REVIEW ARTICLE

Surgical Treatment Strategies in Chronic Pancreatitis

A Meta-analysis

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Objective: To research the optimal surgical strategy for chronic pancreatitis.

Data Sources: PubMed, EMBASE, Science Citation Index, SpringerLink, and secondary sources from inception through December 31, 2011, with no restrictions on languages or regions.

Study Selection: All controlled experimental (randomized and nonrandomized) studies in which duodenum-preserving pancreatic head resection was compared with pancreaticoduodenectomy in chronic pancreatitis.

Data Extraction: Data were extracted independently and in duplicate by 2 reviewers; discrepancies were resolved by discussion.

Data Synthesis: A total of 1007 patients from 15 studies were included in the meta-analysis. The relative risks for postoperative pain relief and postoperative morbidity in the Beger procedure were 1.29 (95% CI, 1.03-1.61; $P = .03$) and 0.55 (0.21-1.39; $P = .20$), respectively, compared with pancreaticoduodenectomy. These results are just the opposite in the Frey procedure, in which a significantly better outcome was shown in postoperative morbidity compared with resection (relative risk, 0.60; 95% CI, 0.46-0.78; $P < .01$) but not in postoperative pain relief (1.03; 0.90-1.17; $P = .67$). In terms of quality of life, pancreatic exocrine function, and delayed gastric emptying, the results also favored duodenum-preserving strategies.

Conclusions: For the duodenum-preserving strategy of the Beger procedure, complete pain relief is achieved in most patients, but there is no evidence that it has a better result in postoperative morbidity. For the Frey procedure, a significantly lower postoperative morbidity is demonstrated, but complete pain relief is not provided in most cases. Thus, compared with conventional pancreaticoduodenectomy, both new strategies should be recommended on the basis of the patients' appropriate individual preferences.

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CHRONIC PANCREATITIS (CP), a potentially debilitating disease, is characterized by intractable abdominal pain, continuing morphologic and functional damage to the pancreas, and finally a deteriorated quality of life (QoL). Conservative treatment such as medication or diet modification can relieve the symptoms of CP to some extent. Endoscopic drainage is another option.[1,2] However, a randomized controlled trial (RCT)[3] indicated that surgical drainage was superior to the endoscopic technique in patients with CP. Surgical intervention is unavoidable when the disease has progressed for years or even decades and coexisting complications of adjacent organs (ie, duodenal stenosis, bile duct stenosis, portal vein constriction with portal hypertension, pancreatic necroses, formation of pseudocysts, pancreatogenic ascites, or the formation of pancreatic fistulas/leaks) are presented.

Classic partial pancreaticoduodenectomy (PD)—the Whipple procedure[4]—has been the standard procedure for the surgical treatment of CP. Pylorus-preserving PD (PPPD)—the so-called Traverso-Longmire procedure[5]—is another conventional resection based on the Whipple procedure. Several studies comparing the short- and long-term outcomes of the 2 PD procedures showed no clear advantages for either of the procedures. Pancreaticoduodenectomy was associated with a high rate of complications (40%-60%) and a high mortality (up to 5%), which may be due to its extensive re-

See Invited Critique at end of article

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section, including the removal of the duodenum and the biliary tree and a large portion of the pancreas.[6-8] To provide a better long-term outcome, duodenum-preserving pancreatic head resection (DPPHR) strategies have been introduced. In recent years, 2 main duodenum-preserving techniques, the Beger procedure[9] and the Frey procedure[10] (a combination of resection and drainage with longitudinal pancreaticojejunostomy and local pancreatic head excision), have been widely used in many medical centers all over the world. The value of these new gastrointestinal reconstructive strategies is worthy of summary.

METHODS

The methods of literature search, inclusion and exclusion criteria, outcome measures, and methods of statistical analysis were defined in a protocol according to the Preferred Items for Systematic Reviews and Meta-Analyses[11] and Meta-analysis of Observational Studies in Epidemiology[12] recommendations for study reporting.

DATA SOURCES AND SEARCHES

The primary sources of the reviewed studies through December 31, 2011, without restriction on the languages or regions, were PubMed, EMBASE, Science Citation Index, and SpringerLink. We combined the following database-specific search terms for CP: PD (*pancreatoduodenectomy* or *duodenopancreatectomy* or *pancreatectomy* or *pylorus-preserving* or *Traverso-Longmire* or *Whipple* or *PD* or *PPPD*) and DPPHR (*duodenum-preserving* or *organ-preserving* or *Beger* or *drainage* or *longitudinal pancreaticojejunostomy* or *longitudinal pancreaticojejunoanastomosis* or *Frey* or *LPJ* or *PJS*). The computer search was supplemented with manual searches for reference lists of all retrieved review articles, primary studies, and abstracts from meetings to identify other studies not found in the computer search. Authors of relevant abstracts were contacted to obtain any unpublished data (if available). When the results of a single study were reported in more than 1 publication, only the most recent and complete data were included.

STUDY SELECTION

We selected all controlled experimental (randomized and nonrandomized) studies in which DPPHR was compared with PD in CP. The studies had to meet the following inclusion criteria:

1. Patients presented with pancreatic head enlargement based on the diagnosis of CP (defined as a diameter of >35 mm in a contrast-enhanced computed tomography scan) or with intractable pain and obstruction of the common bile duct or pancreatic duct or duodenum or other adjacent organ complications.
2. Patients had no contraindication for the surgical management of CP.
3. Postoperative pain relief and postoperative morbidity were assessed as outcome measures of the effect of the treatment.
4. The studies had been published or accepted for publication as full-length articles.
5. The study included at least 30 patients. Smaller studies were excluded because of poor reliability.

The exclusion criteria were nonhuman studies, nonexperimental trials, review articles, editorials, letters/case reports, and articles not reporting outcomes of interest.

OUTCOME MEASURES

Primary outcomes assessed were pain control (incidence of pain relief postoperatively and pain score) and postoperative morbidity. Secondary outcome measures assessed were the newly acquired endocrine insufficiency and exocrine insufficiency postoperatively, nutritional status, professional rehabilitation, QoL, operative time, and length of hospital stay. Moreover, long-term QoL was assessed in this study.

DATA EXTRACTION AND QUALITY ASSESSMENT

Two reviewers (J.S. and D.Y.) independently considered the eligibility of potential abstracts and titles. Retrieval strategies were refined with a smaller set of reports. When there was a disagreement about a study or insufficient information for an accurate assessment of eligibility, the authors were contacted for further information to ensure accuracy. Data were extracted independently and in duplicate by both reviewers, and discrepancies were resolved by discussion. The quality of RCTs was assessed by the Cochrane Risk of Bias Tool.[13] The quality of observational studies was assessed by the Newcastle-Ottawa Scale[14] (also see the eTable; http://www.archsurg.com). The loss to follow-up and the way in which missing data were handled for all studies were also assessed.

DATA SYNTHESIS AND ANALYSIS

We performed the meta-analysis using the software package RevMan, version 5.1.[15] Dichotomous variables were presented as relative risks (RRs) with 95% CIs and continuous variables as weighted mean differences with 95% CIs. Fixed-effects models and random-effects models were used, with significance set at $P = .10$. Medians were converted to means using the technique described by Hozo et al.[16] Statistical heterogeneity was assessed using the I^2 statistic.[13] Subgroup analysis was used to assess the efficacy of different procedures. Sensitivity analysis was performed by exclusion of observational studies. Funnel plots were used to screen for publication bias.

RESULTS

STUDY CHARACTERISTICS

The characteristics of the included studies[17-35] are listed in the **Figure** and **Table 1**, which includes details regarding the enrolled participants and methods of pain evaluation and metabolism function test. All were single-center studies, and the total number of patients per study ranged from 39 to 123. Most patients were men and underwent DPPHR or PD by the diagnosis of CP based on contrast-enhanced computed tomography scan, duodenoscopy, endoscopic retrograde cholangiopancreatography, and endocrine and exocrine functional test results. The Beger and Frey procedures were included in DPPHR, whereas PD comprised the Whipple procedure and PPPD. Pain evaluation was by the incidence of pain relief postoperatively or pain score.[17,19-23,25-29] The tests of the pancreatic endocrine function were assessed according to the need to treat diabetes mellitus with diet modification, oral hypoglycemic agents, or insulin. Serum C-peptide levels and glycohemoglobin concentrations were also used in 2 studies.[22,24] Exocrine function

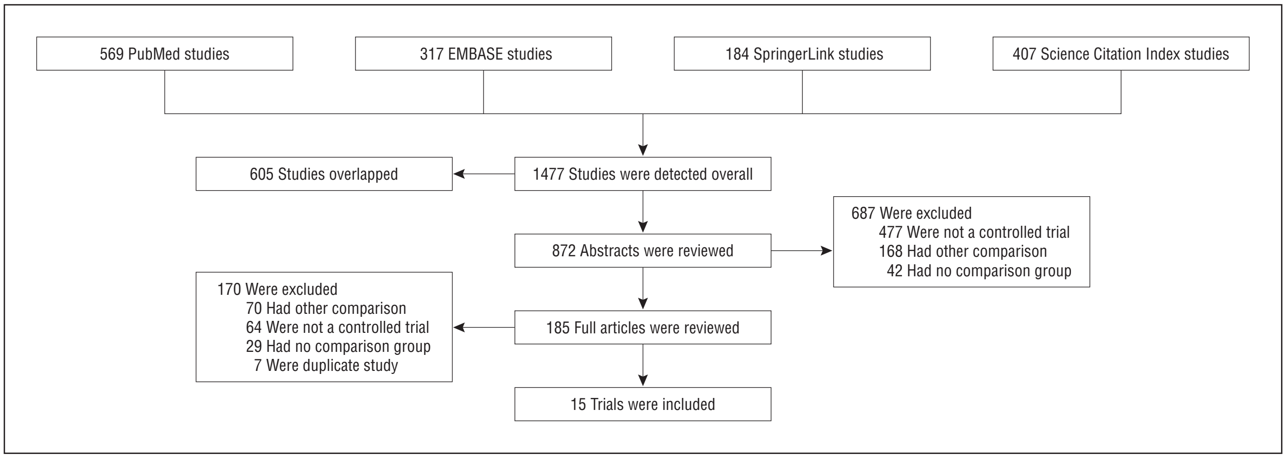

Figure. Flowchart of publication search and selection.

was estimated by means of the fecal human elastase concentration test or the need to treat maldigestion with enzyme substitution therapy in most trials. Nine studies[17-22,27,30,31] reported QoL of the patients, and long-term results were available in 4 studies.[32-35] The follow-up period ranged from 6 months to 14 years in these trials.[32]

QUALITY OF INCLUDED STUDIES

The agreement between 2 reviewers for study selection was 0.93 and for quality assessment of trials was 0.90. The studies were generally of moderate quality with minimal publication bias. We evaluated the risk of bias in the 5 published RCTs[20,22,23,26,27] by the Cochrane Risk of Bias Tool[13] (**Table 2**). Allocation sequence generation and allocation concealment were confirmed for 2 studies.[22,27] No study clearly described masking of the patient, personnel, or observer. Adequate assessment of each outcome and selective outcome reporting was available in 5 randomized trials, but none of the included studies reported intention-to-treat analysis. Two studies[22,27] have initially estimated the sample size for study. For the 10 observational studies,[17-19,21,24,25,28-31] the risks of bias were evaluated by modification of the Newcastle-Ottawa Scale.[14] Also, the outcomes may have been influenced by the selection bias in all trials for allocation to different strategies. Although Chiang et al[24] and Witzigmann et al[21] reported a protocol for the DPPHR and the PD group, respectively, allocation may have been at the surgeon's discretion in most studies. No study adequately described the patient flow. Methods for handling missing data were not adequately described in most studies.

PAIN CONTROL AND POSTOPERATIVE MORBIDITY

Table 3 presents summary estimates, 95% CIs, and *P* values for the test for heterogeneity for each of the strategies under study. Duodenum-preserving pancreatic head resection resulted in a higher incidence of postoperative pain relief (RR, 1.08; 95% CI, 0.97-1.20; $P = .15$; $I^2 = 20\%$) and a lower pain score (−4.67; −13.47 to 4.12; $P = .30$; $I^2 = 91\%$) postoperatively compared with PD. The overall pooled estimate of postoperative morbidity showed no statistical difference between DPPHR and PD (RR, 0.67; 95% CI, 0.44-1.03; $P = .07$; $I^2 = 60\%$). The RRs for postoperative pain relief and postoperative morbidity in the Beger procedure were 1.29 (95% CI, 1.03-1.61; $P = .03$) and 0.55 (0.21-1.39; $P = .20$), respectively, compared with PD. These results are just the opposite in the Frey procedure, which had a significantly better outcome in postoperative morbidity compared with resection (RR, 0.60; 95% CI, 0.46-0.78; $P = .01$) but not in postoperative pain relief (1.03; 0.90-1.17; $P = .67$).

SECONDARY OUTCOMES

With respect to newly acquired endocrine insufficiency, the RR for DPPHR was 0.42 (95% CI, 0.15-1.22) compared with PD; this difference was not significant ($P = .11$). A significant decrease in postoperative exocrine insufficiency was found in DPPHR (RR, 0.30; 95% CI, 0.13-0.70; $P \leq .01$) and in the drainage procedure (0.69; 0.47-1.00; $P = .05$). As for blood transfusion and hospital stay, DPPHR had significantly lower RRs in contrast to PD with pooled estimates of −1.28 (95% CI, −2.32 to −0.25; $P = .02$) and −3.93 (−4.48 to −3.38; $P \leq .01$), respectively. Nutritional status (as shown in postoperative weight gain) and professional rehabilitation favored the DPPHR or drainage procedure.

SUBGROUP AND SENSITIVITY ANALYSES

Subgroup analyses were performed to evaluate whether the RRs of outcome measures were different according to the various surgical techniques. As shown in Table 2, although no significant difference was found in overall morbidity between both arms, DPPHR had a significantly decreased incidence of delayed gastric emptying postoperatively (RR, 0.11; 95% CI, 0.04-0.35; $P \leq .01$). Short- and long-term global QoL both favored DPPHR. Similar primary outcomes were obtained when the analysis was restricted to the 4 RCTs[20,22,23,26] of DPPHR vs PD with a total sample size of 192 patients: the RR for postoperative pain relief was 1.13 (95% CI, 0.96-1.33) ($P = .13$) and the RR for postoperative morbidity was 0.54 (0.20-1.46) ($P = .22$).

Table 1. Characteristics of Included Trials in Surgical Management of Chronic Pancreatitis

Source	Comparison	DPPHR/PD Male Sex, No. (%)	DPPHR/PD Age, Mean (Range or SD), y	Pain Evaluation	DPPHR/PD Postop Morbidity, No. (%)	Metabolism Function Test, Endocrine/ Exocrine	DPPHR/PD Global QoL, Mean (SD)	Follow-up
Belina et al,[17] Czech Republic (2005)	Frey vs PD (Retro)	56 (98)/ 48 (81)	45 (23-71)/ 48 (29-71)	Pain score	22 (39)/ 23 (48)	NA	62.85 (22.87)/ 58.21 (19.42)	Median global QoL improved by 30.4% in the Frey group; improvement was significant in all scales except cognitive function
Büchler et al,[20] Germany (1995)	Beger vs PPPD (Pro)	23 (90)/ 25 (90)	43 (9)/ 48 (11)	Pain score and postop relief	3 (15)/ 4 (20)	Oral glucose load/ Serum pancreolauryl	72.40 (21.40)/ 67.90 (18.60) (long term)[32]	After 6 mo, patients in the DPPHR group had less pain, greater weight gain, better glucose tolerance, and higher insulin secretion capacity; long-term follow-up was undertaken after 7 and 14 y[32]
Chiang et al,[24] Taiwan, China (2007)	Frey vs Whipple (Pro)	25 (80)/ 17 (94)	40 (12)/ 40 (15)	NA	5 (20)/ 2 (12)	According to the need to treat DM with diet modification, OHA, or insulin and serum C-peptide levels and HbA_{1c} concentrations/ By estimating the fecal human elastase I concentration and BT-PABA testing	NA	Pain evaluation and metabolism, including endocrine and exocrine function, were assessed 3 and 6 mo after surgical intervention
Farkas et al,[23] Hungary (2006)	Frey vs PPPD (Pro)	20 (75)/ 20 (75)	43 (5)/ 40 (15)	Postop relief	0/8 (40)	Glucose tolerance test/Stool elastase tests	NA	Follow-up ranged 12-35 mo; no patient died
Hildebrand et al,[25] Germany (2010)	Frey vs Whipple (Retro)	39 (77)/ 12 (83)	47 (9)/ 54 (10)	Pain score	8 (21)/ 5 (42)	According to the need to treat DM with diet modification/ According to the need to treat maldigestion with enzyme substitution therapy	NA	During the median follow-up of 50 mo, pain relief was observed in 93% of the Frey group and 67% of the Whipple group
Izbicki et al,[27] Germany (1995)	Frey vs Beger (Pro)	22 (73)/ 20 (75)	44 (6)/ 45 (8)	Pain score and postop relief	2 (9)/ 4 (20)	By the need to treat DM with diet modification, OHA, or insulin and C-peptide levels and HbA_{1c} concentrations/ By estimation of fecal chymotrypsin concentration and the pancreolauryl test	58.35 (20.85)/ 66.7 (25.00) (long term)[35]	During the mean follow-up of 1½ y, total relief of symptoms was observed in 95% of the Beger group and 89% of the Frey group (NS); for both groups, the global QoL improved by 67% and working ability scores improved by 50%
Izbicki et al,[22] Germany (1998)	Frey vs PPPD (Pro)	31 (81)/ 30 (87)	43 (7)/ 45 (5)	Pain score and postop relief	6 (19)/ 16 (53)	By the need to treat DM with diet modification, OHA, or insulin and C-peptide levels and HbA_{1c} concentrations/ By estimation of fecal chymotrypsin concentration and the pancreolauryl test	85.70 (7.15)/ 57.10 (16.68); 58.35 (20.85)/ 50.00 (25.00) (long term)[34]	During a median follow-up of 24 mo, patients were reassessed in the outpatient clinic. The median global QoL improved by 200% in the extended drainage group and by 100% in the resection group ($P < .05$); long-term follow-up was undertaken after 7 y by Strate et al[34]
Keck et al,[28] Germany (2010)	Frey vs Beger (Retro)	50 (78)/ 42 (86)	45 (27-78)/ 41 (30-62)	Postop relief	15 (30)/ 17 (40)	According to the need to treat DM with diet modification/ According to the need to treat maldigestion with enzyme substitution therapy	NA	Median (range) follow-up was longer in the Beger than in the Frey group (62 [6-137] mo vs 43 [8-126] mo) (NS)
Kelemen and Horváth,[29] Hungary (2002)	Frey vs Beger + PPPD (Retro)	13 (100)/ 53 (90)	46 (36-58)/ 45 (36-64) (Beger); 48 (31-70) (PPPD)	Postop relief	0/21 (40)	By measurement of the fasting blood glucose level and the need of antidiabetic medication or insulin/By Lipiodol test	NA	The mean follow-up was 20.6 mo for the Frey group and 41.5 mo for the Beger group; at least two-thirds of the patients participated in the follow-up examination

(continued)

Table 1. Characteristics of Included Trials in Surgical Management of Chronic Pancreatitis (continued)

Source	Comparison	DPPHR/PD Male Sex, No. (%)	DPPHR/PD Age, Mean (Range or SD), y	Pain Evaluation	DPPHR/PD Postop Morbidity, No. (%)	Metabolism Function Test, Endocrine/ Exocrine	DPPHR/PD Global QoL, Mean (SD)	Follow-up
Klempa et al,[26] Germany (1995)	Beger vs PD (Pro)	22 (77)/ 21 (77)	47 (7)/ 47 (7)	Postop relief	4 (18)/ 6 (29)	According to the need to treat DM with diet modification and C-peptid/According to the need to treat maldigestion with enzyme substitution therapy	NA	60 mo after surgical intervention
van Loo et al,[30] Netherlands (2010)	PJS vs Beger + PPPD (Retro)	27 (69)/ 78 (69)	50 (42-56)/ 50 (42-56)	NA	9 (33)/ 26 (33)	According to the need to treat DM with diet modification/ According to the need to treat maldigestion with enzyme substitution therapy	94.30 (7.78)/ 58.40 (15.33)	Median follow-up was 5.6 y
Maartense et al,[31] Netherlands (2004)	PJS vs Beger (Retro)	12/27[a]	55 (3)/ 51 (2)	NA	0/5 (19)	By a glucose tolerance test, serum C-peptide measurements, and plasma PP levels/By urinary PABA recovery and 24-h fecal fat excretion	74.00 (21.00)/ 64.00 (15.00)	Follow-up was conducted by telephone or return visit; the median follow-up was 2.9 y
McClaine et al,[18] USA (2009)	DPPHR vs PD (Retro)	22 (36)/ 59 (44)	45 (11)/ 47 (11)	NA	12 (55)/ 26 (44)	According to the need to treat DM with diet modification/ According to the need to treat maldigestion with enzyme substitution therapy	52.80 (30.80)/ 48.80 (29.30)	Mean follow-up was 47 mo for the PD group and 14 mo for the DPPHR group ($P < .01$), reflecting a change in the authors' management algorithm for head-predominant chronic pancreatitis
Witzigmann et al,[21] Germany (2003)	Beger vs Whipple (Pro)	38 (74)/ 32 (78)	42 (10)/ 47 (12)	Postop relief	3 (8)/ 6 (19)	According to the need to treat DM with diet modification/By estimating the fecal elastase concentrations	70.00 (26.00)/ 64.00 (15.00); 75.00 (19.00)/ 65.00 (10.00) (long term)[33]	Follow-up ranged from 6-24 mo; long-term follow-up was undertaken after 7 y by Möbius et al[33]
Zheng et al,[19] China (2011)	DPPHR vs Whipple (Retro)	66 (77)/ 57 (89)	46 (9)/ 47 (10)	Postop relief	2 (3)/ 11 (19)	Determined via symptoms of diabetes/Determined via symptoms of steatorrhea	74.00 (21.00)/ 64.00 (15.00)	Follow-up was conducted by telephone or return visit; the median follow-up was 2.9 y

Abbreviations: BT-PABA, *N*-benzoyl-L-tryosyl para-amino benzoic acid; DM, diabetes mellitus; DPPHR, duodenum-preserving pancreatic head resection; HbA_{1c}, glycohemoglobin A_{1c}; NA, not available; NS, not significant; OHA, oral hypoglycemic agent; PD, pancreaticoduodenectomy; PJS, pancreaticojejunoanastomosis; postop, postoperative; PPPD, pylorus-preserving PD; Pro, prospective; QoL, quality of life; Retro, retrospective.

[a] No sex ratio was reported.

Table 2. Risk of Bias in the Published Randomized Controlled Trials[a]

Source	Allocation Sequence Described	Allocation Concealment	Other Potential Bias
Büchler et al,[20] 1995	No	No	Not powered; no ITT analysis
Farkas et al,[23] 2006	No	No	Not powered; no ITT analysis
Izbicki et al,[27] 1995	Yes	Yes	No ITT analysis
Izbicki et al,[22] 1998	Yes	Yes	No ITT analysis
Klempa et al,[26] 1995	No	No	Not powered; no ITT analysis

Abbreviation: ITT, intention-to-treat.

[a] In all studies, there was no masking of patients, personnel, or assessors; each outcome was adequately assessed; and the handling of missing data was unclear. All studies avoided selective outcome reporting, that is, there was no discrepancy in the findings reported in the final article vs the earlier conference proceedings.

COMMENT

The most common surgical indication for CP is intractable pain with the presence of an inflammatory mass in the pancreatic head or pancreatic head–related complications experienced by patients in whom conservative or endoscopic therapy has failed. Therefore, while retaining low morbidity, the aims of the optimal surgical approach should include pain relief, the elimination of CP-associated complications of adjacent organs, the possibility for preserva-

Table 3. Meta-analysis Including Subgroup Analysis and Sensitivity Analysis

Outcome, Comparison	Pooled Estimates, RR (95% CI)	*P* Value	I^2, %
Duration of operation, WMD			
DPPHR vs PD[a]	−93.15 (−135.05 to −51.25)	≤.01	95
Postop pain relief			
DPPHR vs PD	1.08 (0.97 to 1.20)	.15	20
Beger vs PD	1.29 (1.03 to 1.61)	.03	20
Drainage vs resection[b]	1.03 (0.90 to 1.17)	.67	0
Frey vs PD	1.00 (0.87 to 1.16)	.97	0
Exclusion of observational studies	1.13 (0.96 to 1.33)	.13	43
Postop morbidity			
DPPHR vs PD	0.67 (0.44 to 1.03)	.07	60
Drainage vs resection	0.60 (0.46 to 0.78)	≤.01	35
Beger vs PD	0.55 (0.21 to 1.39)	.20	0
Frey vs PD	0.58 (0.31 to 1.07)	.08	52
Exclusion of observational studies	0.54 (0.20 to 1.46)	.22	74
Delayed gastric emptying			
DPPHR vs PD	0.11 (0.04 to 0.35)	≤.01	0
Frey vs PPPD	0.06 (0.01 to 0.45)	≤.01	0
Pancreatic fistula/leak			
DPPHR vs PD	0.59 (0.25 to 1.37)	.22	0
Frey vs PD	0.62 (0.10 to 3.94)	.61	0
Wound infection			
DPPHR vs PD	1.51 (0.71 to 3.21)	.29	0
Pulmonary complication			
DPPHR vs PD	0.64 (0.28 to 1.47)	.29	0
Postoperative mortality			
DPPHR vs PD	0.73 (0.14 to 3.65)	.70	0
Endocrine insufficiency (newly acquired)			
DPPHR vs PD	0.42 (0.15 to 1.22)	.11	54
Drainage vs resection	1.00 (0.64 to 1.56)	.98	48
Frey vs PD	0.44 (0.08 to 2.42)	.35	71
Frey vs PPPD	0.67 (0.05 to 8.36)	.76	65
Exocrine insufficiency (newly acquired)			
DPPHR vs PD	0.30 (0.13 to 0.70)	≤.01	52
Drainage vs resection	0.69 (0.47 to 1.00)	.05	48
Frey vs PD	0.40 (0.20 to 0.78)	≤.01	47
Frey vs PPPD	0.32 (0.15 to 0.70)	≤.01	37
Blood transfusion, WMD			
DPPHR vs PD	−1.28 (−2.32 to −0.25)	.02	89
Hospital stay, WMD			
DPPHR vs PD	−3.93 (−4.48 to −3.38)	≤.01	41
Professional rehabilitation			
DPPHR vs PD	1.40 (1.10 to 1.78)	≤.01	0
Postop weight gain			
DPPHR vs PD	1.95 (1.49 to 2.54)	≤.01	27
Global QoL, WMD			
DPPHR vs PD	11.20 (0.87 to 21.53)	.03	87
Global QOL (long term), WMD			
DPPHR vs PD	8.33 (2.24 to 14.42)	≤.01	0

Abbreviations: DPPHR, duodenum-preserving pancreatic head resection; I^2, degree of statistical heterogeneity (0%-25%, moderate; 26%-50%, average; 51%-100%, high); PD, pancreaticoduodenectomy; postop, postoperative; PPPD, pylorus-preserving PD; QoL, quality of life; RR, relative risk; WMD, weighted mean difference.

[a] DPPHR includes Beger and Frey procedures; PD includes Whipple procedure and PPPD.

[b] Resection includes PD and Beger procedure; drainage includes Frey procedure.

tion of the endocrine and exocrine pancreatic functions, and finally an improvement of the patient's global QoL.[22] The Whipple and PPPD procedures, originally introduced to eliminate malignant lesions of the periampullary and pancreatic head region, were commonly used for surgical management of CP, although they amounted to surgical overtreatment in a benign pancreatic disorder and were associated with poor long-term results in patients with CP.[36] Duodenum-preserving pancreatic head resection procedures (in which the pylorus, duodenum, and extrahepatic bile duct are preserved) were developed in the past decades and have gradually replaced PD as standard surgical treatment for CP in some medical centers.[37] However, as yet, no procedure has met all the criteria for an ideal surgical treatment for CP.[22]

Pain is the crucial symptom in severe CP, and the progressive fibrotic inflammation in the pancreatic head acts as the pacemaker of the disease. Büchler et al[20] demonstrated better pain relief and pancreatic function when Beger's DPPHR was compared with PPPD. Almost the same results were published by Klempa et al,[26] who compared the Beger and Whipple procedures and found that the degree of pain relief was equal, but the Beger procedure provided quicker recuperation. When assessing preoperative and postoperative pain scores, Belina et al[17] showed significant pain relief in both groups; the *P* value was smaller ($<.01$) in the DPPHR group than in the PD group ($<.05$). In this systematic review and meta-analysis, DPPHR and PD were equally effective in achieving complete pain relief, as illustrated by a visual analog scale of pain or by assessment of the frequency of pain attacks and the need for strong analgesia. These results were also confirmed in the 5-year follow-up of a prospective nonrandomized study.[33]

As for postoperative morbidity, Büchler et al[20] reported morbidity rates of 15% and 20% for the DPPHR and PPPD groups, respectively. In PD, the resection extent is wide and the digestive tract needs to be reconstructed. This process changes the normal anatomy of the upper gut and the normal food passage through the stomach and duodenum.[38] Thus, the risk of postoperative complications should increase in theory. Several RCTs[22,23] comparing DPPHR and PD for the treatment of CP have confirmed the result. Although the pooled estimate in this meta-analysis detected no significant difference in overall postoperative morbidity between PD and DPPHR, the result favored DPPHR (*P* = .07). In the study by McClaine et al,[18] the 30-day morbidity rates did not differ significantly between the PD (44%) and DPPHR (55%) groups, and neither did the rates of delayed gastric emptying. However, our results showed DPPHR significantly decreases the incidence of delayed gastric emptying postoperatively (*P* = .01). Also, in the randomized trial by Müller et al,[39] delayed gastric emptying was described as one of the leading causes of postoperative morbidity after PPPD. In PD, the elimination of the duodenum may impair gastric peristalsis, injure the nerves of Latarjet, lead to ischemia of the duodenal stump, and influence the antropyloric muscle mechanisms. From this point, the duodenal pacemaker (which is located distally 0.5-1 cm from the pylorus) should be preserved to avoid gastric peristalsis disturbances.[39] As for drainage procedures, significantly lower postoperative morbidity was detected in the pooled estimate compared with resection procedures, but drainage procedures failed to provide complete pain relief in most cases.[27]

In 1 investigation, a correlation was found between diabetes and mortality for patients with CP.[40] It is not clear whether disease progression or surgery substantially influences the risk of diabetes development. In the study by Witzigmann et al,[21] more patients seemed to develop diabetes following the Whipple procedure. After a 14-year follow-up, Müller et al[32] reported that the rates of patients with insulin-dependent diabetes were 50% and 79% in the Beger and PPPD procedures, respectively, but the difference was not statistically significant, and the need for pancreatic enzyme substitution was similar in both groups. Theoretically, the islets of Langerhans containing β cells are distributed predominantly in the tail of the pancreas; thus, the endocrine function should not be affected greatly.[24] Furthermore, this meta-analysis identified significant improvement of the pancreatic exocrine function in DPPHR. Also, DPPHR significantly reduced the length of hospitalization compared with PD and had better short- and long-term QoL results in this meta-analysis.

In reviewing the literature, we were surprised to discover very few randomized studies evaluating the surgical interventions in CP. Thus, the main limitation of this review is the low number of RCTs, which makes it difficult to acquire enough data for meaningful results. In most observational controlled trials, whether the patient underwent DPPHR was decided by the surgeon, and allocation to DPPHR or PD was based on the surgeon's preference according to intraoperative findings and the experience of the surgeon, which tended to increase the risk of bias in the results. In addition, universal definitions of postoperative complications were not available among the included studies; thus, subjectivity remained a potential limitation in assessing complications in each trial. However, strict inclusion and exclusion criteria were established to judge the quality of the trials and observational studies following an extensive literature search performed to provide the most up-to-date information. Besides, the Preferred Items for Systematic Reviews and Meta-Analyses and Meta-analysis of Observational Studies in Epidemiology guidelines were used for the reporting of our systematic review, and non-English studies were included to minimize publication bias. This enabled us to include the most valid studies currently published from established centers of excellence.

This review and meta-analysis were conducted at an appropriate time because enough data have accumulated for inspection by meta-analytical methods. We found that DPPHR is used more commonly. Finally, subgroup and sensitivity analyses demonstrated more detailed information on Beger and Frey procedures, which are equally safe and effective compared with PD. For the duodenum-preserving strategy of the Beger procedure, complete pain relief is achieved in most patients, but no evidence showed a better result for postoperative morbidity. For the extended drainage strategy of the Frey procedure, a significantly lower postoperative morbidity is demonstrated, but complete pain relief is not provided in most cases. Thus, compared with conventional PD, both new strategies should be recommended on the basis of the patients' appropriate individual preferences.

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