view with increased dexterity. These benefits may provide a greater opportunity for spleen preservation.[32,49,50] The surgeon who performed the majority of the procedures had the impression that the separation of the splenic vessels from the surrounding pancreatic tissue was better facilitated by the robotic technique because it provides a 3D, magnified visual field and 7 degrees of freedom due to the Endowrist technology. This impression is supported by a previous retrospective study that noted that the vessel-preserving SP rates were significantly higher after RA-LDP than after C-LDP.[30] In contrast, Butturini et al conducted a prospective non-randomized study in 43 patients and demonstrated no benefit of RA-LDP over C-LDP.[1] This controversy can be resolved only by conducting a large-scale, prospective controlled trial. The size of the present study is too small to demonstrate a possible superiority of the robotic approach in terms of achieving a higher spleen preservation rate. Nonetheless, we believe that the superior technical characteristics of the robot, such as the augmented, high-quality, 3D vision and the precise, Endowrist instrument motion, are sufficient to explain the potential superiority of the robot, which has already been established in larger studies.[33,37,51] It has been hypothesized that this superiority is due to the increased dexterity of the robotic arms and the superiority of the robot in suturing in tight spaces, which facilitates the dissection of the small arterial branches and venous tributaries from the splenic artery and vein.[49,52] The EBL is another critical factor in the success of minimally invasive distal pancreatectomy. The analysis demonstrated that the mean EBL in RADP was similar to those in LDP and ODP. Intraoperative bleeding can be influenced by many factors, including local extension of the tumour, tumour size, and surgical expertise.

The total postoperative complication rate for RADP was similar to that for LDP but significantly less than that for ODP. In the present study, the total complication rates were similar between RADP and LDP. With respect to SCs, there were no statistically significant differences between RADP and the other procedures. Currently, distal pancreatectomy remains associated with a high morbidity rate regardless of the surgical approach. Similarly, these findings also demonstrated the safety of robotic surgery, especially relative to ODP. Pancreatic fistula is the most

common abdominal complication after distal pancreatectomy and remains the main postoperative complication of pancreatic surgery.[53] Regarding the rate of pancreatic fistula (including TPFs and SPFs), there was also no significant difference between the RADP, LDP and ODP groups, which is in accordance with the findings of previous reports, regardless of the technique used to surgery. To date, there is no strong evidence that the surgical approach (RADP vs. LDP vs. ODP) affects the pancreatic fistula rate.[36] However, it is uniformly accepted that the risk of fistula formation is increased when the pancreas has a soft texture and the pancreatic duct is small.

The most consistent finding in this meta-analysis was a shorter hospital LOS for RADP than for LDP and ODP. The LOS was significantly shorter by 1.33 days in patients undergoing RADP than in those undergoing LDP. However, the LOS for RADP was significantly shorter (by 4.66 days) than that for ODP. This result was mainly attributed to two reasons, namely, there was a higher rate of patients with severe PF in the LDP than in the RADP group, and there were higher rates of other complications, such as wound dehiscence, lung embolism and postoperative ileus, in the LDP than in the RADP group. Both factors resulted in a longer LOS in the LDP group.[30]

We found that the study heterogeneities were high for several outcomes, and we were unable to identify the sources for operative time and EBL. We suggest that the heterogeneity for operative time could potentially be due to the experience of the surgeons, the different types of DaVinci robotic systems used and the use of a total or hybrid robotic technique. Larger errors in blood loss measurements may be associated with the difficulty of measuring this value precisely during surgery and the fact that it is estimated by surgeons. Additionally, it is possible that surgeons have been reporting positive results in terms of EBL because the system is popular in most countries and regions and because of its high cost. Moreover, the surgeons' experience and proficiency with this system may also have contributed to the heterogeneity for EBL.

The assessments of the quality of the evidence are presented in Tables 2 and 3 and indicated that the overall quality of the evidence was poor for the operative time, LOS, SP, and TPFs in the RADP vs. ODP and LDP comparisons. Moreover, the overall quality of evidence was moderate for TCs in the RADP vs. ODP comparison. This result also suggested that additional research in the future may influence the confidence of this evaluation of the effect and likely change the estimate. The major reason for this poor assessment was that the studies were observational studies, and, consequently, the risk of confounding bias was unclear. Another factor that decreased the quality of the evidence was the wide CIs for the outcomes of operative time, LOS, spleen-preservation rate, and TPFs in distal pancreatectomy.

This meta-analysis has several limitations that must be taken into account when the results are considered. First, the quality of the primary studies determines the quality of the meta-analysis, and the studies included in this meta-analysis had shortcomings in their methodologies. All of the included studies were observational and included the likelihood of selection bias. It has been reported that NRCTs can either exaggerate or underestimate the magnitude of measured effects in an intervention study regardless of the quality scores. However, Abrahama et al[54] found that meta-analyses of well-designed NRCTs of surgical procedures are probably as accurate as those of RCTs. Second, there was heterogeneity between the two groups in operative time, EBL, LOS, and SP because it was impossible to match the patient characteristics in all studies. We applied a random-effects model to consider the between-study variation, and this approach may have been expected to suggest a limited influence. Although sensitivity analysis using matched data should reduce this bias, it cannot be eliminated. Robotic procedures include the initial learning period, which may have resulted in an unequal surgical quality comparison. Most of the studies had small sample sizes, with fewer than 50 RADP procedures. Results with marginal statistical significance should be interpreted with caution. Third, Egger's test yielded some results that suggested the possibility of publication bias. This meta-analysis could not address the problems introduced by confounding factors that may have been inherent in the included studies. These confounders may have biased the results either towards overestimation or underestimation of the risk. Additionally, the primary emphasis of this meta-analysis was to provide a short-term outcome to elucidate the value of RADP in pancreatic resection. The long-term efficacy of the surgical treatment was not thoroughly discussed in some of the included trials. Therefore, further RCTs that focus on long-term outcomes are needed to identify potential advantages and disadvantages of robotic surgery in distal pancreatectomy.

To date, there have been several meta-analyses comparing RADP vs. LDP[43,44,54] and LDP vs. ODP, but no study comparing RADP with LDP and ODP has been published. Essentially, the results of our study are different from those of other published studies that have not compared RADP with the two other possible approaches (robotic and open); in this aspect, our study can be considered a novel study. Furthermore, the number of previous studies was relatively small, and limited numbers of patients were included. We collected 1569 articles in the literature using a comprehensive research strategy. The present meta-analysis included seventeen studies with a total of 2133 patients, which resulted in a comparison of 409 patients who underwent RADP vs. 970 who underwent LDP and 754 who underwent ODP. Finally, we decided to perform a strategic double comparison to minimize the possible bias because we realized that not all of the seventeen selected articles had sufficient quality-level data and because the overall number of patients was relatively small. We also summarized and rated the evidence qualities of the primary outcomes based on the five GRADE considerations (i.e., risk for bias, consistency of effect, imprecision, indirectness, and publication bias).

In summary, our meta-analysis is the most accurate and current study present in the literature and can be considered as a foundation for subsequent investigations. Despite the poor quality of evidence in the published studies to date, our study revealed that RADP for pancreatic resection is a promising new surgical technique that reduces the duration of hospitalization and increases the SP rate compared with LDP and reduces the TCs and duration of hospitalization compared with ODP. However, these advantages come at the price of an increased operative time.

Additional studies with larger sample sizes and high-quality controlled clinical trials are needed to evaluate the benefits and costs of RADP in patients undergoing distal pancreatectomy.

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Conflicts of interest

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Appendix A. Supplementary data

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