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ORIGINAL ARTICLE

Preservation versus Non-preservation of the Duodenal Passage Following Total Gastrectomy: A Systematic Review

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Abstract
Background Various reconstruction procedures have been proposed for restoring the alimentary tract continuity after total gastrectomy. However, so far there is no consensus on the ideal post-gastrectomy reconstruction procedure. The necessity of preserving the duodenal passage is one of the major focuses of the debate concerning gastrointestinal reconstruction and is the objective of this study.
Methods A systematic literature search of PubMed, EMBASE, the Cochrane Library, SCI, and Chinese Biomedical Literature Database (CBM) was carried out before March 2012 to obtain studies of randomized controlled trials (RCT). Analysis was performed using RevMan 5.0 software.
Results Nine RCTs involving 642 participants met the selection criteria. The results of the meta-analyses showed that operative mortality and morbidity were not significantly different between the two procedures (preservation vs. non-preservation of duodenum). However, operative time was considerably prolonged by preserving the duodenal passage. Patients in the preservation group had an improved nutritional parameters (body weight, levels of serum iron and hemoglobin) in the short term (<6 months) after surgery. Beneficial effect on preventing postgastrectomy symptom (heartburn, dumping syndrome) was not found by maintaining the duodenal passage throughout a 2-year follow-up. Moreover, a qualitative measurement showed that no significant quality of life improvement for patients with a preserved duodenal passage.
Conclusion This systematic review failed to demonstrate obvious advantage in preserving duodenal passage after total gastrectomy.

Keywords Alimentary tract reconstruction · Total gastrectomy · Duodenal preservation · Systematic review

Introduction

The selection of an appropriate reconstruction approach after total gastrectomy has important clinical significance in reducing the incidence of postoperative complications, maintaining nutritional status, and improving quality of life for patients.[1–5] To date, more than 60 types of digestive tract reconstruction have been proposed for total gastrectomy.[6] However, the choice of digestive tract reconstruction remains controversial.[6] The broad spectrum of reconstruction methods can be subdivided into whether or not to preserve the duodenal passage and whether or not to perform pouch construction.[6,7] Duodenal passage preservation (DPP), in theory, is the more physiological sound approach to reduce postoperative complications and improve nutritional status.[4,6,7] Its real clinical effect, however, lacks convincing proof. Some reports have showed a similar functional result for the two procedures.[8–12] Therefore, the necessity of maintaining the continuity of the duodenal passage has become one of the major focuses of debates in the area of gastrointestinal reconstruction.[1,6,7,13] Several randomized controlled trials (RCT) concerning this

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issue are characterized by small sample sizes, uneven quality, and different endpoints. Because of the lack of formal meta-analyses and the heterogeneity of reconstruction techniques, evidence from general reviews related to this topic have failed to show reliable results to support reconstruction with DPP as a preferable choice.[1–4,6–8,13,14] In this study, we reviewed the published literature and aimed to assess the clinical value of DPP after total gastrectomy by rigorous screening of related literature and implementing normative meta-analyses in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[15]

Methods

Inclusion and Exclusion Criteria

Only RCTs were considered in our study. Studies on the issue whether DPP after total gastrectomy for gastric malignancies had an impact on one or more of the clinical outcome regarding operative safety, quality of life, nutritional status and symptoms as compared with reconstructions without DPP were considered for inclusion. Since most reconstructions of DPP were done by interposing jejunal passage between the esophagus and duodenum or double tract techniques, our study was restricted to the jejunal interposition and double tract. Any procedure associated with colonic interposition after total gastrectomy was excluded. The double tract reconstruction maintains the duodenal passage by performing esophagojejunostomy and jejunojejunostomy as in the Roux-en-Y technique and adding a side-to-end duodenojejunostomy distal from the esophagojejunal anastomosis.

Literature Search and Data Extraction

A systematic literature search to March 2012 was conducted in the PubMed, EMBASE, the Cochrane Library, SCI, and Chinese Biomedical Literature Database. The main search terms were “gastric malignancy”, “gastric cancer”, “gastric carcinoma”, “gastric neoplasm”, “stomach malignancy”, “stomach cancer”, “stomach carcinoma”, “stomach neoplasm”, “jejunal” or “jejunum” combined with “interpos*”, “preserv*” or “restor*” or “maintain*” or “maintenance” combined with “duoden*” and all of the above combined with “randomized controlled trial” or “RCT”, etc. Reference lists from all relevant articles were reviewed to identify additional studies. No language exclusion criterion was applied.

Two reviewers (Yang and Yan) read titles, abstracts and full texts independently to determine whether they met the inclusion criteria or not, then cross checked the results. Disagreements were resolved by consensus or discussing with the third researcher (Chen). The following information was abstracted from each included study: the authors, year of publication and source of the study, study design, intervention, outcome, etc. When key information was deficient or not available in the published study, we obtained the data by contacting the author through mail or telephone.

Risk of Bias Assessment

The quality of eligible trials was evaluated using the tools for assessing risk of bias provided by *Cochrane Handbook 5.0.2* (Chapter 8) and the assessment took into account the sequence generation, allocate concealment, blinding, incomplete outcome data, selective outcome reporting, other source of bias. The judgment for each domain included: “Yes” (low risk of bias), “No” (high risk of bias), “Unclear” (uncertain risk of bias).[16]

Statistical Analyses

A meta-analysis was performed using Review Manager (Version 5.0) statistical software provided by the Cochrane collaboration. We expressed results for dichotomous outcomes as risk ratio (RR) or odds ratio (OR) and continuous outcomes as mean difference (MD) or standard mean difference (SMD). All the effect measures above were represented as 95 % of confidence intervals (CIs).[17] We used the chi-square test and inconsistency statistic (I^2) to assess the heterogeneity between trials.[18] In this study, summary estimates and their 95 % CI were calculated by the random-effect statistical model.[19,20] A stratified meta-analysis was performed to explore potential causes of heterogeneity. Subgroup analyses were carried out for different follow-up periods and different reconstruction techniques (e.g., reconstruction with or without pouch formation). For the multi-arm studies that had more than two intervention groups, we combined those groups which were independent from each other and correlated on the intervention of DPP or non-duodenal passage preservation (NDPP) based on the comments of the *Handbook 5.0.2* for multiple interventions groups and the relevant formula recommended for combining groups.[16] A descriptive analysis was provided when the heterogeneity in included trials was excessive or the data was not extractable.

Results

In all, nine RCTs including a total of 642 participants, of whom 325 were allocated to group NDPP and 317 to DPP group, were included.[5,9–12,21–24] Figure 1 specifies the selection of the studies. The characteristics and methodological quality of included studies are shown in

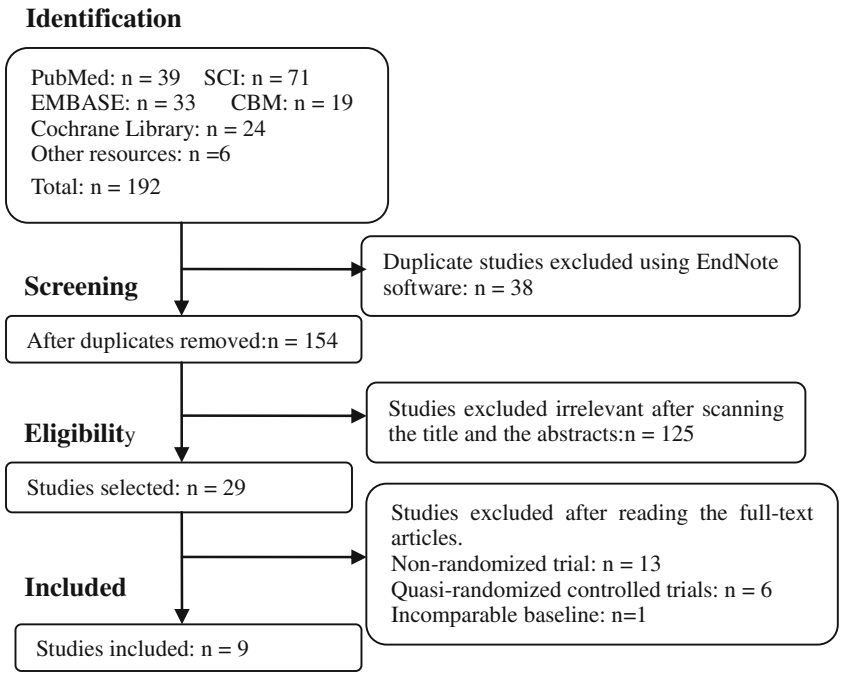

Fig. 1 PRISMA flow diagram for study selection for meta-analysis

Table 1 Characteristics of included studies

Study	Group	Additional pouch	Cases	Age (yr)	Gender (M/F)	Tumor staging	I/R (cm)	Nutrition support	Follow-up
Nakane et al.[9]	DPP[a]	Yes	14	58.9 (46–69)	10/4	I + II (14) III + IV (0)	30	Parenteral nutrition	6 yr
	NDPP[b]	Yes	13	53.8 (40–63)	11/2	I + II (10) III + IV (3)	40		
Fuchs et al.[10]	DPP[a]	Yes	53	59	37/16	I + II (27) III + IV (27)	n.r	Nasojejunal tube	5 yr
	NDPP[b]	Yes	53	58	32/21	I + II (25) III + IV (28)	50		
Nakane et al.[11]	DPP[a]	Yes	10	58.1	7/3	I + II (6) III + IV (4)	40	Parenteral nutrition	5 yr
	NDPP[b]	Yes	10	53.2	6/4	I + II (7) III + IV (3)	40		
Adachi et al.[12]	DPP[a]	Yes	10	59.0 (43–74)	9/1	I (5) II (5)	40	n.r	5 yr
	NDPP[b]	Yes	10	57.5 (48–75)	6/4	I (5) II (5)	40		
Schwarz et al.[21]	DPP[a]	Yes (20 cm)[c]	12	59.0±3.10	9/3	I + II (6) III + IV (6)	35	n.r	6 mo
	DPP[a]	Yes (10 cm)[c]	12	62.00±3.59	4/8	I + II (8) III + IV (4)	25		
	NDPP[b]	Yes (20 cm)[c]	12	63.00±3.47	7/5	I + II (5) III + IV (7)	n.r		
	NDPP[b]	Yes (10 cm)[c]	12	65.00±3.74	10/2	I + II (4) III + IV (8)	n.r		
Zhang et al.[23]	DPP[a]	Yes	30	n.r	n.r	n.r	n.r	n.r	6 mo
	DPP[a]	Yes	29	n.r	n.r	n.r	n.r		
	NDPP[b]	Yes	30	n.r	n.r	n.r	n.r		
	NDPP[b]	Yes	30	n.r	n.r	n.r	n.r		
Zherlov et al.[22]	DPP[a]	No	75	59 (36–72)	52/23	II (7) IIIa (44) IIIb (24)	15–18	Nasojejunal tube	3 yr
	NDPP[b]	No	80	60 (40–77)	62/18	II (11) IIIa (47) III b (22)	n.r		
Ishigami et al.[24]	DPP[a]	No	51	<80	n.r	Ia–IIIb	20–40	n.r	3 yr
	NDPP[b]	No	52		n.r	Ia– IIIb	40		
Iwahashi et al.[5]	DPP[d]	No	21	58.2±10.7	14/7	I (14) II (5) IIIa (0) IIb (2)	35	n.r	1 yr
	NDPP[b]	No	23	65.4±8.3	18/5	I (15) II (6) IIIa (2) IIb (0)	40		

I/R length of the Roux limb/jejunal interposition, *n.r* not reported, *mo* months, *yr* years

[a] Jejunal interposition reconstruction

[b] Roux-en-Y reconstruction

[c] Length of the pouch

[d] Double tract reconstruction

Table 2 Risk of bias in included studies

Study	Sequence generation	Allocate concealment	Blinding	Incomplete outcome data addressed	Selective outcome reporting	Free of other bias
Nakane et al.[9]	Yes[a]	Yes[b]	Unclear	Yes	Unclear	Unclear
Fuchs et al.[10]	Unclear	Unclear	Unclear	Yes	Unclear	Unclear
Nakane et al.[11]	Yes[a]	Yes[b]	Unclear	Yes	Unclear	Unclear
Zherlov et al.[22]	Yes[c]	Unclear	Yes[d]	Unclear	Unclear	Unclear
Adachi et al.[12]	Yes[a]	Yes[b]	Unclear	Unclear	Unclear	Unclear
Schwarz et al.[21]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Iwahashi et al.[5]	Yes[c]	Unclear	Unclear	Unclear	Unclear	Unclear
Zhang et al.[23]	Yes[a]	Yes[b]	Unclear	Yes	Unclear	Unclear
Ishigami et al.[24]	Unclear	Unclear	Unclear	Yes	Unclear	Unclear

[a] Shuffling envelopes

[b] Sealed envelopes

[c] A table of random numbers

[d] Blinding only for interviewer

Tables 1 and 2. The main results of included RCTs are listed in Tables 3 and 4.

Postoperative Morbidity and Mortality

Postoperative morbidity and mortality were reported in four RCTs and five RCTs, respectively.[5,10–12,22] The meta-analyses showed that DPP did not increase morbidity and mortality (Table 5).

Operative Time

Data on operative time was provided in six RCTs.[5,12,21–24] The meta-analyses showed that keeping the duodenum passage prolonged operative time significantly (Table 5).

Quality of Life

The methods used to evaluate the quality of life varied among available RCTs.[5,10,21,23,24] Given the heterogeneity among trials, a descriptive analysis was performed on the five RCTs. Except for Schwarz's study at 6 months postoperatively, related RCTs highlighted that there was no significant difference between the DPP group and the NDPP group in the short- and long-term periods (Table 4).

Body Weight

Seven RCTs stated the dynamics of body weight at different follow-up periods.[5,9,10,21–24] Of these, three studies reported body weight 3 and 6 months after operation.[21,23] The meta-analyses showed that group DPP was superior to group NDPP in improving body weight after total gastrectomy at 3 and 6 months postoperatively (Table 6).

A descriptive analysis was applied to the remaining five RCTs due to a lack of specific data.[5,9,10,22,24] Iwahashi et al.[5] found no significant differences between the two reconstruction procedures 12 months after surgery. For longer follow-up, no significant results were observed throughout the entire follow-up of 2 years by Nakane et al,.[9] during a 3-year follow-up by Fuchs et al,.[10] and 5 years postoperatively by Ishigami et al..[24] In the Zherlov's study,[12] patients in the DPP group had an improved body weight at 1 and 2 years postoperatively. However, statistical analysis was not available.

Serum Nutritional Parameters

Serum albumin (Alb) levels were reported in two trials[5,23] at 3 and 6 months postoperatively and hemoglobin (Hb) value was provided in two trials[21,23] 6 months after operation. The level of serum iron (SI) was evaluated in two trials[5,23] at 3 months and in three trials[5,21,23] at 6 months postoperatively. Meta-analyses for these time points during follow-up showed that the duodenal passage was conducive to improving the levels of the serum nutritional parameters (SNP). Except for the results of Alb 6 months after surgery, statistically significant differences could be seen between the two reconstruction techniques (Table 6). No significant differences were found in Hb value by Zhang et al.[23] at 3 months postoperatively and in the levels of SI and Alb by Fuchs et al.[10] 12 months after surgery.

Gastrointestinal Symptoms

Meta-analyses could be carried out on three trials regarding heartburn.[9,10,12] The results showed that DPP did not significantly relieve the symptom as compared with NDPP

Table 3 Main result of included RCTs

Study	Group	*n*	Morbidity (%)	Mortality (%)	OP time (min)	Body weight				Dumping incidence				Heartburn incidence			
						% Preop		Loss/Abs									
						3 m	24 m			3 m	6 m	12 m	24 m	3 m	6 m	12 m	24 m
[9]	DPP	14	n.r	n.r	265	86.8 %	91.5 %	n.r		0/14	0/14	0/14	0/14	2/14	3/14	1/14	1/14
	NDPP	13	n.r	n.r	280	86.9 %	89.6 %	n.r		1/13	0/13	0/13	0/13	3/13	2/13	3/13	1/13
[10]	DPP	53	14	1	n.r	n.r		−3.5 (0–18)[a]		0[a]				n.r			
	NDPP	53	13	2	n.r	n.r		−3.4 (0–25)[a]		2[a]				n.r			
										3 m	6 m	12 m	24 m	3 m	6 m	12 m	24 m
[11]	DPP	10	2	0	n.r	n.r		n.r		0/6	0/6	1/6	0/5	0/6	0/6	0/6	0/5
	NDPP	10	2	0	n.r	n.r		n.r		0/9	0/9	0/9	0/8	3/9	0/9	0/9	0/8
						60 m				12 m	36 m	60 m					
[12]	DPP	10	5	0	312±69	95.1 %		n.r		0/10	1/10	0/10		n.r			
	NDPP	10	2	0	259±43	94.5 %		n.r		0/10	0/10	0/10		n.r			
								3 m	6 m								
[21]	DPP	24	n.r	n.r	355±41	n.r		60±10	64±10.	n.r				n.r			
	NDPP	24	n.r	n.r	328±43	n.r		60±10	58±11	n.r				n.r			
								3 m	6 m								
[23]	DPP	30	n.r	n.r	230±23	n.r		−2±1.6	−1±1.9	n.r				n.r			
	NDPP	30	n.r	n.r	208±23	n.r		−3±3.2	−4±2.5				n.r	n.r			
						12 m	24 m			3 m	6 m	12 m	24 m				
[22]	DPP	75	6	0	211±25.2	89.8 %	89.7 %	n.r		3/75	4/75	5/75	4/75	n.r			
	NDPP	80	7	0	198±22.7	64.4 %	59.2 %	n.r		12/80	14/80	19/80	22/80	n.r			
						12 m											
[5]	DPP[c]	21	n.r	0	254±43	77.8 %		n.r		n.r				n.r			
	NDPP	23	n.r	1	260±69	70.0 %		n.r		n.r				n.r			
[24]	DPP	51	n.r	n.r	287±72	n.r		n.r		n.r				n.r			
	NDPP	52	n.r	n.r	252±64	n.r		n.r		n.r				n.r			

Abs absolute value, *n.r* not reported, *m* months

[a] Time not specified

Table 4 Main result of included RCTs

Study	Group	*n*	Hb (g/l)		SI (μmol/l)			Alb (g/l)			Quality of life				
											Method	*P* value*			
					3 m	6 m	12 m	3 m	6 m	12 m	UC	3 m	12 m		
[5]	DPP	21	n.r		17+6	18+7	19+7	41+3	41+3	42+3		>0.05	>0.05		
	NDPP	23	n.r		17+6	17+6	21+7	40+3	40+3	40+3					
			3 m	6 m	3 m	6 m		6 m	12 m			3 m	6 m		
[23]	DPP	59	114+12	110+12	24+5	25+3		37+4	36+4		Visck	>0.05	>0.05		
	NDPP	60	116+10	106+11	22+3	12+7		38+3	38+3						
			6 m		6 m							3 m	6 m		
[21]	DPP	24	139+43		18+5						UC	>0.05	<0.05		
	NDPP	24	125+44		11+5										
												36 m			
[10]	DPP	20	n.r		n.r			n.r			Visck, pitzer	>0.05 (Visck, pitzer)			
	NDPP	26	n.r		n.r			n.r							
												3 m	6 m	12 m	60 m
[24]	DPP	18	n.r		n.r			n.r			UC	>0.05	>0.05	>0.05	>0.05
	NDPP	24	n.r		n.r			n.r							

n.r not reported, *m* months, *UC* unclear, *Hb* hemoglobin, *Alb* albumin, *SI* serum iron

*$P<0.05$ was considered statistically significant

Table 5 Comparison of perioperative parameters

Outcomes	No. of studies	No. of cases		OR/MD (95 % CI)	Test of homogeneity		*P* value[c]
		DPP	NDPP		I^2 (%)[a]	*P* value[b]	
Morbidity	4[10–12,22]	148	153	1. 71 (0.63–2.20)	0	0.64	0.62
Mortality	5[5,10–12,22]	169	176	0.43 (0.06–3.04)	0	0.87	0.40
Operation Time	6[5,12,21–24]	207	222	18.63 (10.16–27.11)	34	0.18	*P*<0.0001

DPP duodenal passage preservation, *NDDP* non-duodenal passage preservation, *OR* odds ratio, *MD* mean difference, *CI* confidence interval

[a] Inconsistency statistic (I^2)

[b] Chi-square test

[c] Test for overall effect and $P<0.05$ was considered statistically significant

during a 2-year follow-up (Table 7). Moreover, no significant differences in the incidence of heartburn between the two groups were found by Adachi et al.[17] at 3- and 5-year follow-up postoperatively. The incidence of dumping syndrome was reported in five RCTs and meta-analyses could be carried out in four studies at four time points (3, 6, 12, and 24 months) during follow-up.[9–12,22] The results showed that the incidence of dumping syndrome in the DPP group is significantly lower than that in the NDPP group at 3, 6, and 24 months after surgery. For longer follow-up, no significant differences were found by Adachi et al.[12] at 3 and 5 years postoperatively, and 3 years after surgery by Fuchs et al.[10]

Subgroup Analyses

Potential causes of heterogeneity of pouch formation were explored by performing a subgroup analysis whenever feasible. The results are listed in Table 8. Except for the results of dumping syndrome, the results of these meta-analyses based on possible risk factors of pouch formation were in line with the aforementioned results.

Discussion

As a technique that restores the anatomy and physiology of the digestive tract, DPP should, in theory, result in better physiological regulation of gastrointestinal hormones and physiological enrichment of the chyme with bile and pancreatic juice, thereby preventing bacterial overgrowth, improving appetite and eating capacity, as well as enabling superior digestion and absorption.[1,3,4,6,21] In view of the physiological advantage, some investigators have attempted to demonstrate the necessity and efficacy of DPP. However, the merits and demerits of DPP procedures continue to be hotly debated, as conclusions from different clinical studies are inconsistent.[5,9–12,21–23] Meanwhile, previous reviews lacked evidence from systematic review/meta-analysis and were not powerful enough to draw a reliable conclusion.[1–4,6–8,13,14]

In this meta-analysis, no significant differences were found in the incidence of operative mortality and morbidity between the DPP group and the NDPP group, while maintaining the duodenal food passage prolonged operation time which implies an additional safety risk for the operation. Meta-analyses

Table 6 Comparison of nutritional status

Outcomes	No. of studies	No. of cases		MD (95 % CI)	Test of homogeneity		*P* value*
		DPP	NDPP		I^2 (%)[a]	*P* value[b]	
Body weight							
3-month	2[21,23]	83	84	0.98 (0.08 to 1.87)	0	0.74	0.03
6-month	2[21,23]	83	84	3.05 (2.26 to 3.84)	0	0.33	<0.00001
Hb							
6-month	2[21,23]	83	84	9.62 (5.86 to 13.37)	0	0.69	<0.00001
Alb							
3-month	2[5,23]	80	83	1.07 (0.04 to 2.09)	0	0.93	0.04
6-month	2[5,23]	80	83	0.37 (−0.60 to 1.35)	0	0.41	0.45
SI							
3-month	2[5,23]	80	83	1.72 (0.33 to 3.12)	0	0.36	0.02
6-month	3[5,21,23]	104	107	7.27 (1.08 to 13.47)	94	<0.00001	0.02

DPP duodenal passage preservation, *NDDP* non-duodenal passage preservation, *MD* mean difference, *CI* confidence interval

[a]Inconsistency statistic (I^2)

[b]Chi-square test

*Test for overall effect and $P<0.05$ was considered statistically significant

Table 7 Comparison of gastrointestinal symptoms

Outcomes	No. of studies	No. of cases		OR/RR/MD (95 % CI)	Test of homogeneity		*P* value*
		DPP	NPP		I^2 (%)[a]	*P* value[b]	
Dumping							
3-month	3[9,11,22]	95	102	0.24 (0.07–0.82)	0	0.91	0.02
6-month	3[9,11,22]	95	102	0.27 (0.08–0.85)	–	–	0.03
12-month	4[9,11,12,22]	105	112	0.71 (0.04– 13.56)	67	0.08	0.82
24-month	3[9,11,22]	94	101	0.15 (0.05–0.46)	–	–	0.0009
Heartburn							
3-month	2[9,11]	20	22	0.38 (0.07–2.02)	0	0.47	0.26
6-month	2[9,11]	20	22	1.50 (0.21–10.81)	–	–	0.69
12-month	3[9,11,12]	30	32	0.44 (0.07–2.85)	0	0.48	0.39
24-month	2[9,11]	19	21	0.92 (0.05–16.46)	–	–	0.96

DPP duodenal passage preservation, *NDDP* non-duodenal passage preservation, *RR* risk ratio, *CI* confidence interval, – not applicable

[a]Inconsistency statistic (I^2)

[b]Chi-square test

*Test for overall effect and $P<0.05$ was considered statistically significant

on nutritional parameters showed that patients in the group DPP had an improved body weight, and a better Hb and SI level at 6 months postoperatively. Clinically, the advantage in SI and Hb level and a higher body weight are manifested in rarer iron deficiency anemia and good nutritional conditions. Meta-analyses on postprandial symptoms showed a similar incidence of heartburn between the two groups throughout 2-year follow-up, but a lower frequency of dumping in the DPP group at 3, 6, and 24 month postoperatively. The subgroup analyses on dumping syndrome, however, revealed no significant differences between the two reconstruction procedures. Given the data on nutritional parameters and dumping syndrome were provided in only two or three RCTs included, these meta-analyses were limited to draw firm conclusions of the value of reconstruction with DPP in preventing postgastrectomy symptoms and malnutrition. Meta-analysis for quality of life is not feasible, as the methods utilized varied in the available five RCTs, and most of the results from the RCTs failed to demonstrate any advantage in quality of life for DPP after total gastrectomy.

The formation of a pouch reservoir as a gastric substitute has been repeatedly described as the procedure that has clinical benefit and improves the quality of life after total gastrectomy compared to the Roux-en-Y reconstruction.[11,21,25–30] In addition, a definitive, statistically significant proof of the superiority of this method has been presented in a recent

Table 8 Subgroup analyses for pouch formation

Outcomes	No. of studies	No. of cases		OR/RR/MD (95 % CI)	Test of homogeneity		*P* value*
		DPP	NDPP		I^2 (%)[a]	*P* value[b]	
Morbidity (pouch)	3[10–12]	73	73	1.31 (0.62–2.78)	0	0.49	0.48
Mortality (pouch)	3[10–12]	73	73	0.49 (0.04–5.58)	–	–	0.57
Operation time (pouch)	3[12,21,23]	93	94	23.25 (15.54–30.97)	0	0.47	$P<0.00001$
SI (pouch)							
6-month	2[21,23]	83	84	10.23 (5.03–15.42)	91	0.001	0.0001
Dumping (pouch)							
3-month	2[9,11]	20	30	0.49 (0.05–5.08)	0	0.65	0.55
6-month	2[9,11]	20	30	Not estimable	–	–	–
12-month	3[9,11,12]	30	50	1.74 (0.07–44.48)	50	0.16	0.74
24-month	2[9,11]	19	28	0.29 (0.01–7.70)	–	–	0.46
Mortality (no pouch)	2[5,22]	96	103	0.35 (0.01–9.04)	–	–	0.53
Operation time (no pouch)	3[5,22,24]	114	128	12.46 (0.73–24.19)	13	0.31	$P<0.04$

DPP duodenal passage preservation, *NDDP* non-duodenal passage preservation, *SI* serum iron, *OR* odds ratio, *RR* risk ratio, *MD* mean difference, – not applicable, *CI* confidence interval

[a] Inconsistency statistic (I^2)

[b] Chi-square test

*Test for overall effect and $P<0.05$ was considered statistically significant

meta-analysis with regard to improving nutritional outcomes and ameliorating symptoms.[31] Of the nine included studies, six formed a pouch in the DPP group. In view of the interference effect of pouch formation, which could partially explain the outcome of the DPP group, we have attempted to perform a subgroup analysis in terms of whether pouch reconstruction was applied or not and demonstrate the independent influence of maintaining the duodenal food passage. However, this further subgroup analysis was confined since each outcome included insufficient reports and fewer studies fulfilled the subgroup of different postoperative periods.

The length of follow-up and the time interval employed for assessment were varied among included trials, and most of the studies reported short-term results (<2 years). As discussed above, the diversity in study methodology leads insufficient reports to be combined for multiple time points and fails to manifest the long term effect of DPP. Besides that, other considerable factors also play important roles in the outcome and the crucial factor influencing the outcome can change based on follow-up time. For example, Bozzetti et al.[32] indicated that early evaluation can simply reflect a lack of adaptation to the new anatomical condition, while long-term evaluation may reflect the influence of a tumor recurrence. To limit this problem, most trials included only patients without recurrence during follow-up and excluded stage IV patients.

Other limitations of the included studies should be considered. Concerning the methodological quality of included studies, as shown in Table 2, information is insufficient on the randomization method in three trials, allocation sequence concealment in three trials, and intent-to-treat analyses in four trials that had patients with missing outcome. The remaining two entries had poorly reported details in RCTs included. Some raw data was illustrated in figures solely or presented in the original publications inadequately, and this precluded the full elucidation of the included studies by meta-analysis. Two of the nine RCTs applied double tract and modified jejunal interposition with an antireflux anastomosis as the reconstruction of DPP, respectively. We have performed subgroup analyses by excluding the two reports[5,22] and no markedly changes were found as compared with aforementioned results.

In summary, maintaining the duodenal passage after total gastrectomy did not significantly increase operative morbidity or mortality, but relevantly prolonged the operating time. Also, results of the meta-analyses demonstrated the superiority of nutritional parameters in the short term after surgery for the DPP group compared with the NDPP group. Beneficial effect on preventing postgastrectomy symptom was not found by maintaining the duodenal passage**.** However, with regard to the unfavorable influence from the aforementioned shortcomings and bias from the pooled data, a definitive clarification of the value of reconstruction maintaining the duodenal passage still warrants further objective validation by large-sample, extended follow-up, multicenter, RCTs.

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