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META-ANALYSIS

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Comparison of Radical Antegrade Modular Pancreatosplenectomy with Standard Retrograde Pancreatosplenectomy for Left-Sided Pancreatic Cancer: A Meta-Analysis and Experience of a Single Center

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Background: Radical antegrade modular pancreatosplenectomy (RAMPS) has been reported as a modified surgical technique used to achieve better margin resection and to retrieve more lymph nodes compared with standard retrograde pancreatosplenectomy (SRPS).

Material/Methods: A systematic literature review was performed to identify studies published in PubMed, EmBase, and Web of Science. Hazard ratio (HR), risk ratio (RR), weighted mean difference (WMD), and their 95% confidence intervals (95% CIs) were used as effect measures. In addition, the clinical data of 27 patients in our center were collected and retrospectively analyzed.

Results: Seven studies containing 474 patients were finally enrolled in this meta-analysis. The pooled results showed that the RAMPS group had a better overall survival (OS) compared with the SRPS group (HR=0.65, 95% CI: 0.43–0.99, P=0.046; I^2=41.8%, P=0.143). Significantly more lymph nodes were harvested in the RAMPS group compared with in the SRPS group (WMD=4.74, 95% CI: 0.36–9.12, P=0.034). Recurrence rate (RR=0.8, 95% CI: 0.66–0.98, P=0.028) and blood loss (WMD=–153.19 ml, 95% CI: –303.95 to –2.42, P=0.046) were both significantly reduced in the RAMPS group. Retrospective analysis results showed that only significantly more harvested lymph nodes were noted in the RAMPS group compared with the SRPS group (7.55±0.91 *vs.* 2.81±0.73, P=0.001).

Conclusions: Our study suggests that RAMPS has better prognosis and surgical outcomes than SRPS for left-sided pancreatic cancer. Nevertheless, more high-quality clinical trials are required to validate the result.

MeSH Keywords: General Surgery • Meta-Analysis • Pancreatic Neoplasms • Prognosis

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/914540

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Background

Pancreatic cancer (PC) is one of the most lethal and aggressive cancers in the modern world with a median survival of 3-6 months and a 5-year survival rate less than 6% [1]. Left-sided PC is often asymptomatic and as a result is more commonly diagnosed at an advanced stage [2]. Surgical resection is considered as the only method to radically cure this type of cancer [3]. The first distal pancreatic resection was performed by Trendelenburg in 1882 and was then standardized by Mayo in 1913 [4]. Extensive studies have demonstrated that for patients with PC, R0 resection is essential for improving the long-term outcome [5,6]. Therefore, how to completely remove the tumor, reduce the recurrence rate without R0 resection and improve the posterior margin has always been a challenge for pancreatic surgeons [7,8]. In 2003, RAMPS was first established and performed by Strasberg as a novel technique for the treatment of left-sided PC, which could achieve a better negative posterior margin and harvest more lymph nodes [9]. However, few publications have compared RAMPS with conventional procedures with respect to surgical outcomes. Among these published studies, the results remain controversial.

Previous studies have identified several prognostic factors of left-sided PC, such as tumor size, resection margin, adjuvant chemotherapy, lymph node metastasis and invasion of splenic artery [10–13]. However, little is known about the short-term and long-term outcomes of patients with left-sided PC undergoing RAMPS.

In this study, we evaluate the prognosis and surgical outcomes of patients with left-sided PC undergoing RAMPS compared with SRPS through a systematic review and meta-analysis combined with a retrospective analysis using a database from our own center.

Material and Methods

Search strategy

A comprehensive literature search for relevant studies was systematically performed without time limitations in PubMed, EmBase, and Web of Science. The following search terms were used in various combinations to identify potentially related studies: “radical antegrade modular pancreatosplenectomy” or “RAMPS” and “Pancreatic Neoplasms”, “Pancreatic Neoplasm”, “Pancreas Neoplasms”, “Pancreas Neoplasm”, “Cancer of Pancreas”, “Pancreas Cancers”, “Pancreas Cancer”, “Pancreatic Cancer”, “Pancreatic Cancers” and “Cancer of the Pancreas”. Additional studies eligible were collected from the titles, abstracts, full texts, and reference lists of retrieved publications.

Eligibility criteria

Studies comparing RAMPS with SRPS with at least one outcome were included. The following studies were excluded: (i) abstracts, reviews, letters and case reports; (ii) studies that were noncomparative or not related to RAMPS procedure or PC; (iii) studies not reporting postoperative outcomes or HR and 95% CI; (iv) studies with duplicate data or repeat patients; and (v) studies lacking a consistent surgical approach.

Methodological quality assessment

Methodological quality of included studies was independently assessed by 2 authors (YW and HQ). Newcastle-Ottawa Scale (NOS) was applied to evaluate the quality of each included studies as only nonrandomized studies on this subject were expected. Included studies were ranked with a maximum of 9 points. The methodological quality contains ‘‘selection of patients’’, ‘‘comparability’’ and ‘‘outcome of study participants’’. Articles with an NOS score ≥6 were considered as high-quality studies [14].

Data extraction

The following data were extracted: first author, year of publication, country, general characteristics of population (sample size, gender and age), tumor stage, CA19-9 level, perioperative outcomes (blood loss, operative time, R0 resection and number of harvested lymph nodes) and postoperative outcomes (POPF, length of hospital stay, recurrence rate, HR and 95% CI for OS and DFS). Compared with HR generated from univariate analysis, HR from multivariate analysis was preferable. All data were extracted and cross-checked by 2 authors (ZH and SY Z). Discrepancies were resolved by comprehensive discussion and checked by a third reviewer (XM T).

Selection and characteristics of patients

From January to December 2015, 27 patients with resectable left-sided PC underwent distal pancreatectomy. Of these patients, 11 underwent RAMPS, and 16 received SRPS. The surgical approach was decided by the patient himself with full awareness of the difference between 2 procedures, and the surgery was performed by the same group of surgeons. Baseline data (age, sex, BMI, CA19-9 and CEA level), oncologic (R0 resection, tumor size and stage), and perioperative (operative time, blood loss and harvested lymph nodes) and postoperative outcomes (hospital stay, POPF, recurrence, DFS and OS) of these patients were collected and retrospectively reviewed. Patients who met the following criteria was collected and retrospectively analyzed: (i) diagnosed with left-sided pancreatic cancer; (ii) suggested to receive R0 surgery by MDT; and (iii) without distant metastasis. Exclusion criteria were as follows: (i) patients with

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preoperative chemotherapy or radiotherapy; (ii) distant metastasis or vascular invasion was observed during the operation; (iii) postoperative pathological examination revealed non-pancreatic ductal adenocarcinoma; and (iv) clinical data were missing. The follow-up was performed up to August 2018. The RAMPS procedure was previously described in detail [15].

Statistical analysis

Meta-analysis was performed according to the Cochrane guidelines for systematic reviews. The RR and HR were used as effect measures for categorical variables and WMD for continuous variables. All values were reported with their corresponding 95% CI. Cochran's Q test and I-squared statistic were used to evaluate the heterogeneity between the included studies. $P_{heterogeneity}$ <0.1 or I^2>50% indicates significant heterogeneity, and a random-effect model was applied [16]. Otherwise, the fixed-effect model was adopted. Subgroup and meta-regression analysis were performed to reveal and explain the heterogeneity of pooled analysis. Sensitivity analysis was performed by sequential omission of each individual study to test the stability of the result of meta-analysis. Publication bias was assessed by Begg's funnel plot [17]. Clinical data were calculated by t test for continuous variables and χ^2 analysis (or Fisher's exact test) for categorical variables. DFS and OS were analyzed using Kaplan-Meier curves. P<0.05 was considered statistically significant. All statistical analysis was performed using Stata software, version 12.0 (2011) (Stata Corp, College Station, TX, USA).

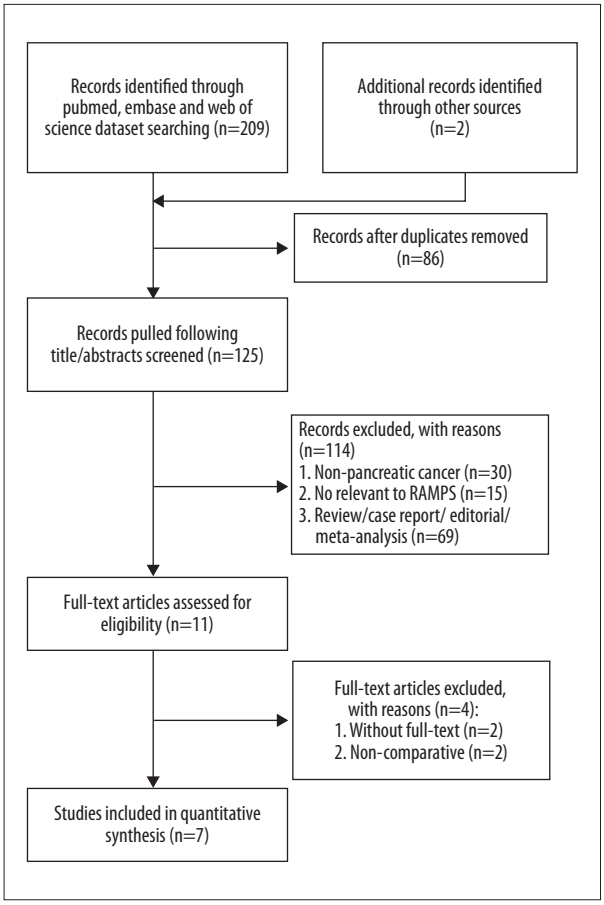

Figure 1. Flow diagram of the study selection process.

Results

Search results and characteristics of included studies

According to the search strategies mentioned above, a total of 209 studies were retrieved, and 2 additional eligible articles were obtained by manual screening. Seven studies comparing RAMPS with SRPS, including 168 patients undergoing RAMPS and 306 patients undergoing SRPS, were identified and ultimately enrolled in this meta-analysis [18–24]. The detailed process of selection is shown in Figure 1. The studies were conducted in 5 countries (China, Italy, Japan, Korea and USA). Three of them were prospective studies [20,22,23], and 4 were retrospective studies [18,19,21,24]. The outcomes contained both OS and DFS in 3 studies [18–20] and only OS in 2 articles [21,22]. The baseline characteristics of enrolled studies are summarized in Table 1. Perioperative and postoperative outcomes are shown in Table 2. The results of methodological quality assessment are listed in Table 3. Of all studies, 6 were of high quality [18,19,21–23], and 1 was of poor quality [20]. Detailed follow-up information was not found in all studies.

Effect of RAMPS over SRPS on DFS and OS

Five studies provided OS data [18–22], and 3 reported DFS data [18–20]. The pooled analysis showed that patients undergoing RAMPS had a better OS compared with patients undergoing SRPS (HR=0.65, 95% CI: 0.43–0.99, P=0.046) with low heterogeneity between studies (I^2=41.8%, P=0.143) (Figure 2A). However, no significant difference was observed in DFS (HR=0.99, 95% CI: 0.6–1.63, P=0.956) with no between-study heterogeneity (I^2=0.0%, P=0.804) (Figure 2B). The results suggested that RAMPS was associated with better patient prognosis.

Effect of RAMPS over SRPS on surgical outcomes

Seven studies provided perioperative and postoperative data. The pooled results indicated that the number of lymph nodes harvested in RAMPS was significantly increased compared with the SRPS group (WMD=4.74, 95% CI: 0.36–9.12, P=0.034; I^2=74%, P=0.004) (Figure 3A). Recurrence rate in the RAMPS group was significantly lower (RR=0.8, 95% CI: 0.66–0.98, P=0.028; I^2=0.0%, P=0.445) (Figure 3B) and blood loss in the RAMPS group was significantly less than that in

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Table 1. Characteristics of all studies included in the meta-analysis.

Reference	Year	Country	Group	Sample size	Age (year)	Gender (M/F)	Tumor size (cm)	Tumor stage	CA19-9 level (U/ml)	Study type	Endpoints
Abe [18]	2016	Japan	RAMPS	53	68.6±10.7	1.40/1	NA	I–III	136.4±291.0	R	OS/DFS
			SRPS	40	65.2±8.6	2.63/1		I–II	390.4±1157.1		
Kim [19]	2016	Korea	RAMPS	30	63.7±8.2	13/17	4.6±1.6	II	NA	R	OS/DFS
			SRPS	19	62.1±8.5	7/12	4.5±1.5	I–II			
Latorre [20]	2013	Italy	RAMPS	8	61	5/3	5.1±1.9	NA	NA	P	OS/DFS
			SRPS	17	60	11/6					
Lee [21]	2014	Korea	RAMPS	12	63.3±9.9	7/5	NA	NA	NA	R	OS
			SRPS	78	51.2±9.9	47/31					
Park [22]	2013	Korea	RAMPS	38	62.17 (40–75)	23/15	3.1 (2–8.0)	II–IV	18.2 (3.0–82.1)	P	OS
			SRPS	54	61.25 (37–79)	35/19	3.8 (1–11)	I–III	15.7 (4.4–148.5)		
Trottman [23]	2014	USA	RAMPS	6	NA	NA	NA	NA	NA	P	NA
			SRPS	20							
Xu [24]	2016	China	RAMPS	21	62±11	11/10	5 (4.3–6.6)	II–IV	70.2 (20.7–594.2)	R	NA
			SRPS	78	63±9	41/37	3.8 (3.0–5.0)	I–IV	158.7 (35.6–692.2)		

M/F – Male/Female; NA – not available; R – retrospective; P – prospective; OS – overall survival; DFS – disease-free survival.

Table 2. Clinicopathological features of included studies.

Reference	Group	Intraoperative blood loss (ml)	Operative time (min)	Harvested lymph node	Hospital stay (days)	R0 resection	POPF	Recurrence	HR (95%CI) for OS	HR (95%CI) for DFS
Abe [18]	RAMPS	485.4 ±63.3	267.3 ±11.5	28.4 ±11.6	35.7 ±19.6	48 (90.6%)	6 (11.3%)	32 (60.4%)	0.35 (0.13–0.95)	0.94 (0.51–1.73)
	SRPS	682.3 ±72.8	339.4 ±13.2	20.7 ±10.1	26.7 ±25.5	27 (67.5%)	6 (15.0%)	30 (75.0%)		
Kim [19]	RAMPS	300 ±220	277.8 ±55.6	21.5 ±8.3	6.4 ±4.3	22 (84.6%)	4 (13.3%)	8 (30.8%)	1.11 (0.28–4.37)	0.74 (0.16–3.45)
	SRPS	260 ±180	253.3 ±41.0	13.7 ±7.4	8.2 ±3.3	11 (64.7%)	2 (10.5%)	8 (47.1%)		
Latorre [20]	RAMPS	342	315	20.7 ±8.9	12.1	7 (87.5%)	1 (12.5%)	NA	1.26 (0.45–3.57)	1.32 (0.45–3.92)
	SRPS	369	265	16.2 ±4.2	9.9	15 (88.2%)	3 (17.6%)			
Lee [21]	RAMPS	445.8 ±346.1	324.3 ±154.2	10.5 ±7.1	12.3 ±6.8	5 (41.7%)	2 (16.7%)	5 (41.7%)	2.14 (0.47–9.65)	NA
	SRPS	669.5 ±776.1	270.1 ±140.4	13.8 ±11.1	22.4 ±21.6	49 (62.8%)	18 (23.1%)	58 (74.4%)		

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Table 2 continued. Clinicopathological features of included studies.

Reference	Group	Intraoperative blood loss (ml)	Operative time (min)	Harvested lymph node	Hospital stay (days)	R0 resection	POPF	Recurrence	HR (95%CI) for OS	HR (95%CI) for DFS
Park [22]	RAMPS	325 (50–3400)	210 (125–480)	14 (5–52)	11.5 (7–32)	34 (89.5%)	1 (2.6%)	25 (65.6%)	0.49 (0.27–0.9)	NA
	SRPS	400 (50–3300)	185 (80–390)	9 (1–36)	10.7 (6–42)	46 (85.2%)	6 (11.1%)	35 (64.8%)		
Trottman [23]	RAMPS	500.0 ±260.8	300.0 ±87.0	11.2 ±6.0	7.7 ±3.0	6 (100%)	0 (0.0%)	NA	NA	NA
	SRPS	581.3 ±559.2	295.3 ±83.8	4.3 ±5.4	6.9 ±1.4	19 (95%)	6 (30.0%)			
Xu [24]	RAMPS	400 (350–650)	235 (180–278)	NA	15 (13–23)	19 (90.5%)	13 (61.9%)	6 (33.3%)	NA	NA
	SRPS	225 (200–400)	180 (130–210)		12 (10–16)	71 (91.0%)	36 (46.2%)	31 (45.6%)		

NA – not available; POPF – postoperative pancreatic fistula; HR – hazard ratio; CI – confidence interval; OS – overall survival; DFS – disease-free survival.

Table 3. Methodological assessment.

Reference	Selection				Comparability	Outcome			Total points
	Representativeness	Selection	Ascertainment	Conflicted Interest		Assessment	FU length	Adequacy of FU	
Abe	•	•	•	○	••	•	•	○	7
Kim	•	•	•	○	••	•	•	○	7
Latorre	•	•	•	○	••	•	○	○	6
Lee	•	•	•	○	••	•	•	○	7
Park	•	•	•	○	••	•	•	○	7
Trottman	•	•	•	○	NA	•	○	○	4
Xu	•	•	•	○	••	•	•	○	7

• – low risk of bias; ○ – unclear or high risk of bias; Comparability contains a maximum of 2 points (••); NA – not available; FU – follow-up.

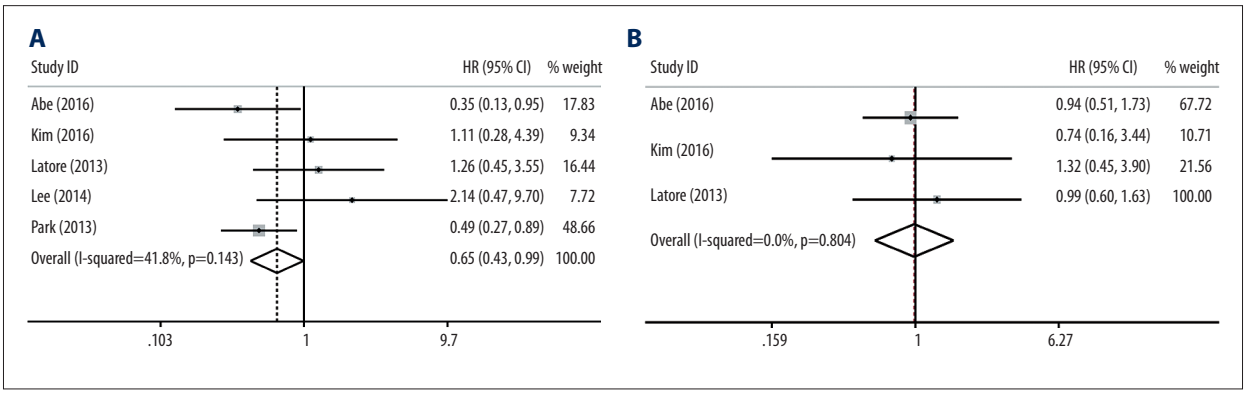

Figure 2. Forest plots of the prognosis of patients with left-sided PC. The association between RAMPS *vs.* SRPS and (**A**) OS and (**B**) DFS.

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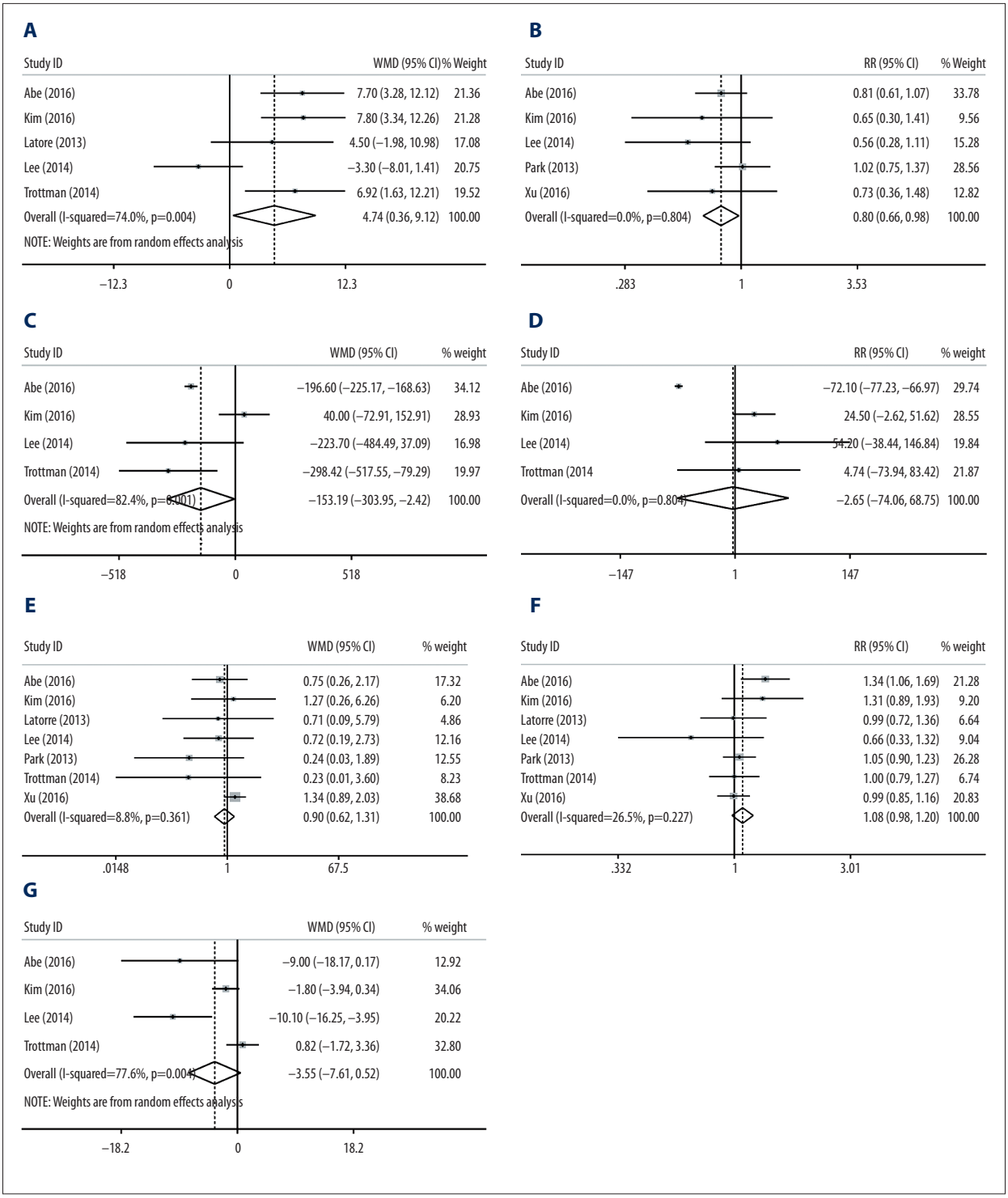

Figure 3. Forest plots of surgical and oncologic outcomes. (**A**) Harvested lymph nodes, (**B**) recurrence rate, (**C**) blood loss, (**D**) operative time, (**E**) POPF, (**F**) R0 resection rate and (**G**) hospital stay.

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Table 4. Summary of meta-analysis results.

Analysis	N	Reference	Random-effect model		Fixed-effect model		Heterogeneity	
			HR (95%CI)	P	HR (95%CI)	P	I^2	Ph
OS	5		0.652 (0.428–0.992)	0.046	0.738 (0.404–1.347)	0.322	41.8%	0.143
DFS	3		0.986 (0.596–1.630)	0.956	0.986 (0.596–1.630)	0.956	0.0%	0.804
Subgroup 1								
Year <2015	3		0.914 (0.379–2.206)	0.842	0.709 (0.434–1.160)	0.171	57.3%	0.096
Year ≥2015	2		0.563 (0.185–1.715)	0.312	0.520 (0.233–1.165)	0.112	43.8%	0.182
Subgroup 2								
Sample size <70	2		1.203 (0.526–2.751)	0.661	1.203 (0.526–2.751)	0.661	0.0%	0.885
Sample size ≥70	3		0.586 (0.265–1.296)	0.187	0.527 (0.324–0.858)	0.01	50.1%	0.135
Subgroup 3								
Prospective	2		0.713 (0.288–1.762)	0.463	0.652 (0.428–0.992)	0.074	58.1%	0.122
Retrospective	3		0.836 (0.280–2.498)	0.748	0.712 (0.350–1.449)	0.348	54.5%	0.111

N – number of studies; HR – hazard ratio; 95% CI – 95% confidence interval; Ph – p values of Q test for heterogeneity test; OS – overall survival; DFS – disease-free survival.

Table 5. Results of meta-regression for OS.

Variables	Coef.	Std. Err.	P value	Adj R-squared
Year	0.474	0.732	0.564	–64.29%
Sample size	–0.826	0.568	0.242	100.00%
Study type	0.119	0.741	0.883	–95.16%

Coef. – coefficient; Std. Err. – standard error; Adj. R-squared – proportion of between-study variance explained.

SRPS group (WMD=–153.19 ml, 95% CI: –303.95 to –2.42, P=0.046; I^2=82.4%, P=0.001) (Figure 3C). However, no significant differences between 2 groups were found regarding operative time (WMD=–2.65 min, 95% CI: –74.06–68.75, P=0.942; I^2=94.7%, P=0.000) (Figure 3D), POPF (RR=0.90, 95% CI: 0.62–1.31, P=0.577; I^2=8.8%, P=0.361) (Figure 3E), R0 resection rate (RR=1.08, 95% CI: 0.98–1.20, P=0.125; I^2=26.5%, P=0.227) (Figure 3F) and length of hospital stay (WMD=–3.55 days, 95% CI: –7.61–0.52, P=0.087; I^2=77.6%, P=0.004) (Figure 3G).

Subgroup and meta-regression analysis

To explore the source of heterogeneity of OS, subgroup and meta-regression analyses were performed. The 7 included studies were stratified according to publication year, sample size and study type. As shown in Table 4, heterogeneity the in subgroup remains significant, suggesting that these 3 variables cannot account for the heterogeneity. Meta-regression analysis indicated the same result, and the results are shown in Table 5.

Sensitivity analysis and publication bias

To evaluate the robustness of the results in this meta-analysis, we performed a sensitivity analysis excluding one study at a time. The results showed that no study could significantly affect the pooled result of meta-analysis, indicating the stability of our meta-analysis (Figure 4A). Begg's and Egger's test were applied to assess the potential publication bias. P<0.05 indicated the existence of publication bias. The results showed no significant bias in the overall analysis of OS (P_{BEGG}=0.221, P_{EGGER}=0.175). The funnel plot of publication bias of OS is shown in Figure 4B.

General characteristics and surgical outcomes of patients in our center

A total of 27 patients were enrolled in this study, including 11 patients with RAMPS and 16 with SRPS. As is shown in Table 6, baseline parameters (age, sex, BMI, CA19-9 and CEA level) and oncologic outcomes (R0 resection, tumor size and

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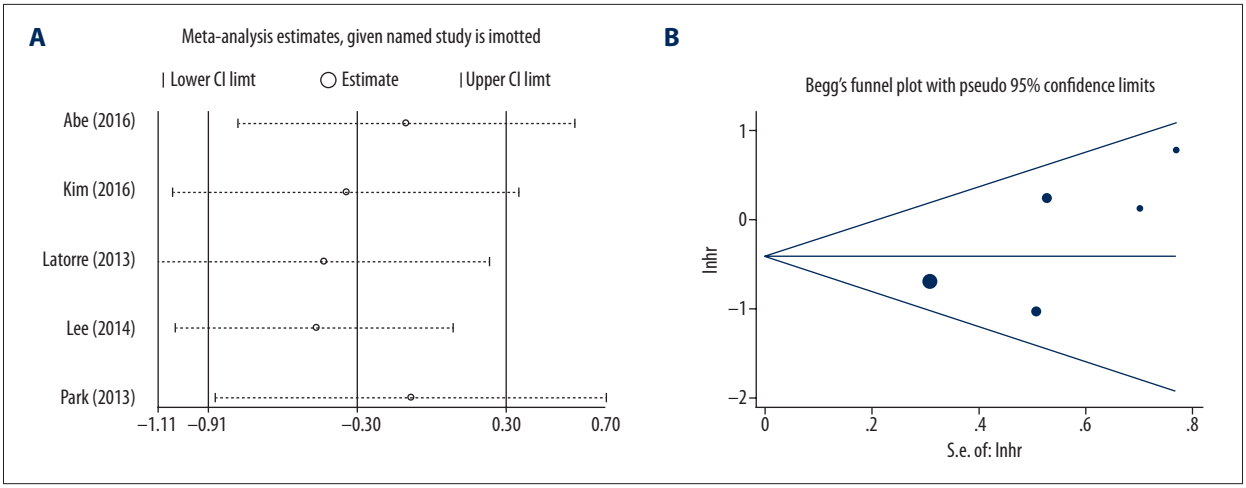

Figure 4. Stability examination of meta-analysis. (**A**) Sensitivity analysis by omitting one study at a time. (**B**) Publication bias detected by Begg's funnel plot.

Table 6. Baseline parameters and surgical outcomes of patients in our center.

Characteristics	RAMPS (n=11)	Standard procedure (n=16)	*P*
Age (year)	63.91±3.22	63.31±2.64	0.887[a]
Sex (M/F)	8/3	5/11	0.054[b]
BMI	23.21±0.91	21.85±0.51	0.172[a]
CA19-9 (U/ml)	340.1±135	895.8±341	0.146[a]
CEA (ng/m)	3.66±0.41	4.08±0.97	0.692[a]
Tumor size (cm)	3.68±0.19	4.44±0.56	0.220[a]
Tumor stage (AJCC)			0.739[b]
Ib	2 (18.2%)	2 (12.5%)	
IIa	3 (27.3%)	7 (43.8%)	
IIb	3 (27.3%)	4 (25.0%)	
III	2 (18.2%)	2 (12.5%)	
IV	1 (9.1%)	1 (6.3%)	
Operative time	171.4±17.04	197.2±19.9	0.206[a]
Blood loss	354.5±124.6	368.8±58.07	0.919[a]
Hospital stay	22.73±2.36	17.31±2.83	0.181[a]
Harvested lymph nodes	7.55±0.91	2.81±0.73	0.001[a]
R0 resection	10 (90.9%)	13 (81.3%)	0.624[b]
POPF	6 (54.5%)	3 (18.8%)	0.097[b]
Recurrence	5 (45.5%)	8 (50.0%)	1.000[b]

BMI – body mass index; CEA – carcinoembryonic antigen; POPF – postoperative pancreatic fistula. *P* value with a superscript 'a' was calculated by t test or Wilcoxon rank sum test; with a 'b', it was calculated by χ^2 test or Fisher exact test.

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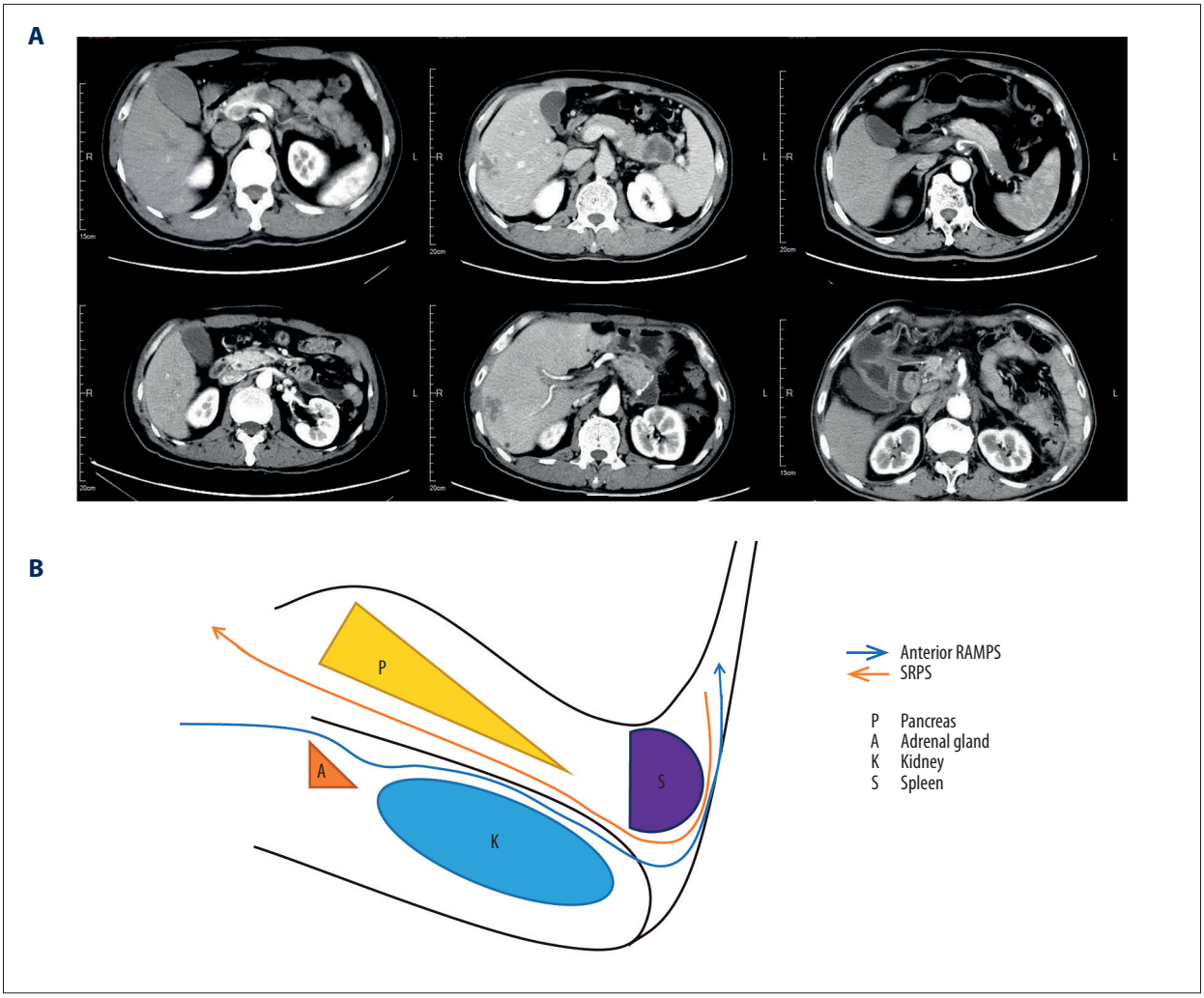

Figure 5. Preoperative preparation. (**A**) Representative preoperative (upper) and corresponding postoperative (lower) imaging examination of 3 patients. (**B**) Surgical approach of RAMPS and SRPS.

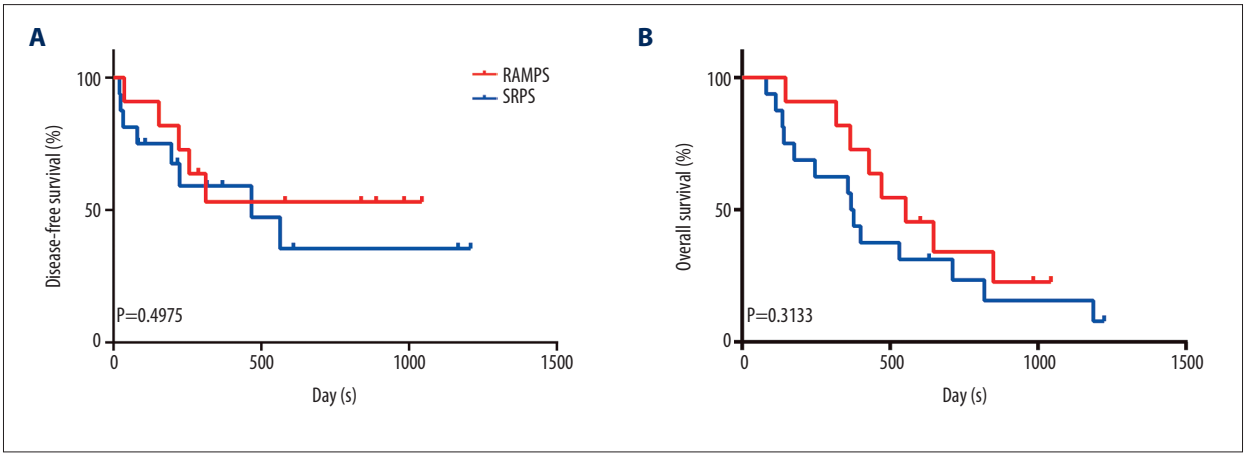

Figure 6. Survival analysis using the data of patients undergoing RAMPS and SRPS in our center. (**A**) DFS, (**B**) OS.

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stage) were not significantly different between RAMPS and SRPS group. In the RAMPS group, preoperative imaging examination of 11 patients suggested no posterior peritoneum and adrenal gland invasion for which anterior RAMPS was performed intraoperatively. The representative images are shown in Figure 5A. The upper 3 images showed the preoperative condition of 3 patients, while the lower 3 showed the corresponding postoperative condition. The surgical approaches of RAMPS and SRPS are shown in Figure 5B. Among surgical outcomes, no significant differences were between 2 groups with the exception of the number of harvested lymph nodes (7.55±0.91 *vs.* 2.81±0.73, *P*=0.001). Kaplan-Meier analysis indicated no significant differences in DFS (*P*=0.4975) and OS (*P*=0.3133) between the RAMPS and SRPS groups (Figure 6)

Discussion

RAMPS is an improved surgical procedure designed to completely dissect D1 lymph nodes and increase the R0 resection rate [25]. However, the number of previously published studies comparing RAMPS with SRPS is limited, and the reported effect of RAMPS on the treatment of left-sided PC is inconsistent. Therefore, we conducted this study systematically reviewing the published studies comparing RAMPS with SRPS and retrospectively analyzing the data of our center, aiming to provide solid evidence on the clinical effect of RAMPS. First, we performed a meta-analysis including 474 patients with left-sided PC, indicating that patients undergoing RAMPS had a better OS, less blood loss, more examined lymph nodes and lower recurrence rate than patients receiving SRPS. Second, the results of retrospective analysis using the database of our center showed that only significantly more harvested lymph nodes were noted in the RAMPS group compared with the SRPS group.

The prognosis of patients is an important factor to assess the clinical effect of a certain surgical procedure [26]. Some original research has proved that RAMPS could improve the OS of patients [18,21,22], while others studies did not [19,20,27]. Dragomir reported that the one-year overall survival was 79.2% in the RAMPS groups compared with 64.29% in the SRPS group with a *P*-value of 0.02 [28]. However, for DFS, the results of published articles remain quite consistent, namely, RAMPS cannot improve the DFS of patients compared with SRPS [18–20]. A meta-analysis published before by Cao concluded that RAMPS was not associated with better OS and DFS [29]. However, our meta-analysis is an update review that demonstrates that RAMPS is related to better OS. In summary, we believe that RAMPS may indeed improve the prognosis of patients with left-sided PC.

Despite considerable discrepancy in intraoperative blood loss between studies, our meta-analysis concludes that blood loss in the RAMPS group is significantly less than that in SRPS group, which is not consistent with a previously published meta-analysis [29]. Previous evidence has suggested that high intraoperative blood loss and blood transfusion are independent risk factors for complications, independent predictors of POPF after pancreaticoduodenectomy, and indicate poor prognosis of patients [30–32]. RAMPS requires early separation of pancreatic neck from pancreas-to-spleen (right-to-left), which can provide an easier approach to control the major blood vessels, including the splenic vessels, renal vessels and adrenal vessels, all of which may account for less blood loss in RAMPS compared with SRPS.

Regarding the harvested lymph nodes, researchers have arrived at a consensus that more lymph nodes are obtained in RAMPS than in SRPS [18–20,22,23,27], which is consistent with the results of our meta-analysis and retrospective analysis. A recent study suggested a positive correlation between the number of positive lymph nodes and the number of lymph nodes analyzed and that at least 21 lymph nodes should be analyzed to ensure a reliable assessment of the nodal status [33]. Although an extended lymphadenectomy shows no survival benefit to patients with pancreatic cancer, more positive lymph nodes may indicate more accurate N staging, which contributes to more accurate tumor staging [34–36]. As a result, patients may benefit from more individualized postoperative treatment and thus have better survival. The number of harvested lymph nodes in our retrospective study is relatively lower than that in other studies, which may be attributed to the fact that anterior RAMPS involved in a more superficial anatomical level than posterior approach was performed in the RAMPS group. In addition, en-block tumor removal was performed in the surgery, which may result in the decreased number of identified lymph nodes; additionally, the pathologist may fail to fully identify the lymph nodes given the morphologic change and physical dissolvement in formalin. Nevertheless, we believe that we have performed a complete surgery. RAMPS has several advantages over SRPS: (i) dissection of N1 lymph nodes, (ii) from pancreas-to-spleen (right-to-left) in accordance with lymphatic drainage, (iii) complete retroperitoneal resection to achieve R0 resection. Therefore, patients with a complete RAMPS could indeed benefit from this procedure and enjoy better survival.

Regarding the recurrence rate, our meta-analysis reveals that recurrence rate in the RAMPS group is significantly lower than that in SRPS group. The results using our own data suggest the same tendency without a significant difference. As previously described, the dissection of RAMPS begins from pancreas to spleen, followed by early division of pancreas neck and early ligation of the splenic vessels; thus, RAMPS can be considered a surgical procedure that applies a no-touch isolation technique [37]. Therefore, RAMPS can theoretically reduce the

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distant metastasis of tumor cells. Interestingly, our pooled results show a significantly lower recurrence rate in the RAMPS group. However, current evidence indicates no significant difference in DFS between the RAMPS group and SRPS group [29], which is consistent with the results of our meta-analysis. Surprisingly, our meta-analysis and retrospective analysis indicate no significant difference in the R0 resection rate between the 2 groups, which is not consistent with previously reported results [18,29]. The meta-analysis indicated better postoperative outcomes for RAMPS.

There are several major limitations in our study. First, the number of studies enrolled in the meta-analysis is inadequate due to the limited number of published articles comparing RAMPS with SRPS. The included studies are mostly retrospective studies with a low level of evidence. Therefore, randomized control clinical trials of high quality are needed, and we plan to conduct one in our center. Second, patients with better OS in the RAMPS group may not benefit only from surgery because there are some characteristics of patients who we failed to take into consideration and thus caused the inevitable heterogeneity among studies, such as tumor size, tumor stage or administration of adjuvant chemotherapy. Hence, a meta-analysis including more homogeneous original studies comparing RAMPS with SRPS is required to draw a more solid conclusion.

Conclusions

The meta-analysis and retrospective analysis both demonstrate that RAMPS is associated with better prognosis and surgical outcomes, indicating that RAMPS is a more safe and feasible surgical procedure than SRPS. However, due to the limited number and insufficient quality of enrolled studies, more homogeneous randomized controlled studies of high quality are required for further investigation.

Conflict of interests

None.

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