Safety and Efficacy for Robot-Assisted Versus Open Pancreaticoduodenectomy: A Meta-Analysis of Multiple Worldwide Centers

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Research

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Abstract

Objectives: To compare the efficacy of robot-assisted pancreaticoduodenectomy with that of laparotomy.

Methods: The PubMed, EMBASE, Cochrane Library, and other databases were searched for literature available from their respective inception dates up to May 2020 to find studies comparing robot-assisted pancreaticoduodenectomy (RPD) with open pancreaticoduodenectomy (OPD). The RevMan 5.3 statistical software was used for analysis to evaluate surgical outcome and oncology safety. The combination ratio (*RR*) and weighted mean difference (*WMD*) and their 95% confidence intervals (*CIs*) were calculated using fixed effect or random effect models.

Results: 18 cohort studies from 16 medical centers were eligible with a total of 5795 patients including 1420 RPD group patients and 4375 OPD group patients. The RPD group fared better than the OPD group in terms of estimated blood loss (EBL) (*WMD* =-175.65, 95% CI (-251.85, -99.44), P<0.00001), wound infection rate (*RR*=0.60, 95%*CI* (0.44,0.81), P= 0.001), reoperation rate (RR=0.61, 95%*CI* (0.41,0.91), P=0.02), hospital day (*WMD* = -2.95, 95% CI (-5.33,-0.56), P = 0.02), intraoperative blood transfusion (*RR* = 0.56, 95% *CI*(0.42, 0.76), P=0.0001), overall complication (*RR* = 0.78, 95% *CI*(0.64,0.95), P = 0.01), and clinical pancreatic fistula (PF) (RR = 0.54, 95% *CI*(0.41,0.70), P < 0.0001). In terms of lymph node clearance (*WMD* = 0.48, 95% *CI*(-2.05,3.02), P = 0.71), R0 rate (*RR* = 1.05, 95% *CI*(1.00,1.11), P = 0.05), postoperative pancreatic fistula (POPF) (*RR*=1, 95% *CI*(0.85,1.19), P = 0.97), bile leakage (*RR* = 0.99, 95% *CI*(0.54,1.83), P = 0.98), delayed gastric emptying (DGE) (*RR* = 0.79, 95% *CI*(0.60,1.03), P = 0.08), mortality (*RR* = 0.82, 95% *CI*(0.62,1.10), P=0.19), and severe complication (*RR* = 0.98, 95% *CI*(0.71,1.36), P = 0.91), there were no significant differences between the two groups. Laparoscopic surgery was inferior to open surgery in terms of operational time (*WMD* = 80.85, 95% *CI* (16.09,145.61), P=0.01).

Conclusions: RPD is not inferior to OPD, and it is even more advantageous for DGE, wound infection rate, reoperation rate, hospital stay, transfusion, overall complication and clinical PF. However, these findings need to be further verified by high-quality randomized controlled trials.

Introduction

Pancreaticoduodenectomy is a method used to treat pancreatic head tumors, periampullary tumors, chronic pancreatitis with biliary stricture, and other diseases. Pancreaticoduodenectomy is one of the most complicated operations in abdominal surgery and is characterized by marked trauma and a high incidence of complications. In 2003, Giulianotti et al. [1] first reported Da Vinci-assisted robotic pancreaticoduodenectomy (RPD). The Da Vinci robot has the following advantages: (1) the operation field of vision can be magnified up to 10 ×, providing a naked-eye, 3D, high-resolution image for the operator; (2) the end of the device simulates the wrist: it is flexible and controllable, the movement can be scaled reasonably, and it can accurately complete various operations and eliminate shaking. These advantages are incomparable to those of traditional laparotomy and robotic surgery. However, the feasibility, safety, and effectiveness of this robot method have not been fully determined. In the past 10 years, many retrospective studies have reported the efficacy of both approaches in PD. Therefore, we conducted this meta-analysis to evaluate the efficacy of robot-assisted PD and open PD in the treatment of pancreatic diseases.

Data And Methods

1. Retrieval strategy

We searched the PubMed, MEDLINE, Cochrane Library, and other databases by computer, and limited the search deadline to May 2020. The search terms used were ((open) OR laparotomy) AND ((pancreaticoduodenectomy) OR pancreatectomy) AND ((robotic) OR robot-assisted). The Boolean operator "OR", "AND" for each keyword was used. The reference lists of identified literatures were also searched manually. In cases of duplicated studies, only the latest study, with the largest sample size and the highest quality, was selected. If a literature involved a study of patients with different types of surgery or operation times, it was still included in the analysis as an independent study.

1. 2. Inclusion criteria: The following studies were included: 1) Reports of patients undergoing pancreaticoduodenectomy. 2) Original research papers, including comparative analysis of various indicators of the two surgical methods, including randomized control studies, and prospective and retrospective non-control studies. 3) Reports with any study sample size. 4) Reports with any length of follow-up. 5) Reports in English. Study indicators included operation time, EBL, wound infection rate, reoperation rate, hospital stay, transfusion, POPF, clinical PF, R0 rate, lymph node dissection, overall complication, bile leakage rate, DGE, mortality, and severe complication.
2. 3. Exclusion criteria: The following reports were excluded: 1) Those with incomplete information, those for which it was impossible to extract data effectively or for which contacting the author yielded no reply, duplicated reports. 2) Reports on non-robotic surgery, such as laparoscopic surgery. 3) Reports on surgery in other parts of the pancreas, non-PD surgery, such as central and distal pancreatectomy. 4) Literature written in languages other than English. 5) Review studies, case reports, and animal experiments.

This meta-analysis included prospective and retrospective cohort studies. In all the included studies, CSs was evaluated according to the Newcastle–Ottawa scale (NOS), specifically including study population selection, comparability, exposure evaluation, or outcome evaluation. The semi-quantitative star system was adopted for evaluation of document quality by NOS, with a full score being 9 stars. The details were attached to the *Appendix file 1*.

Statistical Analyses

The Review Manager 5.3 software was used for meta-analysis. For binary data, relative risk (RR) was used, and for continuous data, the weighted mean difference (WMD) and its 95% confidence interval (CI) were used to represent the combined statistics. Heterogeneity among the included studies was qualitatively evaluated using a χ2-based Q test. P values less than 0.05 showed statistically significant heterogeneity across the studies. The level of heterogeneity among studies was evaluated using I^2 statistics. $I^2 < 30\%$ was considered to indicate low heterogeneity; for these studies, a fixed-effects model was applied. Moreover, $30\% \leq I^2 \leq 60\%$ was considered to indicate moderate heterogeneity, and $I^2 > 60\%$ represented high heterogeneity. A random-effects model was applied when $I^2 \geq 30\%$. Sensitivity analysis was performed by removing 1 study at a time to assess whether the results could have been markedly affected by any single study. The results with less heterogeneity between the studies were selected if results were reversed after sensitivity analysis. Deleted literatures were described in the results section. Funnel plot was used to qualitatively evaluate publication bias. (*Appendix file 2*) Stata software (version SE15.0) was used to calculate Begg's test and Egger's test for quantitative evaluation of publication bias of the included studies, with the significant level limited to 0.05. The details were attached to the *Appendix file 3*.

Results

Literature search results

A total of 25 articles [2–26] were retrieved, of which 18 articles [2, 4–8, 10, 12–15, 17–20, 22, 23, 25] were included in the analysis. The flow chart of the literature screening is shown in Fig. 1. There were 11 cohort studies from prospective databases and 7 cohort studies from retrospective databases. A total of 5795 patients were included in the 18 articles, comprising 1420 patients in the RPD group and 4375 cases in the OPD group. Table 3 shows the basic characteristics and quality evaluation of the included documents.

Table 3
Basic characteristics and quality evaluation of the included documents

Study	Country	Organization	Period	Types	Case	Age		Gender(m/f)		Quali
Included studies					RPDvs.OPD	RPD	OPD	RPD	OPD	ty
Baimas-George 2020	[2]USA	Department of General Surgery, Carolinas Medical Center	2008–2019	PSM(P)	38 vs. 38	66 (38–84)	68 (42–81)	16/22	16/22	8
Bao 2014[4]	USA	Stony Brook University Medical Center,NK	2009–2011	R	39 vs. 38	68.0 ± 11.2	67.7 ± 12.5	13/15	13/15	7
Buchs 2011[6]	USA	Division of General, Minimally Invasive and Robotic Surgery Department of Surgery, University of Illinois at Chicago	2002–2010	P	44 vs. 39	63 ± 14.5	56 ± 15.8	22/22	14/25	8
Cai 2019[7]	China	Department of Hepatobiliary and Pancreatic Surgery, First Affiliated Hospital, Sun Yat-sen University, Guangzhou	2011–2018	P	460 vs. 405	66.5 ± 11.0	67.5 ± 10.7	253/207	211/194	7
Chalikonda 2012[8]	USA	Department of general Surgery, Cleveland Clinic Foundation	2009–2010	p	30 vs. 30	62	61	16/14	16/14	7
Gall 2020[10]	UK	HPB Surgical Unit Dept. of Surgery & Cancer Imperial College London Hammersmith Hospital Campus, London	2017–2019	P	25 vs. 37	60.93 ± 12.52	62.23 ± 10.76	16/19	21/16	8
Ielpo 2019[12]	Spain	Sanchinarro University Hospital, San Pablo CEU University of Madrid	2008–2016	P	17 vs. 17	66.8 ± 9.5	61.4 ± 11.9	8/9	10/7	7
Boggi 2016[5]	Italy	Division of General and Transplant Surgery,University of Pisa	2008–2014	P	83 vs. 36	58(21–84)		77/123		8
Kauffmann 2019[14]	Italy	Division of General and Transplant Surgery,University of Pisa	2014–2017	PSM(P)	24 vs. 26	65 (58.5–74.75)	72.5 (59.75–78.75)	10/10	13/11	7
Kim HS 2018[15]	Korea	Seoul National University College of Medicine,	2015–2017	PSM(P)	51 vs. 186	60.7 ± 11.9	65.4 ± 10.1	24/27	108/78	8

Note: RPD, robot-assisted pancreaticoduodenectomy; OPD, open pancreaticoduodenectomy; P-review of prospectively collected databases; R-review of retrospective databases;PSM- Propensity score matching; No.-number of; NA, data not accessible; vs., versus; Quality- quality assessment;

PRISMA 2009 Flow Diagram

Study	Country	Organization	Period	Types	Case	Age		Gender(m/f)		Quali
Lai 2012[17]	China	Pamela Youde Nethersole Eastern Hospital, Hong Kong	2000–2012	R	20 vs. 67	66.4 ± 11.9	62.1 ± 11.2	12/8	38/29	8
Marino 2019[18]	Italy	Department of Surgery, Palermo University	2014–2016	P	35 vs. 35	60.4 (43–72)	62.3 (45–73)	19/16	15/20	8
McMillan 2017[19]	USA	University of Pittsburgh Medical Center	2003–2015	PSM(P)	185 vs. 2661	64(56–72)		51.5%male		8
Mejia 2020[20]	USA	Methodist Dallas Medical Center	2013–2019	R	102 vs. 54	66 ± 10.6	61.7 ± 14.1	53/49	30/24	8
Jin J 2019[13]	China	the Pancreatic Disease Center of the Shanghai Ruijin Hospital	2003–2017	R	39 vs. 44	29 (21–41)	30 (25–38)	3/15	1/32	7
Shi 2020[22]	China	the Pancreatic Disease Center of the Shanghai Ruijin Hospital	2017–2018	PSM(R)	200 vs. 634	60.9 ± 11.4	60.1 ± 10.8	109/78	107/80	7
Tan 2019[23]	Singapore	Yong Loo Lin School of Medicine	2014–2016	PSM(R)	20 vs. 20	65 (37–82)	64 (46–84)	11/9	11/9	7
Zhou 2011[25]	China	General Hospital of PLA Second Artillery, Beijing	2009,1-2009,11	R	8 vs. 8	65(48–75)	57(47–77)	5/3	4/F	5
Excluded studies										
Baker 2015[3]	USA	Department of General Surgery, Carolinas Medical Center	2012–2013	R	22 vs. 49	63 (38–82)	63 (26–86)	31/18	13/9	
Napoli 2017[21]	Italy	Division of General and Transplant Surgery,University of Pisa	2007–2014	P	82 vs. 227	61.6 (51.9–70.7)	67.4 (59.7–74.8)	36/46	125/102	
Kowalsky 2019[16]	USA	University of Pittsburgh School of Medicine	2014–2015	P	159 vs. 95	66.8 ± 9.8	67.9 ± 10.9	87/72	47/48	
Varley 2018[24]	USA	University of Pittsburgh Medical Center	2011–2016	P	133 vs. 149	66.3 ± 10.6	66.3 ± 10.6	64/69	79/70	
ZureiKat 2016[26]	USA	multicenter: University of Pittsburgh School of Medicine etc.	2011–2015	R	211 vs. 817	67 (15–86)	65 (15–93)	425/392	117/94	
Girgis M 2019[11]	USA	the National Cancer Database (NCDB) from the University of Pittsburgh Medical Center	2011–2016	P	163 vs. 198	66.6 ± 10.9	67.6 ± 10.3	87/76	105/93	

Note: RPD, robot-assisted pancreaticoduodenectomy; OPD, open pancreaticoduodenectomy; P-review of prospectively collected databases; R-review of retrospective databases;PSM- Propensity score matching; No.-number of; NA, data not accessible; vs., versus; Quality- quality assessment;

PRISMA 2009 Flow Diagram

Study	Country	Organization	Period	Types	Case	Age		Gender(m/f)		Quali
Chen S 2015[9]	China	Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine	2010–2013	P	60 vs. 120	53.6 ± 13.5	53.8 ± 14.3	34/26	65/55	
Note: RPD, robot-assisted pancreaticoduodenectomy; OPD, open pancreaticoduodenectomy; P-review of prospectively collected databases; R-review of retrospective databases;PSM- Propensity score matching; No.-number of; NA, data not accessible; vs., versus; Quality- quality assessment;										
PRISMA 2009 Flow Diagram										

Data synthesis and analysis

In this study, 15 postoperative efficacy outcomes of RPD and OPD were analyzed, and sensitivity analysis was performed for each outcome. The outcomes as shown in Table 1. Subgroup analysis was conducted according to whether studies were prospective, retrospective, or propensity score matching (PSM) cohort, as shown in Table 2.

Table 1
Meta-Analysis Results of All Available Studies in Measured Outcomes

Measured Outcomes	No. Studies	No. Patients		Heterogeneity Test		Model	RR /WMD	95% CI	*P*
		RPD	OPD	I^2*(%)*	*P*				
Operative time (min)	9	468	598	96	< 0.00001	Random	80.85	16.09,145.61	**0.01**
Estimated blood loss (ml)	9	410	599	82	< 0.00001	Random	-175.65	-251.85,-99.44	**< 0.00001**
Hospital day (d)	10	615	757	87	< 0.00001	Random	-2.95	-5.33,-0.56	**0.02**
Lymph node dissection	6	222	217	72	0.003	Random	0.48	-2.05,3.02	0.71
R0 rate	13	589	513	1	0.44	Fixed	1.05	1.00,1.11	0.05
Overall complication	10	409	458	33	0.14	Random	0.78	0.64,0.95	**0.01**
Bile leakage rate	6	317	378	0	0.6	Fixed	0.99	0.54,1.83	0.98
POPF	15	1037	1006	0	0.75	Fixed	1	0.85,1.19	0.97
Delayed gastric emptying	11	549	681	0	0.46	fixed	0.79	0.60,1.03	0.08
Wound infection	8	391	433	0	0.65	Fixed	0.6	0.44,0.81	**0.001**
Mortality	14	1178	1218	0	0.53	Fixed	0.82	0.62,1.10	0.19
Reoperation	9	842	843	0	0.69	Fixed	0.61	0.41,0.91	**0.02**
Transfusion	9	817	678	36	0.13	Random	0.56	0.42,0.76	**0.0001**
Clinical PF	8	969	1078	0	0.68	Fixed	0.54	0.41,0.70	**< 0.0001**
Severe complications	6	341	322	0	0.89	Fixed	0.98	0.71,1.36	0.91
Note: RPD- robot-assisted pancreaticoduodenectomy; OPD-open pancreaticoduodenectomy; POPF- postoperative pancreatic fistula; PF-pancreatic fistula; CI- Confidence Interval; RR/WMD-Relative Risk/ weighted mean difference; No.-number of; Statistical significant results are shown in bold									

Table 2
Meta-Analysis Results of subgroup analysis in Measured Outcomes

Measured Outcomes	Subgroup analysis	No. Studies	No. Patients		Heterogeneity Test		Model	RR /WMD	95% CI	*P*
			RPD	OPD	I^2(%)	*P*				
Operative time (min)	R	4	243	290	97	< 0.00001	Random	120.4	-16.02,256.83	0.08
	P	5	225	308	96	< 0.00001	Random	57.52	-30.98,146.02	0.2
Estimated blood loss (ml)	R	4	243	290	79	0.002	Random	-136.55	-230.64,-42,45	0.004
	P	5	167	309	84	< 0.0001	Random	-222.80	-361.50,-84.10	0.0002
Hospital day (d)	R	4	243	290	84	0.0003	Random	-5.35	-9.89,-0.81	0.02
	P	6	372	467	88	< 0.00001	Random	-1.67	-4.92,1.59	0.32
	PSM	3	390	525	54	0.11	Random	-3.04	-5.28,-0.81	0.008
Lymph node dissection	R	2	48	95	71	0.06	Random	2.22	-6.63,2.19	0.32
	P	4	174	122	58	0.07	Random	1.84	-0.75,4.42	0.16
R0 rate	R	5	327	285	0	0.42	Fixed	1.04	0.98,1.10	0.25
	P	8	262	228	0	0.52	Fixed	1.08	0.98,1.19	0.1
	PSM	4	265	269	0	0.49	Fixed	1.02	0.95,1.09	0.59
Overall complication	R	3	130	82	73	0.02	Random	0.6	0.23,1.56	0.29
	P	8	431	528	20	0.27	Fixed	0.94	0.84,1.06	0.31
	PSM	4	247	384	45	0.14	Random	0.98	0.77,1.25	0.87
POPF	R	6	281	343	0	0.55	Fixed	1.1	0.84,1.44	0.5
	P	9	756	663	0	0.74	Fixed	0.96	0.78,1.18	0.7
	PSM	4	269	271	0	0.7	Fixed	1.08	0.75,1.54	0.69
Delayed gastric emptying	R	3	227	274	2	0.36	Fixed	1.07	0.49,2.37	0.86
	P	8	322	407	10	0.35	Fixed	0.73	0.56,0.97	0.03
	PSM	5	320	457	48	0.1	Random	0.72	0.31,1.65	0.44
Wound infection	R	3	227	274	0	0.48	Fixed	0.67	0.49,0.92	0.01
	P	5	164	159	0	0.73	Fixed	0.28	0.10,0.79	0.02
	PSM	3	245	245	0	0.46	Fixed	0.66	0.48,0.90	0.009
Mortality	R	4	243	243	0	0.73	Fixed	0.73	0.3,1.77	0.48
	P	10	935	975	15	0.31	Fixed	0.84	0.62,1.13	0.25
	PSM	5	448	583	0	0.5	Fixed	1.01	0.69,1.47	0.97
Reoperation	R	2	207	254	0	0.71	Fixed	0.58	0.25,1.31	0.19
	P	7	635	589	0	0.49	Fixed	0.63	0.40,0.98	0.04
Transfusion	R	3	150	102	0	0.76	Fixed	0.69	0.48,0.99	0.04
	P	6	667	576	43	0.12	Random	0.48	0.31,0.75	0.001
Clinical PF	R	2	205	220	30	0.23	Fixed	0.61	0.36,1.03	0.06

Note: RPD, robot-assisted pancreaticoduodenectomy; OPD, open pancreaticoduodenectomy; P-review of prospectively collected databases; R-review of retrospective databases;PSM- Propensity score matching; No.-number of; POPF- postoperative pancreatic fistula; PF- pancreatic fistula; CI- confidence interval

Measured Outcomes	Subgroup	No. Studies	No. Patients		Heterogeneity Test		Model	RR /WMD	95% CI	*P*
	P	6	764	858	0	0.6	Fixed	0.5	0.36,0.71	< 0.0001
	PSM	3	389	439	0	0.85	Fixed	0.63	0.42,0.96	0.03
Severe complications	R	3	140	107	0	0.78	Fixed	0.75	0.33,1.71	0.5
	P	3	210	215	0	0.71	Fixed	1.04	0.73,1.49	0.84
	PSM	3	196	198	0	0.64	Fixed	1.01	0.70,1.46	0.96

Note: RPD, robot-assisted pancreaticoduodenectomy; OPD, open pancreaticoduodenectomy; P-review of prospectively collected databases; R-review of retrospective databases;PSM- Propensity score matching; No.-number of; POPF- postoperative pancreatic fistula; PF- pancreatic fistula; CI- confidence interval

1.1 Comparison of operation time

Nine studies [4–6, 8, 12, 15, 17, 22, 25] reported the operation time. There was a high degree of heterogeneity (I^2 = 96%, P < 0.00001) among studies. Using a random-effects model, the *WMD* was 80.85 (95% *CI*: 16.09 ~ 145.61; P = 0.01). The operation time in the RPD group was significantly longer than that in the OPD group. Subgroup analysis showed that, in the retrospective cohort studies, the operation time of the RPD group was significantly longer than that of the OPD group (*WMD* = 120.4, 95% *CI*: -16.02 ~ 256.83, *P* = 0.08) and the difference was significant. In the prospective cohort study, the operation time in the RPD group was not significantly different from that in the OPD group (*WMD* = 57.52, 95% *CI*: -30.98 ~ 146.02, *P* = 0.2) (Figs. 2A).

1.2 Comparison of estimated blood loss

Nine studies [4, 6, 8, 10, 12, 15, 17, 22, 25] reported estimated blood loss (EBL). There was a high degree of heterogeneity among the studies (I^2 = 82%, P < 0.00001). Using the random-effects model, the combined *WMD* was − 175.65, 95%*CI* (-251.85, -99.44), P < 0.0001, the EBL in the RPD group was significantly less than that in the OPD group. Using a random-effects model, the combined WMD was − 175.65,95%CI (251.65, -99.44), P < 0.00001. The EBL in the RPD group was still significantly less than that in the OPD group. Subgroup analysis showed that in both retrospective and prospective cohort studies, the EBL in the RPD group was significantly less than that in the OPD group (*WMD* =-136.55, 95%*CI* -230.64, -42.45, P = 0.004; and *WMD*=-222.8, 95%*CI*(-361.50, -84.10), P = 0.0002, respectively) (Figs. 2B).

1.3 Comparison of intraoperative blood transfusion

Nine studies [3–5, 7, 8, 11, 13–15] reported the rate of transfusion. There was moderate heterogeneity among these studies (I^2 = 36%, P = 0.13). Using a random-effects model, the combined *RR* was 0.56, 95%*CI* (0.42, 0.76), *P* = 0.0001, and the rate of transfusion in the RPD group was significantly lower than that in the OPD group. After sensitivity analysis, the meta-results did not show any reversal changes. However, when Cai et al. [14] was eliminated, the heterogeneity was significantly reduced (I^2 = 0%, P = 0.43), the fixed-effects model yielded an *RR* of 0.65, 95%*CI* (0.50, 0.86), *P* = 0.002, and the statistically significant difference remained. In both retrospective and prospective cohort studies, there was a statistically significant difference in the number of transfusion between the RPD group and the OPD group (*RR* = 0.69, 95% *CI*: 0.48, 0.99, *P* = 0.04; *RR* = 0.48, 95% *CI*: 0.31, 0.75, *P* = 0.001, respectively) (Figs. 2C).

1.4 Postoperative hospital stay

Ten studies [4–6, 10, 12, 15, 17, 19, 22, 25] reported the postoperative hospital stay. There was a high degree of heterogeneity among the studies (I^2 = 87%, P < 0.00001). Using a random-effects model, the combined *WMD* was − 2.95, 95% *CI* (-5.33, -0.56), P = 0.02; there was no statistically significant difference between the RPD group and the OPD group. Subgroup analysis showed that in the retrospective or PSM cohort studies, the hospital stay in the RPD group was significantly shorter than that in the OPD group (*WMD* = -5.35, 95% *CI* (-9.89, -0.81), *P* = 0.02; *WMD* = -3.04, 95%*CI* (-5.28, -0.81), *P* = 0.008, respectively). In the prospective cohort studies, there was no significant difference between the RPD and OPD groups. (Figs. 2D)

1.5 Number of lymph node dissection

Six studies [4–6, 8, 12, 17] reported the number of lymph node dissection. There was moderate heterogeneity among the studies (I^2 = 72%, *P* = 0.003). Using the random-effects model, *WMD* was 0.48, 95%*CI* (-2.05, 3.02), P = 0.71), and there was no statistically significant difference between the two operative methods. Subgroup analysis showed that there was no statistically significant difference between the RPD group and OPD group in both retrospective and prospective cohort studies (*WMD* = 2.22, 95% *CI*: -6.63, 2.19, P = 0.32; *WMD* = 1.84, 95% *CI*: -0.75, 4.42, *P* = 0.16, respectively). (Figs. 3A)

1.6 R0 rate

Thirteen studies [2, 4–6, 8, 10, 12, 14, 18, 20, 22, 23, 25] reported the R0 rate of the cutting edge. There was a low degree of heterogeneity (I^2 = 1%, P = 0.44) among the studies. Using the fixed-effects model, the combined RR was 1.05, 95%CI (1.01, 1.11), P = 0.05. The R0 rate of the RPD group was significantly higher than that of the OPD group. However, subgroup analysis showed that there was no statistically significant difference between the RPD group and the OPD group in the prospective or retrospective cohort studies (*RR* = 1.04, 95% *CI*: 0.98, 1.10, *P* = 0.25; and *RR* = 1.08, 95% *CI*: 0.98, 1.19, *P* = 0.1, respectively) (Fig. 3B).

1.7 Overall complication

Eleven studies [5, 6, 10, 12, 14, 15, 18–20, 23, 25] reported the overall complication. There was moderate heterogeneity (I^2 = 55%, P = 0.01) among the studies. Using the random-effects model, the combined RR was 0.83, 95%CI (0.68,1.01), P = 0.27, with no statistically significant difference. After sensitivity analysis, the meta-analysis results show reversal changes. When studies by McMillan et al. [19] was sequentially eliminated, the heterogeneity was significantly reduced (I^2 = 33%, *P* = 0.14). The combined RR of the random effect model was 0.78, 95%*CI* (0.64,0.95), *P* = 0.01, and there was statistically significant difference. Subgroup analysis showed that, in the retrospective, prospective and PSM cohort study, there was no statistically significant difference between the RPD group and OPD group (Fig. 3C).

1.8 Bile leakage rate

Six studies [6, 12, 13, 17, 18, 22] reported the bile leakage rate. There was a low degree of heterogeneity (I^2 = 0%, P = 0.6) among the studies. Using a fixed-effects model, the combined *RR* was 0.99, 95%*CI* (0.54, 1.83), *P* = 0.98. There was no statistically significant difference between the RPD and OPD groups. Subgroup analysis showed that there was no significant difference in bile leakage rate between the RPD group and OPD group in the prospective and retrospective cohort studies. (*Appendix file 4A*)

1.9 Incidence of delayed gastric emptying

Nine studies [2, 4–7, 9, 10, 15, 18] reported the incidence of DGE. There was a low degree of heterogeneity (I^2 = 0%, P = 0.46) among the studies. Using the fixed-effects model, the combined RR was 0.98, 95% CI: 0.60, 1.03, P = 0.08), and the difference was not statistically significant. Subgroup analysis showed that there was no significant difference in the incidence of DGE between the RPD group and OPD group for prospective or PSM studies (*RR* = 1.07, 95% *CI*: 0.49,2.37, *P* = 0.86; and *RR* = 0.72, 95% CI: 0.31, 1.65, *P* = 0.44, respectively). However, DGE in the RPD group was significantly lower than that in the OPD group among the eight prospective cohort studies. (*Appendix file 4B*)

2.0 Severe complication

Six studies [10, 13, 14, 19, 20, 23] reported the severe complication. There was a low degree of heterogeneity (I^2 = 0%, P = 0.89) among the studies. Using the fixed-effects model, the combined *RR* was 0.98, 95%*CI* (0.71,1.36), *P* = 0.91, with no statistically significant difference. After sensitivity analysis, the meta-analysis showed no reversal changes. Subgroup analysis showed that there was no significant difference between the RPD group and OPD group in either prospective, retrospective or PSM cohort studies. (*Appendix file 4C*)

2.1 Incidence of clinical PF

Eight studies [7, 10, 12–15, 18, 19, 22] reported the incidence of clinical PF. There was moderate heterogeneity (I^2 = 58%, P = 0.58) among the studies. Using a fixed-effects model, the combined *RR* was 0.54, 95%*CI* (0.41, 0.70), *P* < 0.0001). Subgroup analysis showed that the incidence of PF in the RPD group was lower than that in the OPD group in prospective, retrospective and PSM cohort studies (*RR* = 0.61, 95%*CI* (0.36, 1.03), P = 0.06; *RR* = 0.61, 95%*CI* (0.36, 1.03), *P* = 0.06; and *RR* = 0.61, 95%*CI* (0.36, 1.03), *P* = 0.06; respectively). (Figs. 4A)

2.2 Wound infection rate

Eight studies [2, 6, 8, 12, 17, 18, 22, 23] reported the number of wound infection rate. There was moderate heterogeneity (I^2 = 0%, P = 0.65) among the studies. Using the fixed-effect model, the combined RR was 0.6, 95%*CI* (0.44,0.81), *P* = 0.001), with statistical significance. Subgroup analysis showed that in the both retrospective and prospective cohort study, the wound infection rate in the RPD group was significantly lower than that in the OPD group (*RR* = 0.67, 95%*CI*: 0.49–0.92, *P* = 0.01, *RR* = 0.28, 95%*CI*: 0.10–0.79, *P* = 0.02, respectively). (Figs. 4B)

2.3 Reoperation rate

Nine studies [6–8, 10, 12, 14, 17, 18, 22] reported the reoperation rate. There was a low degree of heterogeneity (I^2 = 0%, P = 0.69) among the studies. Using the fixed-effects model, the combined *RR* was 0.61, 95% *CI* (0.41, 0.91), *P* = 0.02), with statistical significance. Subgroup analysis showed that there was no significant difference in reoperation rate between the RPD group and the OPD group in the retrospective cohort studies

(*RR* = 0.58, 95% *CI* (0.25, 1.31), *P* = 0.19. In a prospective cohort study, the rate of reoperations in the RPD group was less than that in the OPD group, and the difference was significant (*RR* = 0.63, 95% *CI* (0.40, 0.98), *P* = 0.04). (Figs. 4C)

2.4 Incidence of POPF

Fifteen studies [2–7, 9–15, 17, 18] reported the incidence of POPF. There was moderate heterogeneity (I^2 = 0%, *P* = 0.75) among the studies. Using the fixed-effect model, the combined *RR* was 1.00, 95%*CI* (0.85,1.19), *P* = 0.97, and there was no statistically significant difference. Subgroup analysis showed that there was no significant difference in POPF between the RPD group and the OPD group in the prospective, retrospective and PSM studies, respectively (*Appendix file 5A*).

2.5 Postoperative mortality

Fourteen studies [2, 4–8, 10, 12, 15, 18, 19, 22, 23, 25] reported postoperative mortality. There was a low degree of heterogeneity (I^2 = 0%, P = 0.53) among the studies. Using the fixed-effects model, the combined *RR* was 0.82, 95%CI (0.62,1.10), P = 0.19, with no statistically significant difference. Subgroup analysis showed that there was no significant difference in postoperative mortality between the RPD group and OPD group in the prospective, retrospective and PSM cohort studies (*RR* = 0.73, 95%*CI* (0.3, 1.77), *P* = 0.48; *RR* = 0.84, 95%*CI* (0.62, 1.13), *P* = 0.25; *RR* = 1.01, 95%*CI*(0.69,1.47), *P* = 0.97, respectively) (*Appendix file 5B*).

2.6 Sensitivity analysis and bias risk assessment

Sensitivity analysis was carried out in each meta-analysis. The heterogeneity of operation time, estimated blood loss, intraoperative blood transfusion, lymph node dissection, and hospital day was large. After the relevant literature was removed, the heterogeneity was significantly reduced, but the results were not reversed. After the relevant literature was removed, the heterogeneity of overall complication is reduced, but the result reversed. The sensitivity analysis showed that other results were not reversed after sequential removal of each study. The funnel plots of the publications were found to be symmetrical, which suggested no publication bias. No publication bias was detected by Begg's test and Egger's test, except for the hospital day in the Egger's test (*Appendix file 3*).

Discussion

Pancreaticoduodenectomy was first reported by Whipple et al. in 1935 [27] Traditional pancreaticoduodenectomy is considered to be the most complicated operation in abdominal surgery because it involves multiple organs and complex reconstruction of the pancreatic digestive tract. At present, traditional open surgery remains the main method used. With the development of computer science and technology, a robotic (Da Vinci) surgical system has been introduced into the general surgery field, including pancreatic surgery, and has become one of the most promising surgical techniques. However, the safety and effectiveness of this new technology have not been fully determined. Compared with OPD, robotic surgery is more dependent on surgical instruments and equipment. At present, the Da Vinci surgical robot is the only technical platform used for RPD, and the medical units that have a Da Vinci surgical robot are typically the most advanced hospitals in a region. Therefore, the equipment is homogeneous across regions, making studies comparable. Therefore, we reviewed the existing literature, conducted this meta-analysis, and evaluated the current role of robotics and open surgery in pancreatic disease.

The results of this meta-analysis showed that RPD was significantly better than open surgery in the estimated blood loss, wound infection rate, reoperation rate, postoperative hospital stay, transfusion, overall complication and clinical PF. Additionally, no significantly different were found in the lymph node dissection, R0 rate of cutting edge, bile leakage rate, delayed gastric emptying, postoperative mortality, FOPF, severe complication. In terms of operation time, open surgery was better than robot surgery.

Four previous meta-analyses [28–31] discussed the safety and effectiveness of robot technology in pancreaticoduodenal surgery and concluded that pancreaticoduodenectomy is a safe and feasible alternative to open surgery. However, these meta-analyses also have some limitations. One of the limitations is that their meta-analysis included all the published literature at that time, but the data of many literatures came from the same institution, and there may be overlap. This study provides a comprehensive and up-to-date meta-analysis, in which not only new institutions are included, but also the most recent studies with the largest sample size and highest quality from previous institutions are selected. Up to now, randomized controlled trials (RCTs) were still lack; however, it is difficult to conduct a prospective, randomized study because of ethical issues and patients' concerns for malignant tumors. It has been pointed out that the meta-analysis of carefully designed non-randomized comparative studies of surgery may be as accurate as that of RCTs. [32] And we used comparative meta-analysis, which will be better accepted as a supplementary tool for qualitative review in medical literature [33].

Postoperative complications of pancreaticoduodenectomy are some of the most difficult problems for surgeons. Postoperative complications after pancreaticoduodenectomy occur in 40–50% of patients [34]. POPF is widely considered the most common and most dangerous complication after pancreatectomy, which is the most important factor in death due to pancreaticoduodenectomy. Whether via a new material or new surgical technique, reducing pancreatic fistula has become the focus of surgeons. The results of this meta-analysis showed that there was no significant difference between the RPD group and the OPD group in terms of POPF, while for clinical PF, the incidence in the RPD group decreased by 47% (95%CI: 29%~60%), which was statistically significant. Clinical pancreatic leakage, also known as BC grade pancreatic leakage, requires clinical intervention; hence, the reduction of RPD will undoubtedly reduce the occurrence and development of a series of other problems. As in this meta-analysis, overall complication is also reduced.

This meta-analysis concluded that the estimated blood loss, intraoperative transfusion, and the length of stay of the RPD patients were reduced compared to those of OPD patients, but the operation time was longer for RPD than for OPD. However, there was a high degree of heterogeneity between the studies in the terms. Although the random-effects model is used to combine the effect amount, the high degree of heterogeneity will greatly weaken the interpretation of the results. The most likely reason for the marked heterogeneity is that many studies are still in the initial stage of the learning curve. In the prospective database collection study, there was no significant difference in operative time and postoperative hospital stay between the RPD group and the OPD group, while in the retrospective cohort study, there was a significant difference; but EBL's situation was the opposite. Different types of database studies were included, which may have introduced a bias in these outcome indicators. Thus, there is a need to verify this further by better-designed, high-quality RCTs.

R0 resection and lymph node dissection are two important prognostic factors in patients with pancreaticoduodenectomy [35]. The survival rate can be improved by increasing the number of lymph node dissections, clarifying lymph node metastasis, and guiding postoperative treatment [36, 37]. This meta-analysis showed that the R0 resection rate and lymph node dissection of robotic surgery were not significant different from that of open surgery, which was consistent with the previous meta-analyses by Podda et al. [29], but Zhao et al. [31] and Yan et al [30]. Nevertheless, they may have partially overlapping patients, which may lead to bias. Long-term survival and tumor recurrence rates were not evaluated due to incomplete data. Therefore, it is difficult to make a reliable conclusion regarding tumor safety.

With the development of neoadjuvant chemotherapy, the current treatment strategy for pancreaticoduodenal cancer is a multidisciplinary comprehensive treatment with surgery at the core. The fibrogenic response and cytotoxicity caused by neoadjuvant chemotherapy leads to the loss of a normal tissue plane, which brings great challenges to all surgeries. Whether robotic surgery can overcome the new problems caused by new adjuvant therapy due to its unique advantages remains unclear. Some of the studies included in this meta-analysis, such as those by Baimas-George et al.[2], Cai et al.[7], Ielpo et al.[12],Marino et al.[18], Mejia et al.[20], reported the number of people who had received neoadjuvant therapy in the RPD and OPD groups; however, without a separate subgroup analysis, it was impossible to obtain the RPD and OPD effect comparison after receiving neoadjuvant therapy. In future, the safety and effectiveness of using robots in pancreaticoduodenectomy after neoadjuvant chemotherapy, compared with open surgery, should be further explored.

Conclusions

This meta-analysis showed that RPD is superior to OPD in terms of the rate of R0 at the cutting edge, the rate of infection at the wound site, the rate of reoperation, the length of stay after operation, the number of blood transfusions required during operation, and the rate of clinical pancreatic leakage; however, the operation time is longer than that of open surgery. Robot-assisted surgery is a safe and feasible alternative to OPD with regard to short outcomes. This needs to be further verified by high-quality clinical trials.

Limitations

Most of the studies included in this meta-analysis were retrospective, and there was, consequently, a risk of selection bias. In addition, RPD is a complex process and is still in its infancy; therefore, the number of cases in each study is small, and some studies reported on data obtained during the learning curve stage of these processes.

Declarations

Availability of Data and Materials

All the data comes from databases. The author has sorted out all the data and attached to the attachment at the end of the article.

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Ethics approval and consent

Ethical approval was not necessary, as this study was a “Systematic Review and Meta-analysis.” There are no individual person's data and presentations of case reports involved in this article.

Consent for publication

Consent for publication was not necessary, as this study was a “Systematic Review and Meta-analysis.” There are no any individual person’s data in any form (including individual details, images or videos) in this article.

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Figures

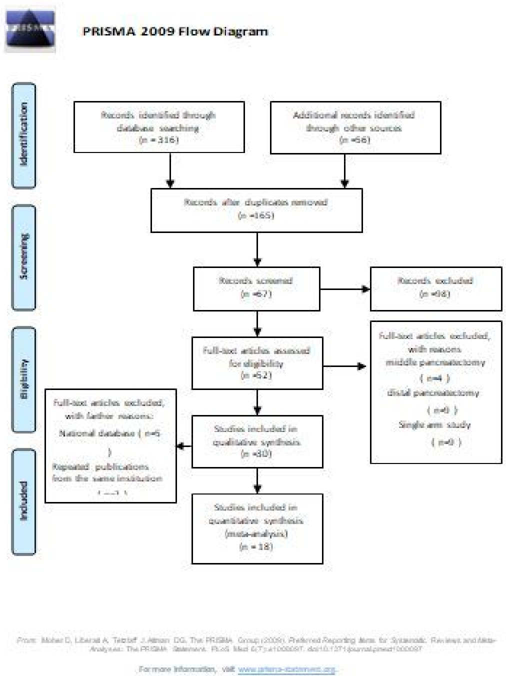

Figure 1

Literature search process (PRISMA 2009 flow diagram of literature screening)

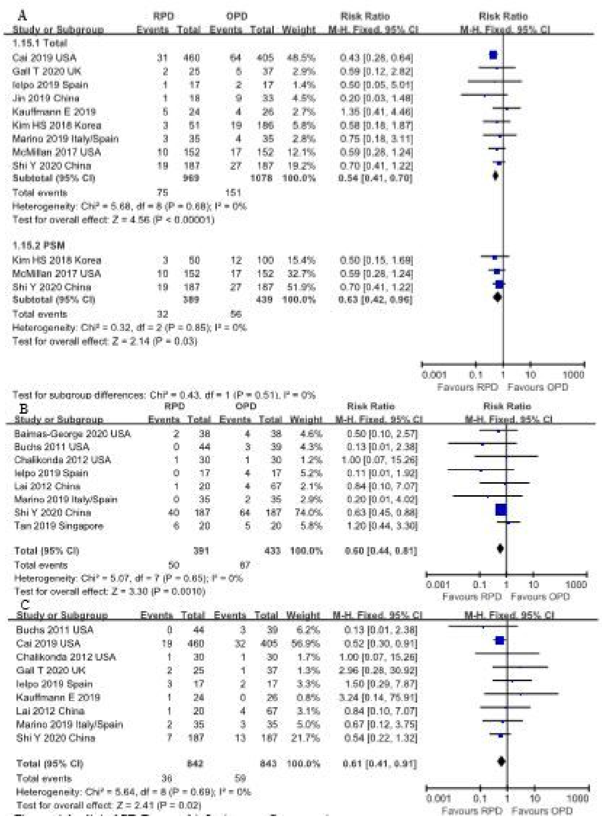

Figure 2

A. operation time B. estimated blood loss C. transfusion D. hospital stay

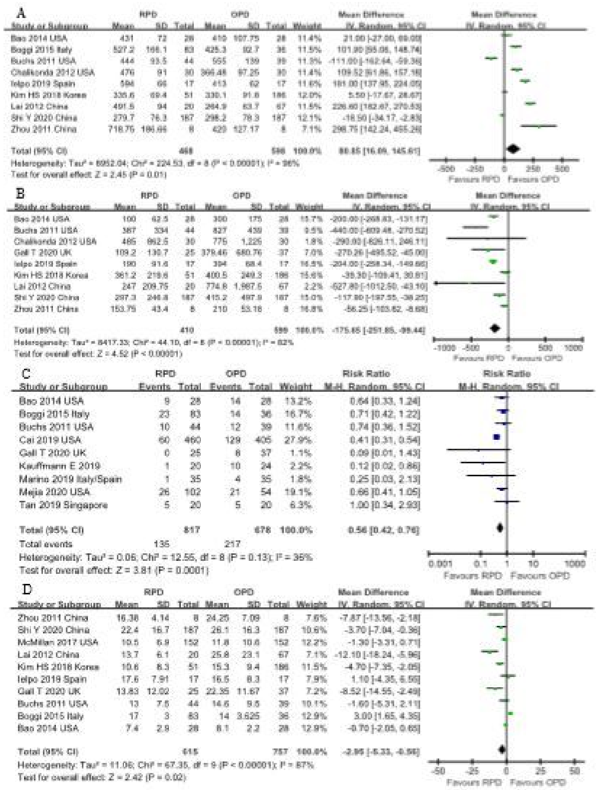

Figure 3

A. lymph node dissection B. R0 rate C. overall complication

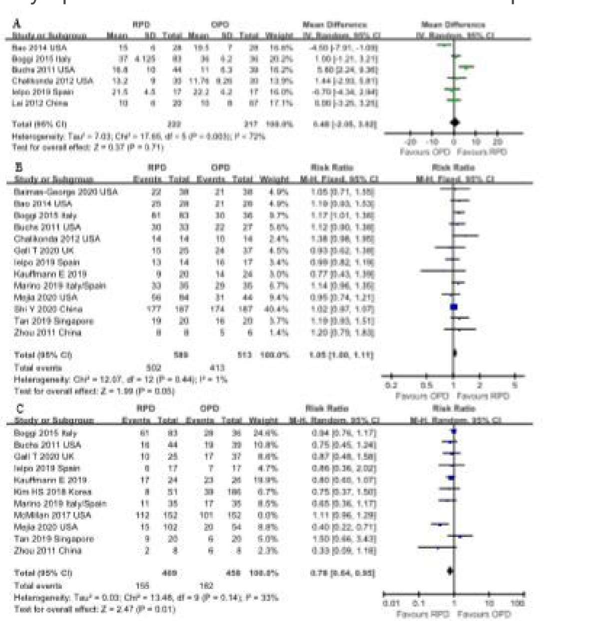

Figure 4

A. clinical PF B. wound infection rate C. reoperation rate

Supplementary Files

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- Appendixfile3.docx
- Appendixfile2R0.pdf
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