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Up-to-date comparison of robotic-assisted versus open distal pancreatectomy

A PRISMA-compliant meta-analysis

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Abstract

Background: Although robot-assisted distal pancreatectomy (RADP) has been successfully performed since 2003, its advantages over open distal pancreatectomy (ODP) are still uncertain. The objective of this meta-analysis is to compare the clinical and oncologic safety and efficacy of RADP vs ODP.

Methods: Multiple databases (PubMed, Medline, EMBASE, Web of Science, and Cochrane Library) were searched to identify studies that compare the outcomes of RADP and ODP (up to February, 2020). Fixed and random effects models were applied according to different conditions.

Results: A total of 7 studies from high-volume robotic surgery centers comprising 2264 patients were included finally. Compared with ODP, RADP was associated with lower estimated blood loss, lower blood transfusion rate, lower postoperative mortality rate, and shorter length of hospital stay. No significant difference was observed in operating time, the number of lymph nodes harvested, positive margin rate, spleen preservation rate, rate of severe morbidity, incidence of postoperative pancreatic fistula, and severe postoperative pancreatic fistula (grade B and C) between the 2 groups.

Conclusions: With regard to perioperative outcomes, RADP is a safe and feasible alternative to ODP in centers with expertise in robotic surgery. However, the evidence is limited and more randomized controlled trials are needed to further clearly define this role.

Abbreviations: CIs = confidence intervals, LDP = laparoscopic distal pancreatectomy, ODP = open distal pancreatectomy, ORs = odds ratios, PPF = postoperative pancreatic fistula, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RADP = robot-assisted distal pancreatectomy, WMD = weighted mean difference.

Keywords: complication, distal pancreatectomy, open surgery, Robot-assisted surgery

1. Introduction

Although pancreatectomy has a history of more than 80 years, it remains the most challenging abdominal surgery with relatively high morbidity and mortality.[1–5] Open distal pancreatectomy (ODP) is safe and feasible, but it could not completely avoid pain, infection, hernia, scarring, and other wound complications.

Laparoscopic distal pancreatectomy (LDP) has been performed for more than 30 years since the 1990s and has been demonstrated as safe and feasible,[6,7] but it still has the intrinsic disadvantages of conventional laparoscopy, including instrument motion, 2-dimensional imaging, poor surgeon ergonomics, and long learning curve. In 2000, the Da Vinci system was approved by the Food and Drug Administration. In 2003, Melvin et al reported the first case

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Core tip: Until now, no consensus exists on whether open or robotic-assisted distal pancreatectomy is more beneficial to the patient. This work is the latest meta-analysis to compare open and robotic-assisted distal pancreatectomy. We found that robotic-assisted distal pancreatectomy was associated with lower estimated blood loss, lower blood transfusion rate, lower postoperative mortality rate, and shorter length of hospital stay compared with open distal pancreatectomy. No significant difference was found in operating time, the number of harvested lymph nodes, positive margin rate, spleen preservation rate, rate of severe morbidity, and incidence of postoperative pancreatic fistula between the two groups.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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of robot-assisted distal pancreatectomy (RADP).[8] Then, Giulianotti et al published his case series that proved the feasibility of robotic pancreatectomy, including 8 robot-assisted pancreaticoduodenectomy and 5 RADP.[9] Since then, several studies[2,10,11] have evaluated the perioperative outcomes of RADP and LDP. Regarding the laparoscopic approach, robotic surgery is an advanced minimally invasive surgery technique and has several benefits, such as enhanced 3-dimensional vision, EndoWrist instruments with a greater range of motion, and short learning curve.

Currently, several studies[2–5,12,13] have compared robotic assisted pancreatectomy with open pancreatectomy, and the former showed potential advantages in terms of intraoperative blood loss, mortality, morbidity, and length of hospital stay. However, all these reports are single-center, non-randomized, controlled studies and did not evaluate the feasibility, safety, and efficacy of RADP compared with ODP. We conducted this meta-analysis to perform a comprehensive evaluation of the safety and efficacy of RADP versus ODP.

2. Methods

This study was conducted in accordance with the framework recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Supplementary PRISMA checklist http://links.lww.com/MD/E373). The design does not require ethical approval because no patient was involved.

2.1. Literature search and selection

A systematic and comprehensive literature search of online databases including the Cochrane Library, Embase, PubMed, Web of Science, and Medline databases published until February 2020 was performed. The following search strategies were employed: (robot* OR "da Vinci surgical system" OR Davinci) AND pancrea*. No other search limits were applied.

2.2. Inclusion and exclusion criteria

All articles were screened by 2 reviewers (Heng Zou and Zhongtao Liu). The inclusion criteria were

1. comparative studies between RADP and ODP,
2. studies reporting at least 1 outcome of interest, and
3. the literature is in English.

Studies would be excluded if they were

1. unoriginal articles or low-quality studies;
2. case reports, expert opinions, reviews, and abstracts; and
3. focal data could not be extracted.

2.3. Quality assessment and data extraction

This procedure was performed independently by two investigators (Heng Zou and Zhongtao Liu), and conflicts were adjudicated by a third investigator (Wenhao Chen). We used the Newcastle–Ottawa Scale to assess the quality of studies. Studies with scores ≥6 were considered to be qualified. The following information was extracted: baseline characteristics of the patient (age, body mass index, gender, and final pathology), intraoperative information (operative time, estimated blood loss, blood transfusion rate, spleen preservation, number of lymph nodes harvested, and rate of R0 resection), and postoperative outcomes (morbidity, postoperative pancreatic fistula [PPF], incidence of severe PPF (grade B and C), length of hospital stay, and 90-day mortality). The R0 resection indicated that no evidence of malignancy was identified at any of the resection margins, and the R1 resection was defined as malignancy that infiltrated at least one of the resection margins on the permanent section. Short-term complications, which were stratified by the Clavien–Dindo classification of surgical complications, indicated morbidities within 90 postoperative days.[14] Major postoperative morbidities were defined and graded using the criteria recommended by the International Study Group of Pancreatic Surgery (ISGPS), including PPF.[15].

2.4. Statistical analysis

Review Manager 5.3 (Cochrane Collaboration, Oxford, England) was used for all statistical analysis. Dichotomous and continuous variables were estimated on the basis of odds ratios (ORs) and the weighted mean difference (WMD) with 95% confidence intervals (95% CIs). The I^2 statistics quantified the heterogeneity. If the I^2 statistic was higher than 50%, random-effects analysis would be performed. Otherwise, the fixed effect model was used. Statistical significance was taken as two-sided ($P < .05$). Publication bias was not examined by a funnel plot as the number of included studies was less than 10.

3. Results

3.1. Study and patient characteristics

The first report of RADP was published in 2003.[8] According to our searching strategy, 1117 studies were published until February 2020. After screening titles, 934 records were excluded. Titles, abstracts, and full text of all articles were assessed, and 7 articles[2–5,12,13,16] met the inclusion criteria, including 2264 patients (515 RADP and 1749 ODP). Our selection protocol is shown in a PRISMA flow diagram chart (Fig. 1). Three studies[2–4] were prospective, whereas 4 other studies were retrospective.[5,12,13,16]Table 1 presents the characteristics of the selected studies and patients. The 2 groups were basically similar in terms of age, gender, body mass index, and malignancy rate.

3.2. Meta-analysis of RADP vs ODP

3.2.1. *Intraoperative outcomes and operative times.* All studies[2–5,12,13,16] reported the operative times. There was no difference observed in the operative times between the 2 groups. (WMD = 12.95; 95% CI = –32.51, 58.41; P = .58, Fig. 2A).

3.2.2. *Estimated blood loss.* Five studies[2,3,5,13,16] reported blood loss in the 2 groups. The mean estimated blood loss of the RADP group was 246.95 mL less than that of the ODP group. This difference was statistically significant (WMD = −246.95; 95% CI = −300.83, −193.07; $P < .00001$, Fig. 2B).

3.2.3. *Blood transfusion rate.* Only 3 studies[2,5,12] reported the blood transfusion rate. Analysis of the pooled data revealed that the blood transfusion rate differed significantly between the groups. The rate was lower in the RADP than in the ODP group (OR = 0.25; 95% CI = 0.15, 0.44; $P < .000001$, Fig. 2C).

3.2.4. *Spleen preservation rate.* Six studies[2–5,12,13] in this review had reported spleen preservation rate. Meta-analysis showed no statistically significant difference between the RADP and ODP groups (OR = 1.97; 95% CI = 0.74, 5.24; P = .17, Fig. 2D).

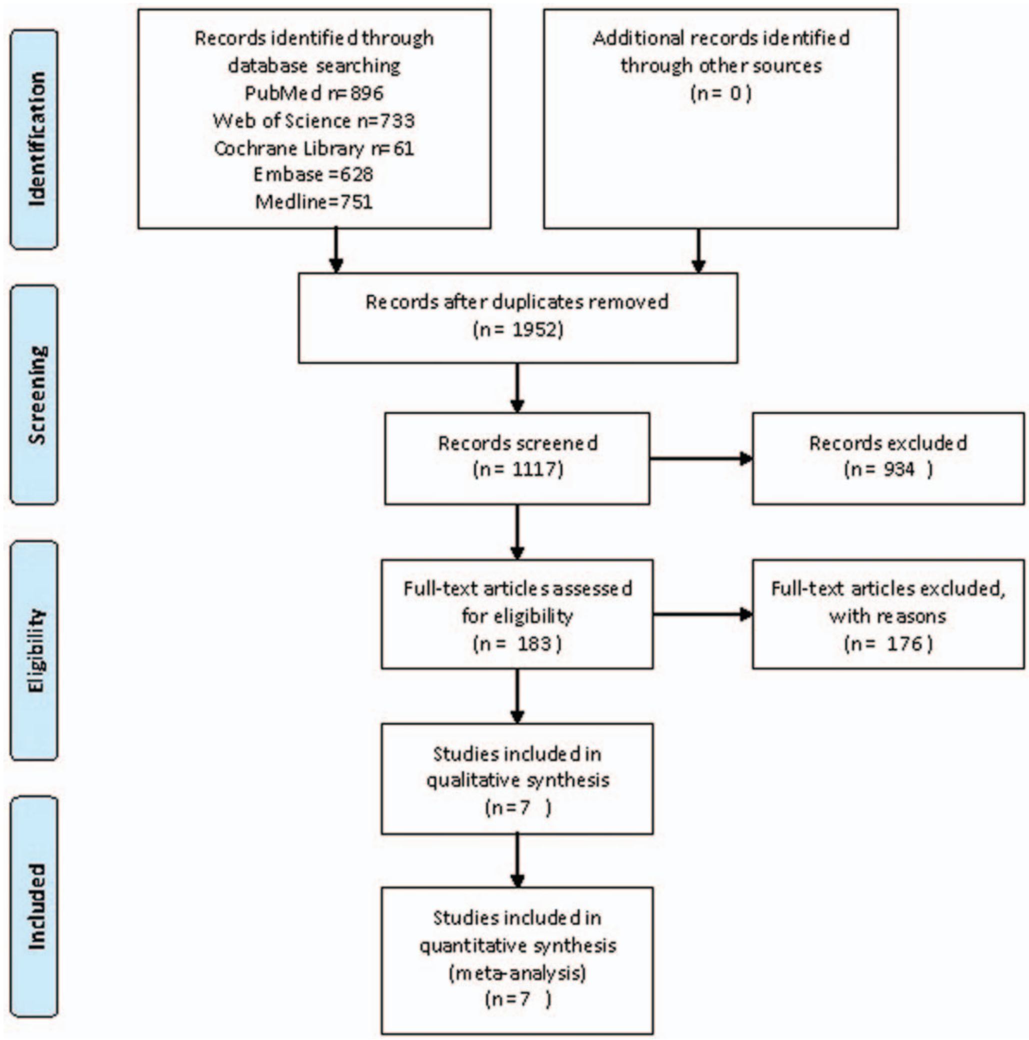

Figure 1. Flow diagram for robot-assisted distal pancreatectomy vs open distal pancreatectomy.

3.2.5. Postoperative outcomes. Major Morbidity (Clavien–Dindo ≥3)

Six studies[2–5,13,16] reported major morbidity. The major morbidity rate was 15.2% (48/315) in the RADP group and 23.3% (193/828) in the ODP group. However, there was no statistic difference (OR=0.73; 95% CI=0.29, 1.85; P=.50, Fig. 3A).

3.2.6. Incidence of PPF. All 7 studies[2–5,12,13,16] reported the incidence rates of PPF. The PPF rate was 26.7% (137/515) for the RADP group and 16.5% (288/1749) for the ODP group. Meta-analysis indicated no significant difference between the 2 groups (OR=1.19; 95% CI=0.90, 1.57; P=.22, Fig. 3B).

3.2.7. Incidence of severe PPF (grade B and C). Five studies[2–5,16] reported the incidence rates of severe PPF (grade B and C). The PPF (grade B and C) rate was 13.8% (41/298) for the RADP group and 11.4% (92/806) for the ODP group. There was no significant difference between the 2 groups (OR=1.19; 95% CI=0.90, 1.57; P=.22, Fig. 3C).

Table 1

Characteristics of the studies and patients reporting the comparison of RADP vs ODP included for meta-analysis.

Author	Country	Study design	Surgery type	Number	Age(y) (R/O)	Male (%) (R/O)	BMI (kg/m^2) (R/O)	Malignant (%) (R/O)
Waters 2010	USA	Retrospective	RADP/ODP	17/22	64.0/59.0 P=.08	35.0/45.0 P=.500	NR	0/50.0 P=NS
Duran 2014	Spain	Retrospective	RADP/ODP	16/13	61.0/63.8 P=NS	56.0/47.0 P=NS	NR	75.0/77.0 P=NS
Lee 2014	USA	Prospective	RADP/ODP	37/637	58.0/63.0 P<.05	27.0/45.0 P=.1	28.4/28.7 P=.88	11/39 P<.05
Xourafas 2017	USA	Retrospective	RADP/ODP	200/921	62.0/61 P=.8577	41.0/44.0 P=.1394	28.8/27.1 P<.0001	54.0/54.0 P=.3243
Magge 2018	USA	Retrospective	RADP/ODP	196/85	62.7/60.6 P=.41	46/45 P=.404	29.7/28.1 P=.123	78/68 P=.005
Rodriguez 2018	France	Prospective	RADP/ODP	21/43	53.0/65.0 P=.05	28.6/51.2 P=.21	25/24.7 P=.1	61.9/79.1 P=.14
Ielpo 2018	Spain	Prospective	RADP/ODP	28/28	59.7/62.5 P>.5	57.1/53.6 P>.5	24.1/23.4 P>.5	53.6/60.7 P>.5

NR=No reported, NS=Non significant (P>.05), R=Robot-assisted distal pancreatectomy, O=Open distal pancreatectomy, ODP = open distal pancreatectomy, RADP = robot-assisted distal pancreatectomy.

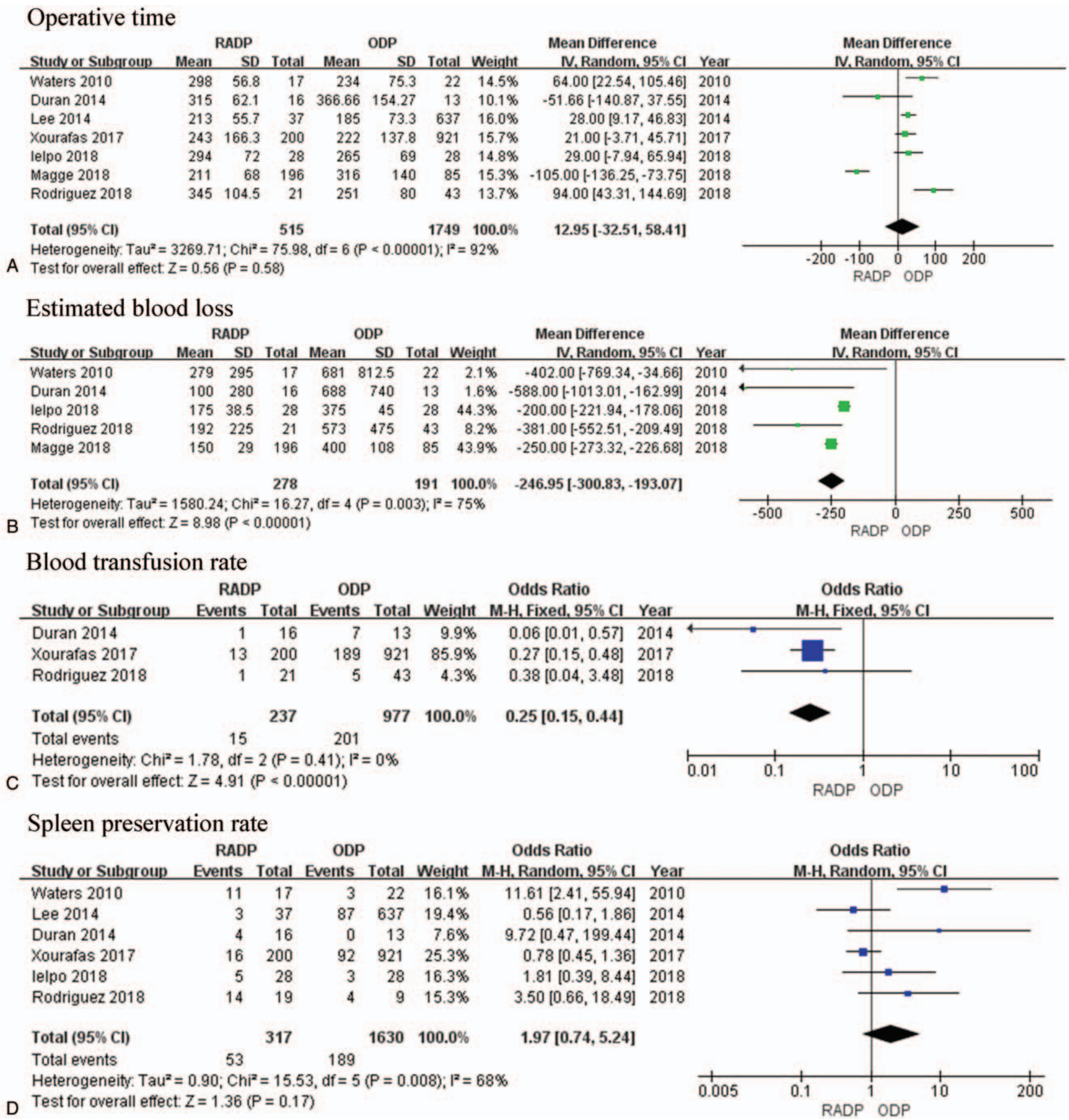

Figure 2. Pooled meta-analysis for Intraoperative outcomes of robot-assisted distal pancreatectomy vs open distal pancreatectomy. A: Operative time; B: Estimated blood loss; C: Blood transfusion rate; D: Spleen preservation rate.

3.2.8. Length of hospital stay. All studies[2–5,12,13,16] reported the length of hospital stay. Meta-analysis showed that RAPD had a significantly shorter length of hospital stay than OPD (WMD = −2.42; 95% CI = −2.99, −1.85; P < .00001, Fig. 3D).

3.2.9. Ninety-day postoperative mortality. All studies[2–5,12,13,16] reported the 90-day postoperative mortality. A total of 24 deaths occurred in the ODP group (1.4%) vs only 1 death in the RADP group (0.2%). Analysis of the pooled data revealed that the postoperative mortality rate in the RADP group was significantly lower than that in the ODP group (OR = 0.29; 95% CI = 0.10, 0.89; P = .03, Fig. 3E).

3.3. Oncological outcomes

3.3.1. Positive margin rate. All 7 studies[2–5,12,13,16] reported the proportion of malignant tumors (Table 1). Malignant histopathologic diagnoses included adenocarcinoma, neuroendocrine tumor, and pseudopapillary solid tumor. Benign diagnoses included intraductal papillary mucinous neoplasm, pancreatitis, and pancreatic cystadenoma. The data about the positive margin for 361 malignant cases (41 in RADP and 320 in ODP) were extracted from 5 studies.[2–5,13] No positive margin case was observed in the in RADP group (0%), but 34 cases were found in the ODP group (10.6%). There was no statistic difference between 2 groups. (OR = 0.70; 95% CI = 0.08, 5.95; P = .74, Fig. 4A).

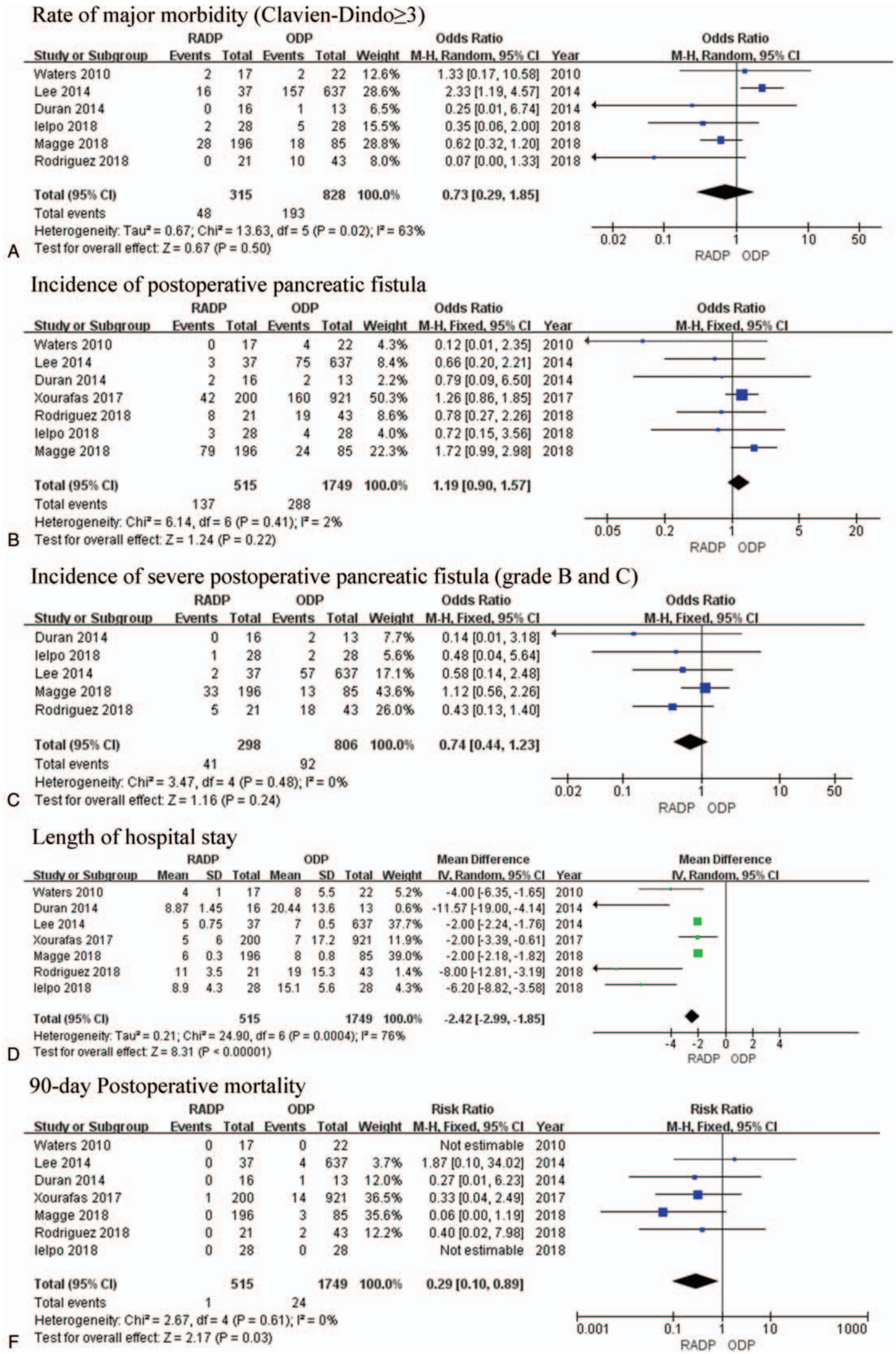

Figure 3. Pooled meta-analysis for Postoperative outcomes of robot-assisted distal pancreatectomy vs open distal pancreatectomy A: Rate of major morbidity; B: Incidence of pancreatic fistula; D: Incidence of severe postoperative pancreatic fistula (grade B and C); E: Length of hospital stay; F: 90-day postoperative mortality

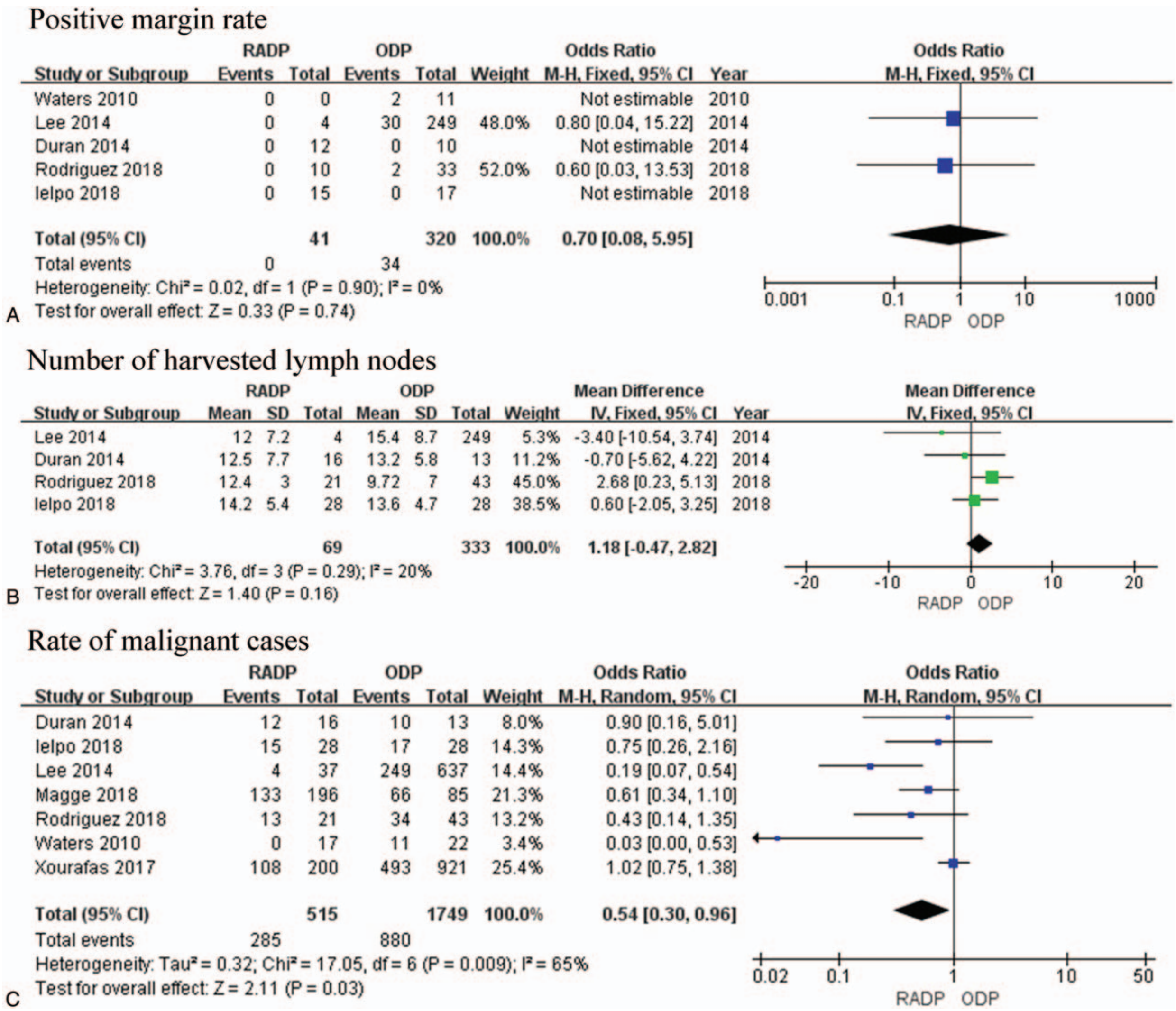

Figure 4. Pooled meta-analysis for oncological outcomes of robot-assisted distal pancreatectomy vs open distal pancreatectomy. A: Positive margin rate; B: Number of harvested lymph nodes; C: Rate of malignant cases.

3.3.2. Number of lymph nodes harvested. Four of the 7 studies[2–5] reported the numbers of lymph nodes harvested for the 2 groups. The highest mean values of lymph nodes harvested for the RADP and ODP groups were reported by Lelpo et al (14.2 ± 5.4) and Lee et al (15.4 ± 8.7), respectively. Meta-analysis indicated no statistically significant difference between the 2 groups (OR = 1.18; 95% CI = −0.47, 2.82; P = .16, Fig. 4B).

3.3.3. Rate of malignant cases. All studies[2–5,12,13,16] reported the rate of malignant cases. Meta-analysis showed that RAPD had a significantly higher proportion malignant cases than OPD (OR = 0.54; 95% CI = 0.30, 0.96; P = .03, Fig. 4C).

4. Discussion

As a minimally invasive technique, robotic surgery has natural advantages that could prevent disproportionately long abdominal incisions, reduce tissue injury, and minimize the rate of incision infection[17]; however, such approach also has the inherent disadvantage of being expensive.[18] Nevertheless, the feasibility, safety, and oncological outcomes of RADP compared with ODP have not been fully determined due to the lack of randomized controlled trials.

According to the results of our meta-analysis, there was no difference in the operation time between 2 groups, which was not in accordance with previous reports.[19] Two reasons may explain this outcome. First, according to our experience and previous literature reports,[19] the docking time for the robotic system was approximately 30 minutes. Second, significant heterogeneity existed, as our results showed an I^2 value of 92%. Certainly, when starting a new technology, surgeons at different stages of the learning curve show different levels of surgical skills.[20,21]

Estimated blood loss and blood transfusion rate are 2 critical indicators for evaluating the success of RADP. This situation may due to the inherent advantages of the robot system, such as a 3-dimensional image, the muscle tremor filter, and the wrist-like movement of the effector instrument (with 7 degrees of freedom) that can enable precise surgery. However, this kind of precise operation was not observed in the surgery for spleen preservation. No significant difference of spleen preservation rate occurred between the 2 groups. The RADP outperformed the LDP in terms of spleen preservation,[22] but not the ODP.

Two article published in *New England Journal of Medicine* in November 2018 declared minimally invasive radical hysterectomy was associated with lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy among women with early-stage cervical cancer, which attracted public concerns about the influences on oncological outcomes of minimal invasive surgery.[23,24] Oncological outcomes including rate of R0 resection and number of lymph nodes harvested were also analyzed in this study. No R1 resection case was found in the RADP group, which confirmed the effectiveness of the RADP for patients with malignant tumors. Only three studies[2,4,13] reported 34 positive margin resection cases in the ODP group, but this difference was not significant. Our results are inconsistent with previous reports.[1,6] Van Hilst et al reported a significantly lower lymph node harvested with minimally invasive distal pancreatectomy than with ODP. Minimally invasive distal pancreatectomy is defined as LDP or RADP. All cases in this analysis involved RADP, which may explain the inconsistency. In our opinion, either robotic or open surgery is technical means. Only if we follow the principle of tumor-free technique, then we are able to achieve radical resection.

With respect to severe morbidity (Clavien–Dindo ≥3), Incidence of PPF and severe PPF (grade B and C), no significant statistical differences were observed between the 2 groups, thereby demonstrating the safety of the RADP. However, when analyzing the 90-day mortality, the RADP group was significantly lower than the ODP group. This outcome also differed from a previous report[25] by Zhao et al They concluded that the rate of overall complications were higher in the RADP group, but the postoperative mortality rate was similar between the 2 groups. Such difference may be due to the variations in the observation indicators and number of included cases. We focused on severe morbidity (Clavien–Dindo ≥3) instead of the rate of overall complications, and our work included more studies and more cases than other works.

Length of hospital stay plays an important role in the evaluation of a minimally invasive technique. Compared with the ODP group, the RADP group had shorter postoperative hospitalization in this meta-analysis and in previous reports.[6,10,26] Robot-assisted surgery meets the requirements of enhanced recovery after surgery.

This study has several limitations. First, no randomized controlled trial was included in this work. Therefore, selection and reporting bias were inevitable and our conclusions must be interpreted with caution. Second, long-term survival is the foremost consideration for malignant cases. However, follow-up investigations among all included studies were short. Finally, this meta-analysis can only elucidate the value of RADP on perioperative outcome.

5. Conclusion

In this meta-analysis, current evidence reveals that RADP is a feasible and safe alternative to ODP in centers with expertise in robotic surgery and has lower postoperative mortality and similar morbidity. RADP was superior to ODP in terms of estimated blood loss, lower blood transfusion rate, and shorter postoperative hospital stay. Overall, randomized clinical trials and long-term follow-up need to be conducted in future research.

Author contributions

Conceived and designed the experiments: Yu Wen and Jiangjiao Zhou.

Performed the experiments: Heng Zou, Wenhao Chen and Zhongtao Liu. Analyzed the data: Xiong Li and Zhuo Lv. Wrote the paper: Jiangjiao Zhou. Proofread and revised the manuscript: Yu Wen, Heng Zou and Li Xiong.

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