ORIGINAL ARTICLE

Evidence-Based Surgical Treatments for Chronic Pancreatitis

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Jörg Kleeff*, Christian Stöb*, Julia Mayerle, Lynne Stecher, Matthias Maak, Peter Simon, Ulrich Nitsche, Helmut Friess

SUMMARY

Background: If conservative treatment of chronic pancreatitis is unsuccessful, surgery is an option. The choice of the most suitable surgical method can be difficult, as the indications, advantages, and disadvantages of the available methods have not yet been fully documented with scientific evidence.

Methods: In April 2015, we carried out a temporally unlimited systematic search for publications on surgery for chronic pancreatitis. The target parameters were morbidity, mortality, pain, endocrine and exocrine insufficiency, weight gain, quality of life, length of hospital stay, and duration of surgery. Differences between surgical methods were studied with network meta-analysis, and duodenum-preserving operations were compared with partial duodenopancreatectomy with standard meta-analysis.

Results: Among the 326 articles initially identified, 8 randomized controlled trials on a total of 423 patients were included in the meta-analysis. The trials were markedly heterogeneous in some respects. There was no significant difference among surgical methods with respect to perioperative morbidity, pain, endocrine and exocrine insufficiency, or quality of life. Duodenum-preserving procedures, compared to duodenopancreatectomy, were associated with a long-term weight gain that was 3 kg higher ($p < 0.001$; three trials), a mean length of hospital stay that was 3 days shorter ($p = 0.009$; six trials), and a duration of surgery that was 2 hours shorter ($p < 0.001$; five trials).

Conclusion: Duodenum-preserving surgery for chronic pancreatitis is superior to partial duodenopancreatectomy in multiple respects. Only limited recommendations can be given, however, on the basis of present data. The question of the best surgical method for the individual patient, in view of the clinical manifestations, anatomy, and diagnostic criteria, remains open.

► Cite this as:

Kleeff J, Stöb C, Mayerle J, Stecher L, Maak M, Simon P, Nitsche U, Friess H: Evidence-based surgical treatments for chronic pancreatitis—a systematic review and meta-analysis of randomized controlled trials. *Dtsch Arztebl Int* 2016; 113: 489–96.
DOI: 10.3238/arztebl.2016.0489

*Jörg Kleeff and Christian Stöb are joint first authors.

Department of General, Visceral, and Pediatric Surgery, Düsseldorf University Hospital, Düsseldorf; Department of Surgery, The Royal Liverpool and Broadgreen University Hospitals NHS Trust, Liverpool, United Kingdom; and Department of Molecular and Clinical Cancer Medicine, Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom: Prof. Kleeff

Department of Surgery, Klinikum rechts der Isar, Technische Universität München, Munich: Stöb, Dr. Nitsche, PhD, Prof. Friess

Department of Internal Medicine A, Faculty of Medicine, University of Greifswald: Prof. Mayerle, Dr. Simon
Institute of Medical Statistics and Epidemiology, Klinikum rechts der Isar, Technische Universität München, Munich: Stecher, PhD

Department of Surgery, University Hospital Erlangen: Dr. Maak

Chronic pancreatitis has an annual incidence of 4 to 23 per 100 000 and a prevalence of 13 per 100 000 population (e1, e2). Etiologically, the disease is classified into genetic, autoimmune, and obstructive or toxic-metabolic forms (e1). In Germany, the most important risk factor for chronic pancreatitis amenable to influence is chronic alcohol abuse (1).

Between 10% and 40% of patients with chronic pancreatitis develop stenosis of the common bile duct and require treatment, which is often endoscopic. However, 61 to 86% of patients who receive endoscopic treatment experience no long-term benefit (e3–e7). The results of two randomized controlled trials, each of which investigated the efficacy of endoscopic treatment compared with a surgical intervention, led the authors to conclude that in the long term surgery is significantly superior to endoscopic treatment with regard to lasting freedom from pain. Respectively, pain was completely eliminated in 40% versus 16% ($p = 0.007$) (2) and in 34% versus 15% of patients ($p = 0.002$) (3). The S3 guideline of the German Society for Gastroenterology, Digestive and Metabolic Diseases (*Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten*, DGVS) (1) also recommends operative treatment if pain reduction cannot be maintained. Early surgery results in less parenchymal injury and lower rates of chronic pain with improved postoperative function of the remaining pancreatic tissue or of the islet cells after autologous transplantation (e8, e9). The basic options for surgical treatment are the following:

- Drainage of the pancreatic duct, e.g., by longitudinal pancreaticojejunostomy
- Resection of the chronically inflamed, painful, and functionally impaired tissue, e.g., duodenum-preserving pancreatic head resection (DPPHR) or partial duodenopancreatectomy
- A combination of these approaches.

To date there is no evidence-based scheme for surgery adapted to the individual etiology and symptoms. We therefore set out to examine the relevant surgical techniques and conduct a meta-analysis of the existing randomized controlled trials.

Methods

Two of us conducted a survey of the literature on 14 May 2015. The PubMed/Medline database was

searched according to the stipulations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement, with no restrictions on date of publication. As well as network meta-analyses, two-armed standard meta-analyses comparing duodenum-preserving procedures (DPPHR according to Beger or Frey, Bern variant of DPPHR, lateral pancreaticojejunostomy according to Puestow) with non-duodenum-preserving operations (classic and pylorus-preserving partial duodenopancreatectomy) were carried out. In contrast with standard meta-analysis, in which only two techniques of surgery are compared, network meta-analysis permits comparison of more than two procedures. With a third intervention as common comparator, comparisons can be performed that were not possible in the original publications (e2). Care must be taken, however, to ensure that study and patient characteristics are comparable and the observed effects sufficiently homogeneous (e10). Details of the methods can be found in the *eBox* and in *eFigure 1*.

Results

The options for the surgical treatment of chronic pancreatitis are presented below, together with the results of our meta-analyses of randomized trials.

Drainage surgery

Longitudinal pancreaticojejunostomy according to Partington and Rochelle: Following Puestow and Gillesby's description of drainage of the pancreatic duct in combination with distal pancreatic resection in 1958 (*eFigure 2*) (11, e13, e14), Partington and Rochelle developed longitudinal pancreaticojejunostomy (*eFigure 2*) (12, 13, e15, e16). The morbidity of this procedure is ca. 20% (13, e17). Dilatation of the pancreatic duct in patients without inflammatory enlargement of the head of the pancreas achieves early postoperative pain reduction in 65 to 93% of cases (14, 15, e18–e22) without significant impairment of endocrine and exocrine function (e20, e23). However, the rate of long-term freedom from pain is <60% (14, 16, e15).

Resection

Partial duodenopancreatectomy: The classic partial en-bloc duodenopancreatectomy described by Allen O. Whipple in 1935 (*eFigure 2*) retained its status as the standard for surgical treatment of chronic pancreatitis for many years (16), but has now been displaced by pylorus-preserving partial duodenopancreatectomy (*eFigure 2*). Although the publications cited here and below are principally observational studies, the current consensus is that preservation of the pylorus leads to a better functional outcome (16, e24, e25). Both procedures result in long-term pain relief in 50 to 95% of patients (17, e21, e26, e27); however, both are associated with relatively high rates of postoperative morbidity (20 to 53%) (6, e28) and 2 to 5% hospital mortality (10, 14, 16, 18, 19, e29). Suspicion of malignancy is currently one of the indi-

cations for partial duodenopancreatectomy in patients with chronic pancreatitis (16).

Duodenum-preserving pancreatic head resection according to Beger: Beger first developed and described DPPHR as an organ-preserving alternative to pylorus-preserving or classic duodenopancreatectomy in patients with chronic pancreatitis in 1972 (20). This subtotal resection of the pancreatic head, with division of the body of the pancreas, was born out of the realization that in many patients with chronic pancreatitis an oncological intervention represents overtreatment (*eFigure 2*). Duodenal passage is preserved (13, 21). DPPHR according to Beger results in long-term pain relief in 70 to 95% of cases (4, 16, 18, 22–24). The associated morbidity is 15 to 45% (4, 18, 22), with hospital mortality of 0.7 to 5% (5, 8, 18, 19, 23, e30).

Duodenum-preserving pancreatic head resection according to Frey: In 1987 Frey and Smith described a modification of DPPHR in combination with longitudinal pancreaticojejunostomy (*eFigure 2*) (25). The Frey operation is associated with morbidity of 9 to 39% (5, 6, 16, 26) and hospital mortality of <1% (4, 5, 25), as well as endocrine and exocrine insufficiency in 11 to 31% of cases (5, 25). Long-term pain relief is achieved in 75 to 92% of patients (4, 5, 25).

Duodenum-preserving pancreatic head resection (Bern variant): The modification of DPPHR developed by Büchler is based on the core concept of the Beger and Frey operations (*eFigure 2*). The head of the pancreas is hollowed out to provide local decompression without dividing the organ (27). With morbidity of <23% (28, e31) and hospital mortality of 0 to 1% (28), the risks attached to the Bern variant of DPPHR are comparable to those for the other established procedures (14).

V-shaped excision: In the variant described by Izbicki, patients with small-duct pancreatitis with pancreatic duct diameter <7 mm and no inflammatory mass in the pancreatic head are treated by decompression of the branch ducts (*eFigure 2*) (14, 28, e28). In Izbicki's original group of 13 patients, with endocrine and exocrine function preserved, 12 were completely free of symptoms after surgery; 2 had postoperative complications. There was no hospital mortality (28). No reports of this procedure exist in larger numbers of cases.

Distal pancreatic resection: Distal pancreatic resection (*eFigure 2*) is indicated in the rare cases in which chronic inflammation is present predominantly in the body or tail of the pancreas (16, 29, e32). Pain is relieved in 90% of patients with this rare manifestation (13), with morbidity of 15 to 31% and hospital mortality of 0 to 4% (e31).

Segmental resection: In the rare cases of circumscribed segmental pancreatitis in the body of the organ, a segment can be resected in isolation (*eFigure 2*). Since large portions of the pancreatic parenchyma remain in place, the rates of endocrine and exocrine insufficiency are low, well under <10% (30, e33). The

TABLE

Results of the evaluable trials*

Year, first author	Comparison	Morbidity (any complication)		Pain (no complete freedom from pain)		Endocrine insufficiency (diabetes mellitus requiring treatment)		Weight change (kg)	Quality of life (EORTC QLQ-C30 score, %)	Hospital stay (days)	Operating time (min)
		Result	Odds ratio, 95% CI	Result	Odds ratio, 95% CI	Result	Odds ratio, 95% CI				
1995, Buehler (19)	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR according to Beger	4/20 (20%) vs. 3/20 (15%)	1.4 [0.3; 7.3]	9/15 (60%) vs. 4/16 (25%)	4.5 [1.0; 20.8]			-2.2 [-3.0; -1.4]		1.0 [-2.4; 4.4]	
1995, Klempa (18)	Partial duodenopancreatectomy (classic) vs. DPPHR according to Beger	8/21 (38%) vs. 10/22 (45%)	0.7 [0.2; 2.5]	8/20 (40%) vs. 6/20 (30%)	1.6 [0.4; 5.8]	10/20 (50%) vs. 5/20 (25%)	3.0 [0.8; 11.4]			5.2 [2.9; 7.5]	
1997, Izbiccki (5)	DPPHR according to Beger vs. DPPHR according to Frey	12/38 (32%) vs. 8/36 (22%)	1.6 [0.6; 4.6]			13/38 (34%) vs. 11/36 (31%)	1.2 [0.4; 3.1]	0.2 [-0.9; 1.3]			31 [-7.8; 69.8]
1998, Izbiccki (6)	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR according to Frey	16/30 (53%) vs. 6/31 (19%)	4.8 [1.5; 14.9]						-28.6 [-35.1; -22.1]	-5.0 [-17.8; 7.8]	83 [48.1; 118]
2001, Hwang (9)	Partial duodenopancreatectomy (classic) vs. lateral pancreaticojejunostomy according to Puestow	3/8 (38%) vs. 0/10 (0%)	13.4 [0.6; 308]	7/8 (88%) vs. 0/10 (0%)	105 [3.7; 2 948]	4/8 (50%) vs. 0/10 (0%)	21.0 [0.9; 477]				125 [73.6; 176]
2006, Farkas (10)	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR (Bern)	8/20 (40%) vs. 0/20 (0%)	27.9 [1.5; 526]	2/20 (10%) vs. 3/20 (15%)	0.6 [0.1; 4.2]	3/20 (15%) vs. 0/20 (0%)	8.2 [0.4; 170]	-3.6 [-4.0; -3.2]		5.3 [3.5; 7.1]	136 [132; 140]
2008, Köninger (33)	DPPHR according to Beger vs. DPPHR (Bern)	6/32 (19%) vs. 7/33 (21%)	0.9 [0.3; 2.9]						-5.7 [-17.0; 5.6]	4.0 [-0.3; 8.3]	46 [9.1; 82.9]
2012, Keck (8)	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR according to Beger and Frey	13/43 (30%) vs. 14/42 (33%)	0.9 [0.3; 2.2]			19/43 (44%) vs. 19/42 (45%)	1.0 [0.4; 2.3]		0 [-9.8; 9.8]	1.5 [-2.0; 4.0]	

* Evaluable for morbidity, postoperative pain, endocrine function, weight change, quality of life, duration of hospital stay, and operating time EORTC QLQ-C30. Quality of Life Questionnaire Version 3.0 of the European Organisation for Research and Treatment of Cancer; DPPHR, duodenum preserving pancreatic head resection; CI, confidence interval

FIGURE 1

Direct comparison of the surgical procedures and their results with regard to morbidity and duration of hospital stay in a network meta-analysis. The diagrams on the left are visual representations of the comparisons shown in quantitative terms on the right.

DPPHR, duodenum-preserving pancreatic head resection; Part. duodenopancreatic, partial duodenopancreatectomy; Lat. pancreaticojejun., lateral pancreaticojejunostomy; CI, confidence interval

hospital mortality is <1%, and the morbidity rate is comparable with that of other types of resection (30, e33).

Total pancreatectomy: Occasionally postoperative recurrence or hereditary chronic pancreatitis requires total pancreatectomy (eFigure 2) (13). This procedure results in complete freedom from pain in 75 to 83% of patients (e32–e35). Insulin dependence (brittle diabetes) and total exocrine insufficiency, necessitating substitution, are inevitable consequences (13). The elevated risk of pancreatic cancer associated with chronic pancreatitis is eliminated (e36).

Since the 1990s it has been possible to isolate pancreatic islet cells and then carry out autologous transplantation following total pancreatectomy (e37). The early results were positive with regard to quality of life and consumption of painkillers (31), but the transplant failure rate has turned out to be high (32). Nevertheless, especially patients with minimal-change chronic pancreatitis or a hereditary or genetic etiology

and high risk of malignancy seem to benefit from early pancreatectomy and autologous transplantation, provided the residual function of the islet cells is satisfactory (e8, e38). Five years after autologous transplantation 59 to 73% of patients are still free of pain, and over the same period the rate of insulin dependency falls from 38% to 27% (e38, e39).

Meta-analysis of randomized studies

Of the 326 publications initially identified, 8 randomized controlled trials with 423 patients were included in the meta-analysis. eTable 1 details the characteristics of these studies, including possible sources of bias.

Morbidity: Izbicki et al. (6) and Farkas et al. (10) found significantly lower rates of complications for DPPHR according to Frey and the Bern variant of DPPHR than for partial duodenopancreatectomy (pylorus-preserving). The other six trials showed no significant differences among the procedures (Table). Network analysis of the seven evaluable studies

FIGURE 2

Results of standard meta-analysis comparing duodenum-preserving operations (DPPHR [Bern], DPPHR according to Beger, DPPHR according to Frey, lateral pancreaticojejunostomy according to Puestow) and partial duodenopancreatectomy (classic and pylorus-preserving) with regard to morbidity, postoperative pain, and endocrine insufficiency (odds ratio, 95% confidence interval)
DPPHR, duodenum-preserving pancreatic head resection; Duodenopancreatic, duodenopancreatectomy

revealed that in comparison with DPPHR according to Beger, the complication rate was non-significantly higher for partial duodenopancreatectomy (pylorus-preserving) (odds ratio [OR] 2.96; 95% confidence interval [CI] [0.77; 11.35]; $p = 0.122$) and non-significantly lower for drainage according to Puestow (OR 0.06, 95% CI [0.00; 2.21]; $p = 0.124$) (Figure 1). A matrix with effect estimators and CIs for all pairwise comparisons in the network analysis can be found in eTable 2. In the standard meta-analysis partial duodenopancreatectomy displayed non-significantly higher morbidity (OR 2.15, 95% CI [0.81; 5.67]; $p = 0.124$) (Figure 2).

Mortality: Five trials reported hospital mortality, but only in one of them (18) did deaths occur. For both partial duodenopancreatectomy (classic) and DPPHR according to Beger, 1 of a group of 20 patients died.

Pain: Among four studies, Büchler et al. (19) and Hwang et al. (9) found a significantly higher rate of freedom from pain after DPPHR (Table). Comparison of DPPHR with partial duodenopancreatectomy showed a higher rate of freedom from pain for the former, but the difference was not significant (OR 2.06, 95% CI [0.69; 6.17]; $p = 0.196$) (Figure 2).

Endocrine insufficiency (diabetes mellitus): The five trials that reported postoperative diabetes mellitus showed no significant differences (Table). Standard meta-analysis revealed a non-significantly higher risk of diabetes after partial duodenopancreatectomy (36 of 91 versus 24 of 92; OR 2.61, 95% CI [0.78; 8.74]; $p = 0.115$) (Figure 2).

Exocrine insufficiency: Exocrine pancreatic insufficiency is generally hard to quantify. Only two trials reported the rate of insufficiency in a comparable manner, and only one of them compared DPPHR with partial duodenopancreatectomy. Therefore, no formal meta-analysis could be carried out. The absolute rate of newly occurring exocrine insufficiency after operation differed widely: 3 of 74 patients (4%) (5) and 20 of 85 probands (23.5%) (8). However, the relative difference within the two studies was small (2.8% versus 5.2% and 21% versus 26%).

Weight gain: Postoperative weight gain was presented in various ways and was reported by only three of the trials (Table), which between them covered four operations. For this reason, network meta-analysis was not feasible. Two studies (10, 19) were suitable for comparison of DPPHR and partial duodenopancreatectomy; they showed significantly greater weight gain after DPPHR in long-term follow-up for 6 to 30 months (mean difference 2.94 kg, 95% CI [1.57; 4.31]; $p < 0.001$) (Figure 2, eFigure 3). These results are in agreement with those of a study that was not amenable to meta-analysis (18).

Quality of life: Three trials provided quantitative data on postoperative quality of life (6). In two cases (6, 8), however, the mean differences could only be estimated after conversion of the original data (Table, eBox). Izbicki et al. (6) found that the patients' quality of life was significantly better after DPPHR according

to Frey than after partial duodenopancreatectomy (pylorus-preserving). Meta-analysis could not be performed owing to the small number of trials and their scant comparability.

Length of hospital stay: Network meta-analysis of six trials showed that classic duodenopancreatectomy was followed by a significantly longer stay in hospital (*Figure 1*). Standard meta-analysis also showed a longer hospital stay for partial duodenopancreatectomy than for DPPHR (mean difference 3.13 days, 95% CI [0.77; 5.49]; $p = 0.009$) (*eFigure 3*).

Operating time: Three of the five evaluable trials compared partial duodenopancreatectomy with DPPHR and found that the average operating time was longer for the former procedure; the differences were 83, 125, and 136 min (*Table*). Furthermore, Koninger et al. (33) reported that the operating time for DPPHR according to Beger was on average 46 min longer than for the Bern variant of DPPHR ($p = 0.020$). Reliable network meta-analysis was not possible. However, standard meta-analysis confirmed the findings of Koninger et al., revealing that the operating time was 117 min (95% CI [80.35; 153]) longer for partial duodenopancreatectomy ($p < 0.001$) (*Figure 2, eFigure 3*).

Discussion

This review compares the surgical treatments for chronic pancreatitis. Potential limitations are the high degree of heterogeneity of the trials in standard meta-analysis and restriction of the systematic literature survey to Medline alone. The data available for analysis permit neither a global recommendation for or against the use of any particular procedure nor unequivocal recommendation of any of the methods in the presence of particular anatomical circumstances, symptoms, or etiology. Duodenum-preserving interventions seem to offer a certain benefit with regard to morbidity, weight loss, hospital stay, and operating time. Pancreatic surgeons should be familiar with all intervention techniques so that whatever the individual situation they can select the least invasive option that will successfully solve the problem.

Long-term analyses show that the benefits of duodenum-preserving operations are time dependent. In the Hamburg cohort initially described by Izbicki et al. (6), DPPHR according to Frey was superior to partial duodenopancreatectomy. Apart from the above-mentioned perioperative factors, the patients also exhibited a higher quality of life with regard to physical performance capacity; after 7 years, however, this was no longer apparent (34). By 15 years after surgery (7), DPPHR according to Frey was superior in this respect, as well as showing lower long-term mortality and less weight loss. However, the data of only 35 of the original 62 patients were available for analysis. The cohort described by Büchler et al. (19) also showed initial superiority of DPPHR, this time according to Beger, over partial duodenopancreatectomy in the first 6 months after operation, particularly with regard to pain, weight loss, and glucose tolerance.

At 7 and 14 years after surgery, respectively, analysis of 27 and 29 of the original 40 patients no longer revealed significant differences for these parameters. At 14 years, DPPHR according to Beger was demonstrably superior in terms of appetite, subjective well-being, and overall time in full employment since the operation (35). Comparing the various duodenum-preserving interventions, apart from the above-mentioned perioperative factors a further Hamburg cohort showed no significant differences in quality of life, pain, and exocrine or endocrine pancreatic function between DPPHR according to Frey and DPPHR according to Beger—neither initially (5) nor after 7 years (36) or 16 years (in 45 of the original 74 patients) (37). However, the greatly reduced number of patients in the long-term follow-up means that these results have to be interpreted with caution.

An earlier meta-analysis of six randomized controlled trials, two prospective studies, and seven retrospective investigations agreed with our review in finding that both operating time (mean difference -93 min, 95% CI $[-135; -51]$; $p < 0.01$; $I^2 = 95\%$) and length of hospital stay (mean difference: -3.9 days 95% CI $[-4.5; -3.4]$; $p < 0.01$; $I^2 = 41\%$) were shorter for DPPHR than for partial duodenopancreatectomy (38). DPPHR according to Beger was significantly superior to partial duodenopancreatectomy ($p = 0.03$; $I^2 = 20\%$) with regard to pain reduction. A further meta-analysis of two randomized controlled trials together with the long-term results of two other randomized controlled trials and a retrospective study also found better quality of life, greater weight gain, and less diarrhea after DPPHR in general than after partial duodenopancreatectomy. Nevertheless, there were no significant differences in pain reduction directly after surgery, mortality, or exocrine and endocrine pancreatic function (39). A recent analysis of five studies, including one randomized trial, agreed with us in finding no important differences among the various DPPHR procedures (40). A feature shared by all reviews published to date is that they only investigate subgroups of operation techniques (38, 39, 40) and potentially display increased bias because they included no randomized controlled trials (38, 40). To our knowledge, no exhaustive evaluation including network meta-analysis has yet been carried out.

In conclusion, patients should always be treated at specialized centers, where they can receive interdisciplinary advice and multimodal treatment. There are several surgical options for the treatment of chronic pancreatitis. Further randomized trials are required as the sole means of establishing evidence-based, personalized treatments—conservative, interventional, or surgical—depending on the patient's individual etiology, anatomy, and symptoms. These studies will have to evaluate the procedures they compare with regard to morbidity, mortality, pain, endocrine and exocrine insufficiency, and quality of life.

KEY MESSAGES

- The usual procedures of choice for the surgical treatment of chronic pancreatitis with predominant inflammatory enlargement of the pancreatic head (>4 cm) are duodenum-preserving pancreatic head resection (DPPHR) and its modifications. In the case of marked bile duct compression with obstructive jaundice, partial duodenopancreatectomy can be considered.
- In isolated dilatation of the pancreatic duct without enlargement of the head of the organ, a parenchyma-sparing drainage procedure or a problem-oriented intervention with partial pancreatic resection should be employed.
- In the presence of chronic pain without enlargement of the pancreatic head and without dilatation of the pancreatic duct, a V-shaped incision or total pancreatectomy with autologous islet cell transplantation may be appropriate.
- If malignancy is suspected, oncological partial duodenopancreatectomy should be carried out.
- In hereditary chronic pancreatitis, total pancreatectomy with autologous islet cell transplantation can be considered.

Conflict of interest statement

The authors declare that no conflict of interest exists.

Manuscript received on 18 January 2016, revised version accepted on 21 April 2016

Translated from the original German by David Roseveare

REFERENCES

1. Chronic Pancreatitis German Society of Digestive and Metabolic Diseases (DGVS), Hoffmeister A, Mayerle J, et al.: [S3-Consensus guidelines on definition, etiology, diagnosis and medical, endoscopic and surgical management of chronic pancreatitis German Society of Digestive and Metabolic Diseases (DGVS)]. *Z Gastroenterol* 2012; 50: 1176–224.
2. Cahen DL, Gouma DJ, Nio Y, et al.: Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med* 2007; 356: 676–84.
3. Dite P, Ruzicka M, Zboril V, Novotny I: A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy* 2003; 35: 553–8.
4. Izbicki JR, Bloechle C, Knoefel WT, Kuechler T, Binmoeller KF, Broelsch CE: Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis. A prospective, randomized trial. *Ann Surg* 1995; 221: 350–8.
5. Izbicki JR, Bloechle C, Knoefel WT, et al.: [Drainage versus resection in surgical therapy of chronic pancreatitis of the head of the pancreas: a randomized study]. *Chirurg* 1997; 68: 369–77.
6. Izbicki JR, Bloechle C, Broering DC, Knoefel WT, Kuechler T, Broelsch CE: Extended drainage versus resection in surgery for chronic pancreatitis: a prospective randomized trial comparing the longitudinal pancreaticojejunostomy combined with local pancreatic head excision with the pylorus-preserving pancreatoduodenectomy. *Ann Surg* 1998; 228: 771–9.
7. Bachmann K, Tomkoetter L, Kutup A, et al.: Is the Whipple procedure harmful for long-term outcome in treatment of chronic pancreatitis? 15-years follow-up comparing the outcome after pylorus-preserving pancreatoduodenectomy and Frey procedure in chronic pancreatitis. *Ann Surg* 2013; 258: 815–20; discussion 20–1.
8. Keck T, Adam U, Makowiec F, et al.: Short- and long-term results of duodenum preservation versus resection for the management of chronic pancreatitis: a prospective, randomized study. *Surgery* 2012; 152: 95–102.
9. Hwang TL, Chen HM, Chen MF: Surgery for chronic obstructive pancreatitis: comparison of end-to-side pancreaticojejunostomy with pancreaticoduodenectomy. *Hepatogastroenterology* 2001; 48: 270–2.
10. Farkas G, Leindler L, Daroczi M, Farkas G Jr.: Prospective randomised comparison of organ-preserving pancreatic head resection with pylorus-preserving pancreaticoduodenectomy. *Langenbecks Arch Surg* 2006; 391: 338–42.
11. Puestow CB, Gillesby WJ: Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. *AMA Arch Surg* 1958; 76: 898–907.
12. Partington PF, Rochelle RE: Modified Puestow procedure for retrograde drainage of the pancreatic duct. *Ann Surg* 1960; 152: 1037–43.
13. Pericoli Ridolfini M, Gourgiotis S, Alfieri S, et al.: [Indications and outcomes of surgical management of chronic pancreatitis: literature review]. *G Chir* 2007; 28: 164–74.
14. Bachmann K, Kutup A, Mann O, Yekebas E, Izbicki JR: Surgical treatment in chronic pancreatitis timing and type of procedure. *Best Pract Res Clin Gastroenterol* 2010; 24: 299–310.
15. Prinz RA, Greenlee HB: Pancreatic duct drainage in chronic pancreatitis. *Hepatogastroenterology* 1990; 37: 295–300.
16. Hartel M, Tempia-Caliera AA, Wente MN, Z'Graggen K, Friess H, Büchler MW: Evidence-based surgery in chronic pancreatitis. *Langenbecks Arch Surg* 2003; 388: 132–9.
17. Traverso LW, Kozarek RA: Pancreatoduodenectomy for chronic pancreatitis: anatomic selection criteria and subsequent long-term outcome analysis. *Ann Surg* 1997; 226: 429–35; discussion 35–8.
18. Klempa I, Spatny M, Menzel J, et al.: [Pancreatic function and quality of life after resection of the head of the pancreas in chronic pancreatitis. A prospective, randomized comparative study after duodenum preserving resection of the head of the pancreas versus Whipple's operation]. *Chirurg* 1995; 66: 350–9.
19. Büchler MW, Friess H, Müller MW, Wheatley AM, Beger HG: Randomized trial of duodenum-preserving pancreatic head resection versus pylorus-preserving whipple in chronic pancreatitis. *Am J Surg* 1995; 169: 65–9; discussion 9–70.
20. Beger HG, Krautzberger W, Gogler H: [Resection of the head of the pancreas (cephalic pancreatectomy) with conservation of the duodenum in chronic pancreatitis, tumours of the head of the pancreas and compression of the common bile duct (author's transl)]. *Chirurgie* 1981; 107: 597–604.
21. Königer J, Friess H, Müller M, Büchler MW: Duodenum preserving pancreatic head resection in the treatment of chronic pancreatitis. *Rocz Akad Med Białymst* 2004; 49: 53–60.
22. Büchler MW, Friess H, Bittner R, et al.: Duodenum-preserving pancreatic head resection: long-term results. *J Gastrointest Surg* 1997; 1: 13–9.
23. Beger HG, Schlosser W, Friess HM, Büchler MW: Duodenum-preserving head resection in chronic pancreatitis changes the natural course of the disease: a single-center 26-year experience. *Ann Surg* 1999; 230: 512–9; discussion 9–23.
24. Frey CF, Amikura K: Local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy in the management of patients with chronic pancreatitis. *Ann Surg* 1994; 220: 492–504; discussion 504–7.

25. Frey CF, Smith GJ: Description and rationale of a new operation for chronic pancreatitis. *Pancreas* 1987; 2: 701–7.
26. Beger HG, Büchler M, Bittner RR, Oettinger W, Roscher R: Duodenum-preserving resection of the head of the pancreas in severe chronic pancreatitis. Early and late results. *Ann Surg* 1989; 209: 273–8.
27. Gloor B, Friess H, Uhl W, Büchler MW: A modified technique of the Beger and Frey procedure in patients with chronic pancreatitis. *Dig Surg* 2001; 18: 21–5.
28. Izbicki JR, Bloechle C, Broering DC, Kuechler T, Broelsch CE: Longitudinal V-shaped excision of the ventral pancreas for small duct disease in severe chronic pancreatitis: prospective evaluation of a new surgical procedure. *Ann Surg* 1998; 227: 213–9.
29. Sawyer R, Frey CF: Is there still a role for distal pancreatectomy in surgery for chronic pancreatitis? *Am J Surg* 1994; 168: 6–9.
30. Müller MW, Assfalg V, Michalski CW, Buchler P, Kleeff J, Friess H: [Middle segmental pancreatic resection: an organ-preserving option for benign lesions]. *Chirurg* 2009; 80: 14–21.
31. White SA, Davies JE, Pollard C, et al.: Pancreas resection and islet autotransplantation for end-stage chronic pancreatitis. *Ann Surg* 2001; 233: 423–31.
32. Lakey JR, Mirbolooki M, Shapiro AM: Current status of clinical islet cell transplantation. *Methods Mol Biol* 2006; 333: 47–104.
33. Königer J, Seiler CM, Sauerland S, et al.: Duodenum-preserving pancreatic head resection—a randomized controlled trial comparing the original Beger procedure with the Berne modification (ISRCTN No. 50638764). *Surgery* 2008; 143: 490–8.
34. Strate T, Bachmann K, Busch P, et al.: Resection vs drainage in treatment of chronic pancreatitis: long-term results of a randomized trial. *Gastroenterology* 2008; 134: 1406–11.
35. Muller MW, Friess H, Martin DJ, Hinz U, Dahmen R, Büchler MW: Long-term follow-up of a randomized clinical trial comparing Beger with pylorus-preserving whipple procedure for chronic pancreatitis. *Br J Surg* 2008; 95: 350–6.
36. Strate T, Taherpour Z, Bloechle C, et al.: Long-term follow-up of a randomized trial comparing the Beger and Frey procedures for patients suffering from chronic pancreatitis. *Ann Surg* 2005; 241: 591–8.
37. Bachmann K, Tomkoetter L, Erbes J, et al.: Beger and Frey procedures for treatment of chronic pancreatitis: comparison of outcomes at 16-year follow-up. *J Am Coll Surg* 2014; 219: 208–16.
38. Yin Z, Sun J, Yin D, Wang J: Surgical treatment strategies in chronic pancreatitis: a meta-analysis. *Arch Surg* 2012; 147: 961–8.
39. Lu WP, Shi Q, Zhang WZ, Cai SW, Jiang K, Dong JH: A meta-analysis of the long-term effects of chronic pancreatitis surgical treatments: duodenum-preserving pancreatic head resection versus pancreatoduodenectomy. *Chin Med J (Engl)* 2013; 126: 147–53.
40. Jawad ZA, Tsim N, Pai M, et al.: Short and long-term post-operative outcomes of duodenum preserving pancreatic head resection for chronic pancreatitis affecting the head of pancreas: a systematic review and meta-analysis. *HPB (Oxford)* 2016; 18: 121–8.

Corresponding author

Prof. Dr. med. Helmut Friess
Chirurgische Klinik und Poliklinik
Klinikum rechts der Isar
Technische Universität München
Ismaninger Str. 22
81675 München, Germany
helmut.friess@tum.de

[Supplementary material](#)
For eReferences please refer to:
www.aerzteblatt-international.de/ref2916

eBox, eTable, eFigure:
www.aerzteblatt-international.de/16m0489

Supplementary material to:

Evidence-Based Surgical Treatments for Chronic Pancreatitis

A Systematic Review and Meta-analysis of Randomized Controlled Trials

by Jörg Kleeff, Christian Stöb, Julia Mayerle, Lynne Stecher, Matthias Maak, Peter Simon, Ulrich Nitsche, and Helmut Friess

Dtsch Arztebl Int 2016; 113: 489–96. DOI: 10.3238/arztebl.2016.0489

eREFERENCES

- e1. Etemad B, Whitcomb DC: Chronic pancreatitis: diagnosis, classification, and new genetic developments. *Gastroenterology* 2001; 120: 682–707.
- e2. Mayerle J, Hoffmeister A, Werner J, Witt H, Lerch MM, Mössner J: Chronic pancreatitis—definition, etiology, investigation and treatment. *Dtsch Arztebl Int* 2013; 110: 387–93.
- e3. Rösch T, Daniel S, Scholz M, et al.: Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. *Endoscopy* 2002; 34: 765–71.
- e4. Kahl S, Zimmermann S, Genz I, et al.: Risk factors for failure of endoscopic stenting of biliary strictures in chronic pancreatitis: a prospective follow-up study. *Am J Gastroenterol* 2003; 98: 2448–53.
- e5. Deviere J, Nageshwar Reddy D, Puspok A, et al.: Successful management of benign biliary strictures with fully covered self-expanding metal stents. *Gastroenterology* 2014; 147: 385–95; quiz e15.
- e6. Perri V, Boskoski I, Tringali A, et al.: Fully covered self-expandable metal stents in biliary strictures caused by chronic pancreatitis not responding to plastic stenting: a prospective study with 2 years of follow-up. *Gastrointest Endosc* 2012; 75: 1271–7.
- e7. Poley JW, Cahen DL, Metselaar HJ, et al.: A prospective group sequential study evaluating a new type of fully covered self-expandable metal stent for the treatment of benign biliary strictures (with video). *Gastrointest Endosc* 2012; 75: 783–9.
- e8. Chinnakotla S, Radosevich DM, Dunn TB, et al.: Long-term outcomes of total pancreatectomy and islet auto transplantation for hereditary/genetic pancreatitis. *J Am Coll Surg* 2014; 218: 530–43.
- e9. Winny M, Paroglou V, Bektas H, et al.: Insulin dependence and pancreatic enzyme replacement therapy are independent prognostic factors for long-term survival after operation for chronic pancreatitis. *Surgery* 2014; 155: 271–9.
- e10. Kiefer C, Sturtz S, Bender R: Indirect comparisons and network meta-analyses. *Dtsch Arztebl Int* 2015; 112: 803–8.
- e11. Rücker G: Network meta-analysis, electrical networks and graph theory. *Res Synth Methods* 2012; 3: 312–24.
- e12. Neupane B, Richer D, Bonner AJ, Kibret T, Beyene J: Network meta-analysis using R: a review of currently available automated packages. *PLoS One* 2014; 9: e115065.
- e13. Ceppa EP, Pappas TN: Modified puestow lateral pancreaticojejunostomy. *J Gastrointest Surg* 2009; 13: 1004–8.
- e14. O'Neil SJ, Aranha GV: Lateral pancreaticojejunostomy for chronic pancreatitis. *World J Surg* 2003; 27: 1196–202.
- e15. Prinz RA, Aranha GV, Greenlee HB: Redrainage of the pancreatic duct in chronic pancreatitis. *Am J Surg* 1986; 151: 150–6.
- e16. Howell JG, Johnson LW, Sehon JK, Lee WC: Surgical management for chronic pancreatitis. *Am Surg* 2001; 67: 487–90.
- e17. Pakosz-Golanowska M, Post M, Lubikowski J, et al.: Partington-rochelle pancreaticojejunostomy for chronic pancreatitis: analysis of outcome including quality of life. *Hepatogastroenterology* 2009; 56: 1533–7.
- e18. Bradley EL 3rd: Long-term results of pancreaticojejunostomy in patients with chronic pancreatitis. *Am J Surg* 1987; 153: 207–13.
- e19. Nealon WH, Thompson JC: Progressive loss of pancreatic function in chronic pancreatitis is delayed by main pancreatic duct decompression. A longitudinal prospective analysis of the modified puestow procedure. *Ann Surg* 1993; 217: 458–66; discussion 66–8.
- e20. Prinz RA, Greenlee HB: Pancreatic duct drainage in 100 patients with chronic pancreatitis. *Ann Surg* 1981; 194: 313–20.
- e21. Sarles JC, Nacchiero M, Garani F, Salasc B: Surgical treatment of chronic pancreatitis. Report of 134 cases treated by resection or drainage. *Am J Surg* 1982; 144: 317–21.
- e22. Warshaw AL: Conservation of pancreatic tissue by combined gastric, biliary, and pancreatic duct drainage for pain from chronic pancreatitis. *Am J Surg* 1985; 149: 563–9.
- e23. Adams DB, Ford MC, Anderson MC: Outcome after lateral pancreaticojejunostomy for chronic pancreatitis. *Ann Surg* 1994; 219: 481–7; discussion 7–9.
- e24. Mobius C, Max D, Uhlmann D, et al.: Five-year follow-up of a prospective non-randomised study comparing duodenum-preserving pancreatic head resection with classic Whipple procedure in the treatment of chronic pancreatitis. *Langenbecks Arch Surg* 2007; 392: 359–64.
- e25. Fitzmaurice C, Seiler CM, Buchler MW, Diener MK: [Survival, mortality and quality of life after pylorus-preserving or classical Whipple operation. A systematic review with meta-analysis]. *Chirurg* 2010; 81: 454–71.
- e26. Stone WM, Sarr MG, Nagorney DM, McIlrath DC: Chronic pancreatitis. Results of Whipple's resection and total pancreatectomy. *Arch Surg* 1988; 123: 815–9.
- e27. Martin RF, Rossi RL, Leslie KA: Long-term results of pylorus-preserving pancreatoduodenectomy for chronic pancreatitis. *Arch Surg* 1996; 131: 247–52.
- e28. Bachmann K, Mann O, Izbicki JR, Strate T: Chronic pancreatitis—a surgeons' view. *Med Sci Monit* 2008; 14: RA198–205.
- e29. Yeo CJ, Cameron JL, Sohn TA, et al.: Six hundred fifty consecutive pancreatoduodenectomies in the 1990s: pathology, complications, and outcomes. *Ann Surg* 1997; 226: 248–57; discussion 57–60.
- e30. Christiansen J, Olsen JH, Worning H: The pancreatic function following subtotal pancreatectomy for cancer. *Scand J Gastroenterol Suppl* 1971; 9: 189–93.
- e31. Sakorafas GH, Sarr MG, Rowland CM, Farnell MB: Postobstructive chronic pancreatitis: results with distal resection. *Arch Surg* 2001; 136: 643–8.
- e32. Rattner DW, Fernandez-del Castillo C, Warshaw AL: Pitfalls of distal pancreatectomy for relief of pain in chronic pancreatitis. *Am J Surg* 1996; 171: 142–5; discussion 5–6.
- e33. Müller MW, Friess H, Kleeff J, et al.: Middle segmental pancreatic resection: an option to treat benign pancreatic body lesions. *Ann Surg* 2006; 244: 909–18; discussion 18–20.
- e34. Warshaw AL, Banks PA, Fernandez-Del Castillo C: AGA technical review: treatment of pain in chronic pancreatitis. *Gastroenterology* 1998; 115: 765–76.
- e35. Sakorafas GH, Farnell MB, Farley DR, Rowland CM, Sarr MG: Long-term results after surgery for chronic pancreatitis. *Int J Pancreatol* 2000; 27: 131–42.
- e36. Ueda J, Tanaka M, Ohtsuka T, Tokunaga S, Shimosegawa T, Research Committee of Intractable Diseases of the Pancreas: Surgery for chronic pancreatitis decreases the risk for pancreatic cancer: a multicenter retrospective analysis. *Surgery* 2013; 153: 357–64.
- e37. Merani S, Shapiro AM: Current status of pancreatic islet transplantation. *Clin Sci (Lond)* 2006; 110: 611–25.
- e38. Wilson GC, Sutton JM, Smith MT, et al.: Total pancreatectomy with islet cell autotransplantation as the initial treatment for minimal-change chronic pancreatitis. *HPB (Oxford)* 2015; 17: 232–8.
- e39. Wilson GC, Sutton JM, Abbott DE, et al.: Long-term outcomes after total pancreatectomy and islet cell autotransplantation: is it a durable operation? *Ann Surg* 2014; 260: 659–65; discussion 65–7.

eBOX

Methods

● Study registration and funding

The study was registered in the PROSPERO database (www.crd.york.ac.uk/PROSPERO) as project number CRD42015023306. No funds were received for this study.

● Literature search

The survey of the Pubmed/Medline database was carried out on 14 May 2015 in accordance with the PRISMA Statement (www.prisma-statement.org), selectively for the systematic review and systematically with the search terms “chronic pancreatitis” and “surgery” for the meta-analysis. Two of the authors conducted the search independently of each other and with no restrictions on language or time of publication. *eFigure 1* shows the study flowchart in accordance with the PRISMA criteria. The identified studies were evaluated on the basis of title, abstract, or full text and their reference lists were also checked. Only randomized controlled trials that compared at least two different surgical procedures were considered. If two or more publications covered the same cohort, owing to an increased number of patients (4, 5) or extension of the follow-up period (6, 7), only the most relevant publication was included (*eFigure 1*).

● Statistics

As far as permitted by the data, network meta-analyses were conducted using the netmeta package of R (e11, e12). The network graphs show the surgical techniques directly compared with each other in the individual studies. For binary outcome parameters we calculated the log odds ratios, in each case relative to the reference procedure, duodenum-preserving pancreatic head resection (DPPHR) according to Beger. For continuous outcome parameters mean differences were calculated. Mean and standard deviation, if not given, were estimated from the median and range. In addition, we conducted a two-arm standard meta-analysis to compare duodenum-preserving and non-duodenum-preserving operations. The random-effects model was used for both forms of meta-analyses. Because of the large number of procedures compared in a relatively small number of studies with heterogeneous patient populations, the analyses should be considered explorative in nature.

Keck et al. (8) compared partial duodenopancreatectomy (pylorus-preserving) with DPPHR according to Beger and Frey; accordingly, this study could be included only in the standard meta-analysis, not in the network meta-analysis of individual operation techniques.

Izbicki et al. (6) and Keck et al. (8) provided only median and range data for postoperative quality of life scores. To calculate confidence intervals for descriptive comparison, we used the medians as means and estimated the standard deviations by dividing the range by four. This rough approximation is not recommended by the Cochrane Handbook for Systematic Reviews of Interventions (www.cochrane-handbook.org), so the results must be interpreted with caution.

In the trials published by Hwang et al. (9) and Farkas et al. (10) the data on range of operating time were unclear. Although numbers described as the standard deviations are given, the low spread of the absolute numbers in each case indicates that these values ought actually to be the standard errors of the mean. For this reason, reliable calculations were not possible. Shown here is the meta-analysis with calculation using standard deviations. The results and the level of significance ($p < 0.001$) do not change to any meaningful degree when the mean is calculated with the aid of the standard error (not shown).

Literature survey

eFIGURE 2

Schematic illustrations

- a) Normal pancreas
- b) Extent of resection in lateral pancreaticojejunostomy according to Puestow/Gillesby
- c) Longitudinal pancreaticojejunostomy according to Partington/Rochelle
- d) Partial duodeno-pancreatectomy (classic)
- e) Partial duodeno-pancreatectomy (pylorus-preserving)
- f) Duodenum-preserving pancreatic head resection (DPPHR) according to Beger
- g) DPPHR according to Frey
- h) V-shaped excision
- i) DPPHR (Bern)
- j) Distal pancreatic resection
- k) Segmental resection
- l) Total pancreatectomy

eFIGURE 3

Results of standard meta-analysis

comparing duodenum-preserving surgical procedures (DPPHR [Bern], DPPHR according to Beger and Frey, lateral pancreaticojejunostomy according to Puestow) with partial annecticoduodenectomy (classic and pylorus-preserving) with regard to weight gain, duration of hospital stay, and operating time (mean difference in kilograms, days, and minutes, respectively; 95% confidence interval).

DPPHR, duodenum-preserving pancreatic head resection; Duodenopanocr., duodenopancreatotomy

eTABLE 1

Characteristics of the eight trials included in meta-analysis*

Year, first author	Study design	Comparison	Patients (n)	Recruitment period	Age (mean)	Sex (male/female)	Selection (sequence generation)	Selection (allocation concealment)	Conduct (blinding of participants)	Detection (blinding of outcome assessment)	Loss (complete documentation)	Reporting (complete data)	Duration of pancreatitis (months)	Diabetes before surgery	Pancreatic head mass	Pancreatic duct stenosis	Pancreatic calcification	Pain before surgery	Duodenal stenosis
1995, Büchler (19)	RCT	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR according to Beger	40	1991–1993	45	36/4	?	+	?	?	+	+	62	n.d.	98%	83%	n.d.	78%	18%
1995, Klempa (18)	RCT	Partial duodenopancreatectomy (classic) vs. DPPHR according to Beger	40	1987–1993	47	33/10	+	+	?	–	+	+	75	28%	n.d.	n.d.	n.d.	100%	14%
1997, Izbiccki (5)	RCT	DPPHR according to Beger vs. DPPHR according to Frey	74	1992–1997	43	54/20	?	+	?	?	+	–	61	28%	100%	73%	n.d.	100%	11%
1998, Izbiccki (6)	RCT	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR according to Frey	61	1995–1998	44	51/10	?	+	?	?	+	–	62	28%	100%	100%	n.d.	100%	8%
2001, Hwang (9)	RCT	Partial duodenopancreatectomy (classic) vs. lateral pancreaticojejunostomy according to Puestow	18	1998–2001	49	16/2	?	+	?	?	+	+	24	n.d.	n.d.	100%	n.d.	n.d.	n.d.
2006, Farkas (10)	RCT	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR (Bern)	40	2002–2004	44	30/10	?	+	?	?	+	–	90	n.d.	98%	83%	n.d.	83%	18%
2008, Königer (33)	RCT	DPPHR according to Beger vs. DPPHR (Bern)	65	2002–2005	47	45/20	?	+	?	?	+	+	40	17%	n.d.	n.d.	n.d.	n.d.	n.d.
2012, Keck (8)	RCT	Partial duodenopancreatectomy (pylorus-preserving) vs. DPPHR according to Beger and Frey	85	1997–2001	42	72/13	–	?	?	?	+	+	48	24%	n.d.	n.d.	75%	88%	13%

DPPHR, duodenum-preserving pancreatic head resection; n.d., no data; RCT, randomized controlled trial

* The risks of bias by selection, conduct, detection, loss, or reporting were classified into low (+), high (–), and unclear or missing data (?) following the recommendations of the Cochrane Handbook (www.cochrane-handbook.org)

TABLE 2

Matrix with effect estimators and confidence intervals for all pairwise comparisons in the network meta-analyses

Morbidity						
	DPPHR according to Beger	DPPHR (Bern)	Partial duodenopancre. (classic)	DPPHR according to Frey	Partial duodenopancre. (pylorus-preserving)	Lateral pancreaticojejun. according to Puestow
DPPHR according to Beger		1.42 [0.33; 6.16]	1.35 [0.27; 6.83]	1.61 [0.46; 5.65]	0.34 [0.09; 1.29]	18.1 [0.45; 722.96]
DPPHR (Bern)	0.70 [0.16; 3.04]		0.95 [0.11; 8.44]	1.13 [0.18; 7.07]	0.24 [0.04; 1.41]	12.7 [0.24; 672.59]
Partial duodenopancre. (classic)	0.74 [0.15; 3.72]	1.05 [0.12; 9.32]		1.19 [0.15; 9.21]	0.25 [0.03; 2.04]	13.4 [0.49; 367.38]
DPPHR according to Frey	0.62 [0.18; 2.18]	0.88 [0.14; 5.52]	0.84 [0.11; 6.51]		0.21 [0.06; 0.76]	11.2 [0.23; 552.19]
Partial duodenopancre. (pylorus-preserving)	2.96 [0.77; 11.35]	4.21 [0.71; 25.14]	4.01 [0.49; 32.85]	4.78 [1.32; 17.31]		53.7 [1.06; 2 715.73]
Lateral pancreaticojejun. according to Puestow	0.06 [<0.01; 2.21]	0.08 [<0.01; 4.16]	0.07 [<0.01; 2.06]	0.09 [<0.01; 4.38]	0.02 [<0.01; 0.94]	

p (Cochran's Q) = 0.229; tau² = 0.30

Hospital stay						
	DPPHR according to Beger	DPPHR (Bern)	Partial duodenopancre. (classic)	DPPHR according to Frey	Partial duodenopancre. (pylorus-preserving)	
DPPHR according to Beger		4.17 [1.32; 7.02]	-5.20 [-7.54; -2.86]	-6.10 [-19.17; 6.96]	-1.10 [-3.84; 1.63]	
DPPHR (Bern)	-4.17 [-7.02; -1.32]		-9.37 [-13.05; -5.68]	-10.27 [-23.15; 2.61]	-5.27 [-6.94; -3.60]	
Partial duodenopancre. (classic)	5.20 [2.86; 7.54]	9.37 [5.68; 13.05]		-0.90 [-14.17; 12.37]	4.10 [0.50; 7.69]	
DPPHR according to Frey	6.10 [-6.96; 19.17]	10.27 [-2.61; 23.15]	0.90 [-12.37; 14.17]		5.00 [-7.77; 17.77]	
Partial duodenopancre. (pylorus-preserving)	1.10 [-1.63; 3.84]	5.27 [3.60; 6.94]	-4.10 [-7.69; -0.50]	-5.00 [-17.77; 7.77]		

p (Cochran's Q) = 0.9189; tau² <0.01

DPPHR, duodenum-preserving pancreatic head resection; duodenopancre., duodenopancreatotomy; pancreaticojejun., pancreaticojejunostomy