Chirurgia (2023) 118: 335-347
No. 4, July - August

http://dx.doi.org/10.21614/chirurgia.2023.v.118.i.4.p.335

From Classic Whipple to Pylorus Preserving Pancreaticoduodenectomy and Ultimately to Pylorus Resecting – Stomach Preserving Pancreaticoduodenectomy: A Review

Dimitrios Symeonidis, Dimitrios Zacharoulis, Labrini Kissa, Athina A. Samara*, Eleana Petsa, Konstantinos Tepetes

Department of Surgery, University Hospital of Larissa, Mezourlo, Larissa, Greece

***Corresponding author:**
Athina A Samara MD, MSc
Department of Surgery
University Hospital of Larissa
Mezourlo, 41110, Larissa, Greece
Tel: +2413501701
E-mail: at.samara93@gmail.com

Received: 10.06.2023
Accepted: 16.08.2023

Rezumat

De la clasicul Whipple la pancreatico-duodenectomia cu prezervarea pilorului și, în cele din urmă, la rezecția pilorului - pancreatico-duodenectomia cu prezervarea stomacului: o revizuire

Pancreato-duodenectomia este procedura de elecție pentru tratamentul chirurgical al tumorilor benigne sau maligne ale regiunii periampulare. Conservarea pilorului a fost stabilită ca cea mai frecventă abordare utilizată în timpul pancreato-duodenectomiei în majoritatea centrelor specializate în tratamentul chirurgical al cancerului pancreatic, din întreaga lume. Factorii care au influențat această predilecție sunt scurtarea duratei intervenției chirurgicale, limitarea pierderilor de sânge intraoperatorii, dificultatea tehnică redusă şi rezultatele destul de asemănătoare pe termen scurt şi lung față de clasicul Whipple. Cu toate acestea, în literatura de specialitate, se evidențiază creşterea incidenței evacuării gastrice întârziate în urma pancreato-duodenectomiei de prezervare a pilorului. Printre alți factori, disfuncția pilorului atribuibilă manevrelor chirurgicale a fost recunoscută în etiologia acestei complicații. În încercarea de a depăşi această limitare a pancreato-duodenectomiei cu prezervarea pilorului, a fost propusă pancreato-duodenectomia de rezecție a pilorului cu prezervarea stomacului. În teorie, pancreato-duodenectomia cu rezecția pilorului ar putea menține avantajele operației de prezervare a stomacului, dar, în acelaşi timp, poate garanta o golire gastrică mai fluidă. Doar trei studii clinice randomizate şi-au propus, până în prezent, să evalueze această tehnică, şi un singur studiu a raportat rezultate în favoarea pancreato-duodenectomiei cu rezecția pilorului în ceea ce priveşte incidența evacuării gastrice întârziate. Studiul

PyloResPres, un studiu german multicentric în curs de desfăşurare care compară PPPD şi PRPD, înrolează în prezent pacienți, iar rezultatele sale ar putea oferi dovezi adecvate cu privire la abordarea optimă.

Cuvinte cheie: cancer pancreatic, procedura Whipple, pancreato-duodenectomie cu prezervarea pilorului, pancreato-duodenectomie cu rezecția pilorului, Chirurgie de prezervare a organelor

Abstract

Pancreaticoduodenectomy is the procedure of choice for benign or malignant tumors of the periampullary region. The preservation of the pylorus has been established as the mostly utilized approach during pancreaticoduodenectomy among the majority of specialized, in the surgical treatment of pancreatic cancer, centers worldwide. The factors that influenced this predilection are the shorter operation times, the less intraoperative blood loss, the decreased technical difficulty, and the quite similar short- and long-term outcomes compared to the classic Whipple. However, there is a notable trend in the literature highlighting the increased incidence of delayed gastric emptying following pylorus preserving pancreaticoduodenectomy. Among other factors, pylorus dysfunction attributable to the surgical maneuvers has been implemented in the etiology of this complication. In an attempt to overcome this limitation of the pylorus preserving pancreaticoduodenectomy, pylorus resecting pancreaticoduodenectomy with the preservation of the stomach was proposed. In theory, pylorus resecting pancreaticoduodenectomy could maintain the advantages of organ sparing surgery, but at the same time guarantee a more seamless gastric emptying. Only three RCTs, to date, aimed to evaluate the approach with only one reporting results in favor of the pylorus resecting pancreaticoduodenectomy in regard to the incidence of delayed gastric emptying. Further well-designed prospective randomized studies are needed for an accurate assessment of the true role of each of these surgical alternatives on the treatment of pancreatic cancer.

Key words: pancreatic cancer, Whipple's procedure, pylorus preserving pancreaticoduodenectomy, pylorus resecting pancreaticoduodenectomy, delayed gastric emptying

Introduction

Deciding on the proper treatment plan for pancreatic cancer is a rather complex equation. A multidisciplinary approach is required and surgery with curative intent, i.e. obtaining an R0 resection, plays a key role (1). In general, pancreatic surgery is a highly demanding field in regards to the technical aspects of the procedure itself but to the perioperative management of patients, as well. Traditionally, pancreatic resections have been regarded as procedures of high associated morbidity and mortality. Nowadays, a significant progress has been documented and mortality rates of less than 5% have been reported (2). Starting from the time of diagnosis, high hospital volume has clearly allowed mastering the whole process (3-4). However, despite the steadily decreased mortality rates, the high associated morbidity, even up to 50%, is still a major concern after any kind of pancreatic surgery (5). The room for improvement is more than obvious.

Pancreaticoduodenectomy (PD) is the procedure of choice for several, both benign

and malignant, tumors of the periampullary region. From the historical perspective, the procedure was first proposed by Kausch in 1909 (6). More than twenty years later, in 1935, Allen Whipple redefined the procedure as a two-stage operation with the second stage performed three to four weeks after the first stage (7). The first, one stage procedure was reported, six years later, simultaneously by Whipple and Trimble et al (8-9). The classic Whipple procedure involves a PD along with the resection of the distal part of the common bile duct, the gallbladder, and finally the gastric antrum. In 1944, Watson proposed a modification of the classic Whipple by omitting the antrectomy (10). Then, in 1978, Traverso and Longmire proposed a similar surgical technique with the preservation of the entire stomach, the pylorus, and the first 2.5 cm of the duodenum in two patients (a patient with chronic pancreatitis and a patient with distal duodenal cancer). The gastrointestinal tract continuity was re-established with a duodenojejunostomy in both cases (11). Two years later, the authors published a follow-up assessment focused on the functional results of the proposed technique. By the time of this publication, the sample size had been increased to 18 patients. The authors reported that pylorus-preserving pancreaticoduodenectomy (PPPD) was associated with decreased incidence of postgastrectomy syndrome defined as postprandial dumping, diarrhea, dyspepsia, nausea and vomiting and better functional results (12).

Since then, the penetration of PPPD among centers, specialized in pancreatic surgery, worldwide has been quite impressive as it was, at least initially, hypothesized to reduce the occurrence of dumping, diarrhea, and bile reflux gastritis and to improve overall nutritional status compared to the classic Whipple (13-14). From the technical viewpoint, the preservation of the pylorus during PD was associated with shorter operation times and less intraoperative blood loss (13-14). The crucial question at this point was whether this organ sparing approach, with its notable advantages, resulted in inferior oncological, long-term results compared to the classic Whipple. In theory, a strategy of "resecting less and preserving more" could increase the risk of positive resection margins and, ultimately, compromise the oncological efficiency of PD. Five randomized controlled trials (RCTs), comparing the PPPD with the classic Whipple in patients with pancreatic and/or periampullary tumors, that provided survival data did not reveal any differences in terms of overall survival between the two approaches (15-19). Similarly, a recent Cochrane database review reported no difference between PPPD and classic Whipple in terms of tumor recurrence, overall survival, and relevant morbidity parameters (20).

As soon as the oncological appropriateness of this organ preserving modification of the classic technique was established, the end points of the comparison between the PPPD and the classic Whipple were inevitably summarized in morbidity and short-term complication issues (21). In general, any form of pancreatic surgery can be complicated by the development of postoperative pancreatic fistulas (POPF), bile leaks, post-pancreatectomy hemorrhage, chyle leaks, intra-abdominal abscess / fluid collections, and delayed gastric emptying (DGE) (22). With the exception of the latter i.e. DGE, all of these complications do not seem to be directly correlated with the extent of gastric resection, if any. Therefore, the incidence of DGE after classic Whipple or PPPD was, commonly, utilized as the primary end point for the comparison of the two techniques in the majority of the relevant studies. In general, DGE is the most frequent complication after PD with a reported incidence ranging between 7 and 61 % (23). PPPD has been associated with an increased rate of DGE compared to the classic Whipple (31.4% vs. 23.5%; OR 3.03, 95% CI, 1.05-8.7, P=0.04) (20). It was hypothesized that, among other factors, the preservation of a dysfunctional pyloric ring because of innervation issues, occurred by the operative maneuvers, may be implemented in the etiology of DGE. (24). In attempt to overcome or, even, limit this bothersome complication associated with the PPPD, the pylorus resecting pancreatico-

duodenectomy (PRPD) with the preservation of the stomach was proposed (25).

The purpose of the present study was to evaluate and compare the various forms of PD i.e. the classic Whipple, the PPPD and the PRPD that arise depending on the extent of gastric resection, by reviewing the relevant literature (*Fig. 1*).

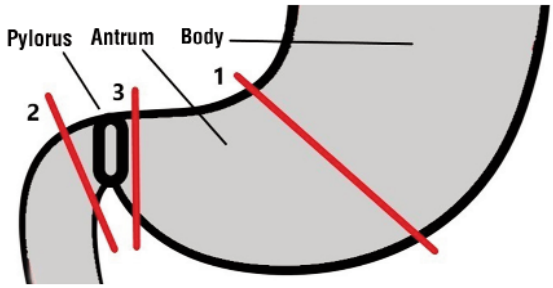

Figure 1. Level of proximal transection in: 1: Classic Whipple, 2: Pylorus preserving Pancreaticoduodenectomy (PPPD), and 3: Pylorus resecting – stomach preserving Pancreaticoduodenectomy (PRPD)

Methods

We conducted a literature search on the MEDLINE (PubMed), Scopus, Google Scholar, and Cochrane library electronic databases for articles published from the beginning of databases to 2023 aiming to include all prospective and retrospective studies assessing and comparing the different forms of PD. However, we have based the comparison mainly on the results of the available randomized control trials, systematic reviews, and meta-analyses. Exclusion criteria included the following: 1. Non-human studies; 2. Case reports; 3. Conference abstracts; 4. Studies with no full text available. The search strategy included combinations of the following key words: "Pancreatic surgery", "Whipple's procedure", "Pancreaticoduodenectomy", "Pylorus preserving pancreaticoduodenectomy", "Pylorus resecting pancreaticoduodenectomy" and "Delayed gastric emptying". After screening the titles and the abstracts of the retrieved studies for relevance, a full text review was conducted. The literature screening and the quality assessment of the retrieved articles were performed by two independent researchers. The opinion of a third senior researcher resolved any cases of disagreement.

Delayed Gastric Emptying

The outcomes of pancreatic surgery have been notably improved over the past three decades. In high volume centers, mortality rates of less than 5% have been reported (2,26-28). However, despite this favorable development, morbidity remains an important problem (2). DGE is one of the most troublesome postoperative complications following pancreatic surgery because it results in increased healthcare costs, increased hospital readmissions rates and compromised postoperative patients' quality of life (29-30). In addition, the risk of aspiration and nosocomial pneumonia is markedly increased (29). In general, the prompt restoration of normal enteral nutrition following any form of gastrointestinal surgery has been associated with several advantages such as the preservation of intestinal integrity, the prevention of intestinal mucosal atrophy, and the avoidance of bacterial translocation (31). Within this context, the occurrence of DGE after pancreatic surgery compromises the goal for early enteral feeding.

The pathogenesis of DGE on the background of pancreatic surgery seems to be multifactorial (32-33). Postoperative infectious and inflammatory complications such as POPF and intraperitoneal abscesses have been implemented in the etiology. These common complications, following any form of pancreatic surgery, cause gastric dysrhythmia due to the induced inflammation of the gastric wall remnant and subsequently increase the incidence of DGE (32-33). In general, after PD gastric motility is decreased (34). The resection of the duodenal pacemaker and the disruption of gastroduodenal neural connections have been also postulated as possible causes as extensive dissections along the common hepatic artery could disrupt crucial for gastric motility nerve pathways (34). Another possible mechanism is the ischemic injury on the antropyloric muscle mechanism due to dissections along the right

gastric artery ultimately causing pylorospasm (35).

Significance alterations at the hormonal level after PD seem to play an important role, as well (36). A reduction of the circulating levels of motilin has been documented following the resection of the duodenum and the proximal jejunum (36). Motilin is a polypeptide hormone that stimulates motility in several parts of the gastrointestinal tract (36-37). In support of the above, patients submitted to distal pancreatectomy rarely develop DGE (37). In addition, duodenum-preserving pancreatic head resection seem to be associated with a decreased incidence of DGE compared to PD (38-39). Preoperative diabetes mellitus has been strongly associated with increased incidence of DGE (40-41). Possible causes include the autonomic neuropathy, the fluctuations in blood glucose levels, and the effect of anti-diabetic medications on gastrointestinal motility (40-41).

However, pure technical parameters seem to significantly affect the incidence of complications and more specifically DGE after PD. The type of surgical reconstruction appears important. Available options include the s-Child reconstruction defined as the reconstruction with pancreaticojejunostomy followed by the hepaticojejunostomy and finally the gastrojejunostomy, the BE-Child reconstruction which includes an additional to the s-Child Braun enteroenterostomy, and the isolated Roux-en-Y pancreaticojejunostomy in which the pancreatic anastomosis is performed in a separate jejunal loop after the gastrojejunostomy (42). A recent meta-analysis of nineteen studies comparing these three reconstruction options concluded that the BE-Child reconstruction is associated with a decreased risk for postoperative complications, particularly a decreased risk for clinically relevant DGE, POPF, and bile leaks compared to the other alternatives (42). In general, DGE is directly related to other common complications of PD and especially POPF. Apart from DGE, POPF can lead to a series of significant secondary injuries such as abdominal cavity infection, false aneurysms, and abdominal bleeding (43-44). The latter i.e. the postoperative hemorrhage is the most serious complication with an associated mortality of as high as 50% (43). In this sense, interventions aiming to reduce the incidence of POPF will ultimately have an impact on DGE, as well. Interventions with documented effectiveness in reducing the rates of POPF include the following: 1. the use of external pancreatic duct drainage, 2. the administration of Ulinastatin, and 3. the adaptation of the invagination (versus duct-to-mucosa) technique for the pancreatojejunostomy (45-46).

However, as soon as a clinically significant POPF develops, a surgical intervention might be required. The surgical options include completion pancreatectomy, the revision of the pancreatic anastomosis or the open drainage and debridement. The secondary DGE on the background of POPF seems to be adequately addressed with the successful management of POPF (47). There is also evidence suggesting the favorable effect of early drain removal on the incidence of complications after PD (48). Apart from the early drain removal, various interventions included in the enhanced recovery protocols after PD have significantly aided in improving the outcomes of pancreatic surgery (49).

Until 2007, a universally accepted, objective, consensus definition of DGE after major pancreatic surgery was not available. The result was that each study dealing with the occurrence of DGE after pancreatic surgery adopted or proposed a different definition. For example, Miedema et al. defined DGE as the inability to tolerate full oral intake on the 14th postoperative day while Patel et al. lowered the threshold to the 7th postoperative day (50-51). Obviously, this approach entailed problems in regard to the interpretation and the comparison of the results out of different studies.

Aiming to overcome this notable limitation, the International Study Group of Pancreatic Surgery (ISGPS), in 2007, developed and proposed an objective and generally applicable definition and grading of DGE (52). This classification was based, primarily, on the severity and the clinical impact of this bothersome and

frustrating complication. According to this definition and grading system, there are three grades of DGE. DGE grade A results only in a transient alteration of the anticipated post-operative course, has no major clinical impact, and does not prolong the length of hospital stay. DGE grade B results in an extended hospital stay and, usually, requires the administration of prokinetic drugs and nutritional support. Finally, DGE grade C warrants a significant alteration on patients' management while the length of hospital stay is substantially prolonged. Parenteral or enteral nutritional support and treatment of any associated post-operative complications, such as pancreatic fistula or intra-abdominal abscesses are usually required in the clinical scenario of a grade C DGE (52).

Classic Whipple vs. PPPH

Historically, the transition, in regard to the surgical trends, from the classic Whipple to the PPPH for the treatment of periampullary tumors was not based on level I evidence. Factors such as the shorter operative time, the decreased level of technical difficulty, and the less intraoperative blood loss influenced the quest for and the adaptation of a valid alternative to the classic approach (21). Nevertheless, despite its less extensive nature as a curative operation, PPPH was associated with similar to the classic Whipple long-term oncological results (22). This fact focused the comparison of the two techniques on the short-term outcomes, the influence on the quality of patients' life and the nutritional recovery of following surgery. In general, the results of the randomized controlled trials (RCTs), published to date, are confusing (*Table 1*).

In 1998, Paquet et al. reported the results of their RCT showing that digestive and exocrine functions were better restored after PPPD and patients exhibited a better nutritional recovery and exocrine function. In addition, they emphasized that PPPD was an easier to perform procedure, technically wise (53). One year later, Wenger et al. randomized 48 patients with pancreatic and periambullary cancers to either classic Whipple or PPPD. They reported shorter operative time for the PPPD group and no differences in regard to morbidity between the two techniques. While there were no recorded differences in the global quality of life scores, gastrointestinal quality of life, defined by the presence of appetite and the absence of nausea and diarrhea, appeared increased in the PPPD group (54). Almost simultaneously with the previous two studies, Lin et al. were the first that highlighted the possibility of increased incidence of DGE after PPPD. In their RCT, DGE was observed in 6 out of 16 patients of the PPPD group and in only 1 out of 15 patients of the classic Whipple group. Although the result was not statistically significant (P=0.08), the authors highlight the trend and the need for increased sample size in order to confirm this finding. No differences were recorded, in this study, in regard to mortality, morbidity, operating time, blood loss, and blood transfusion requirements between the two groups (55).

In 2004, Tran et al. compared classic Whipple with PPPD and reported comparable operation time, blood loss, hospital stay, mortality, morbidity, and incidence of DGE. In this study, the authors compared the two techniques on the basis of their oncological efficiency, as well. Positive resection margins were found in 12 patients of the control group and 19 patients of the PPPD group ($P < 0.23$). Patients were followed up, for up to 115 months. The overall long-term and disease-free survival was comparable in both groups (56). Similar results were reported by Seiler et al. as well i.e. long-term survival, quality of life, and weight gain were identical after classic Whipple or PPPH at a median follow-up of 63.1 months (57). In 2008, Srinarmwong et al. reported that DGE occurred with increased frequency after PPPD (58) while Taher et al., in their 2015 study, reported similar morbidity between the two techniques (59).

Between 2007 and 2016, three meta-analyses were published comparing PPPH with classic Whipple (21,60-61). In the most recent one, the meta-analysis by Hanna et al.

Table 1. Randomized control trials comparing the classic Whipple with the Pylorus Preserving Pancreaticoduodenectomy

Author	Year of publication	Study type	No of patients (Whipple vs. PPPD)	Follow up	No Differences	PPPD Superior	Whipple Superior
Paquet et al. (53)	1998	RCT	23 vs. 17	Up to 12 years	Morbidity Hospital Mortality Long term Survival	Digestive and exocrine function restoration Nutritional recovery	
Wenger et al. (54)	1999	RCT	24 vs. 24	60 months	Morbidity Global quality of life	Operation time Gastrointestinal quality of life (appetite, nausea, diarrhea) Nutritional recovery	
Lin et al. (55)	1999	RCT	15 vs. 16	During hospital stay	Operative mortality – morbidity Operation time Blood loss Blood transfusion		DGE (Non SS)
Tran et al. (56)	2004	RCT	87 vs. 83	up to 115 months	Operation time Blood loss Hospital stay Mortality Morbidity DGE Overall and disease-free survival		
Seiler et al. (57)	2005	RCT	66 vs. 64	Up to 93 months	Perioperative morbidity Long-term survival Quality of life Weight gain	Capacity to work at 6 months	
Srinarmwong et al. (58)	2008	RCT	13 vs. 14	Up to 60 months	Operation time Blood loss Operative mortality and morbidity Hospital stay Survival		DGE
Taher et al. (59)	2015	RCT	8 vs. 12	During hospital stay	Morbidity	Blood loss Blood transfusions Hospital stay	
Burquets et al. (62)	2022	RCT	42 vs. 42	6 Months	DGE Postoperative morbidity Hospital stay	Anthropometric measurements (Triceps fold, upper arm circumference) at 6 months	

RCT: Randomized control trial, PPPD: Pylorus preserving pancreaticoduodenectomy

published in 2016, the authors report a lower incidence of DGE in the classic Whipple compared to the PPPD and when an antecolic approach for the gastrojejunostomy was utilized (61). The same year a Cochrane database systematic review was published by Hüttner et al. summarizing and appraising the existing data (20). The authors concluded that current evidence suggests no difference between the PPPH and the classic Whipple in terms of survival, postoperative mortality, and morbidity. However, a potential benefit, which could not be corroborated by the sensitivity analyses seems to be recorded for the classic operation in regard to the incidence of DGE. On the other hand, PPPD may indeed reduce operating time, intraoperative blood loss, and the need for red blood cell transfusion (20).

The most recent RCT (QUANUPAD trial) was published, in 2022, by Busquets et al. (62). The authors conclude that DGE incidence and severity did not differ between classic Whipple and PPPD although some anthropometric measurements, related with

the patients' nutritional recovery, such as triceps fold and upper arm circumferences may indicate a better recovery following PPPD (62). However, the authors do not advocate the generalized use of PPPD and suggest that the classic Whipple should remain the technique of choice for the surgical treatment of pancreatic cancer because it can be performed in all patients without the fear of duodenal ischemia.

PPPD vs. PRPD

The preservation of the pylorus, during PPPD, and its dysfunction as a cause of the increased frequency of DGE was the rationale behind the introduction of the pylorus resecting but stomach preserving modification of the classic Whipple (PRPD) (24). The theory of this organ preserving approach is to maintain, in total, the physiologic functions of the stomach in terms of storage and mixing of food with gastric secretions, which are important stages of the digestive process, and to simultaneously limit the increased incidence of DGE to the extent that the pylorus is responsible for (63). Three RCTs aimed to provide high quality evidence and determine the true role of PRPD by either confirming or denying the expectations out of the approach (*Table 2*).

In 2011, Kawai et al. randomized 130 patients with pancreatic cancer to either PPPD or PRPD. The authors concluded that PRPD significantly reduces the incidence of DGE (64). Three years later, the authors published the long-term results of their study. The favorable short-term results on DGE observed in the PRPD arm of the study seemed to be equally reflected in the long term follow-up, as well (65). An additional RCT by Matsumoto et al. with 100 patients reported a DGE incidence of 20% and 12 % for PPPD and PRPD, respectively. However, the result was not statistically significant (P 0.414) (66).

In 2019, Hackert et al. published the results of the currently largest RCT comparing PPPD and PRPD (PROPP trial) with 93 patients in each arm (67). According to the results, the DGE rate, within 30 days postoperatively, was not different between PPPD and PRPD (25.3% vs. 31.2%, OR 1.534, 95% CI, 0.788–2.978;

Table 2. Randomized control trials (RCT) comparing Pylorus Preserving Pancreaticoduodenectomy (PPPD) with Pylorus Resecting Pancreaticoduodenectomy (PRPD)

Author	Year of publication	Study type	No of patients (PPPD vs. PRPD)	Follow up	No Differences	PRPD Superior	PPPD Superior
Kawai et al. (64 - 65)	2011 2014	RCT	64 vs. 66	6 months – 24 months	Postoperative morbidity and mortality Quality of life Weight loss Nutritional status Long term outcomes	DGE	
Matsumoto et al. (66)	2014	RCT	50 vs. 50	3 years	DGE Postoperative serum albumin levels Serum total cholesterol levels Body mass index		
Hackert et al. (67)	2018	RCT	95 vs. 93	30 days	DGE		
Klaiber et al. (68)	2020	RCT	45 vs. 51	Up to 57 months (median: 36,2 months)	Endocrine / exocrine pancreatic function Receipt of chemotherapy Cancer recurrence Reoperations Readmissions Quality of life		Late cholangitis

RCT: Randomized control trial, DGE: Delayed gastric emptying, PPPD: Pylorus preserving pancreaticoduodenectomy, PRPD: Pylorus resecting pancreaticoduodenectomy

P=0.208). Thus, the resection of the pylorus did not reduce the incidence or severity of DGE and the authors assumed that the etiology of DGE seems to be multifactorial rather than attributable to the pyloric dysfunction alone. Based on their findings, the authors suggested that PPPD should remain the standard approach (67). The long-term results in terms of morbidity and quality of life of the PROPP trial were published in 2020 (68). The study included only 96 out of the 188 patients of the PROPP trial, as 63 patients died, and 29 patients were lost to follow-up. There was no difference between PPPD and PRPD patients regarding endocrine and exocrine pancreatic function, receipt of adjuvant/palliative chemotherapy, and disease recurrence. However, delayed cholangitis occurred significantly more often in patients following pylorus resection (P = 0.042). The authors concluded that similar to short-term results, long-term follow-up showed no significant differences between PPPD and PRPD (68).

In 2018, Klaiber et al. performed a meta-analysis of DGE after PPPD vs. PRPD including the three available RCTs and eight nonrandomized studies. The quantitative synthesis across all studies showed superiority for PRPD regarding DGE (OR 2·71, 95 per cent c.i. 1·48 to 4·96; P = 0·001) and length of hospital stay (mean difference 3·26 (95 per cent c.i. -1·04 to 5·48) days; P = 0·004). However, the superiority of PRPD was not confirmed in the subgroup analyses only of the available RCTs (69). The most recent attempt to incorporate all the existing data and draw a definite conclusion was conducted by Varghese et al. in their network meta-analysis of randomized trials. The overall incidence of DGE was 25.6 %. According to the results, the pylorus-resecting, antecolic, Billroth II with Braun enteroenterostomy was associated with the lowest rates of DGE and ranked the best in 35 % of all of the comparisons (70).

Discussion

The debate in regard to the optimal technique seems to be ongoing. The existing RCTs have significant limitations that should be taken into account before interpreting the results, such as the small patient samples, the clinical and methodological heterogeneities, and the lack of a clear and universally accepted definition of DGE, especially before 2007. Although RCTs represent the gold standard in finding evidence for a treatment in clinical practice, the new alternative, that can however be used in conjunction to RCTs, is "big data".

Recently, two studies using large patient databases were published. The first one was an analysis of data of 5080 patients entered in the StuDoQ|Pancreas nationwide registry of the German Society of General and Visceral Surgery. The primary aim of the study was to assess the impact of pylorus preservation or resection on the occurrence of DGE in patients undergoing PD. Pylorus preservation had no impact on the occurrence of DGE (20.3% vs. 21.5%, P=0.33), but further risk factors could be identified. Patient factors, intraoperative factors, duration of surgery and postoperative factors (postoperative pancreatic fistula, biliary leakage, and other surgical complications) were identified as risk factors for DGE (71). The second one was a study where 15,154 patients undergoing classic Whipple or PPPD, enrolled in the American College of Surgeons - National Surgical Quality Improvement Program dataset were analyzed. The purpose of the study was to develop a scoring system to aid in easy preoperative identification of patients at risk for DGE. The authors identified nine factors independently associated with DGE (PrEDICT-DGE) score: Procedures (Concurrent adhesiolysis, feeding jejunostomy, vascular reconstruction with vein graft), Elderly (Age>70), Ductal stent (Lack of biliary stent), Invagination (Pancreatic reconstruction technique), COPD, Tobacco use, Disease, systemic (ASA>2), Gender (Male) and Erythrocytes (preoperative RBC-transfusion). PrEDICT-DGE scoring system strongly correlated with the actual DGE rates and classified patients into low, intermediate, and high risk for DGE category (72). Interestingly, the preservation or not of the pylorus was not among the determinants of the risk for DGE.

It becomes clear that the selection of the more efficient technique remains a challenge for the surgical team. A study that could provide more accurate answers into the quest for the optimal technique is The PyloResPres trial. This is an ongoing, German multicenter, single-blind, surgical, registry-based RCT aiming to compare PPPD or PRPD with preservation of the stomach that is currently enrolling patients (73). The primary outcome is the occurrence of DGE grade A, B or C (mild, moderate, and severe forms) up to the 30th postoperative day. Secondary end points represent intraoperative outcomes such as the operation time and blood loss, and post-operative outcomes such as general complications, post-operative length of hospital stay, pancreatic surgery specific complication and necessity for reoperation. Enrolment could be completed by spring 2023 but it may be subjected to alteration based on the results of an interim analysis scheduled when half of the patients (492 patients according to the power analysis) are enrolled.

However, factors that have not been appropriately appreciated by the existing studies and could decisively influence future perspectives still remain. For example, the increasing acceptance of minimally invasive surgical techniques in pancreatic surgery is an indisputable fact. While the open approach is still the standard approach for PD, there are increasing reports of successful laparoscopic and robotic PDs. In a large multi-institutional series including 1028 patients, 211 patients underwent robotic PD and 817 patients open PD. PPPD was performed significantly more often in open surgery (74). However, further studies are required in order to confirm the impact of minimal-invasive PD combined either with the preservation or the resection of the pylorus on the short-term outcomes but especially on the oncological efficiency of the approach.

In the present review, our goal was to assess and ultimately compare the three forms of PD i.e. classic Whipple, PPPD, and PRPD. Our intention was to emphasize on the rationale of the transition process i.e. from the classic form of the procedure to the other proposed alternatives and to highlight the available high quality data that supported this changing trend. However, the results of the present review are subjected to notable limitations. The available RCTs on the subject usually lack the necessary power in regard to sample size while there is also a notable heterogeneity in regard to the end points utilized in each study. Moreover, even when the same end points were used in different studies, there were result interpretation issues arising from the different definitions adopted by the various authors. This fact has been also underlined in the results of the available relevant systematic reviews and meta-analyses that aimed to summarize these data into a refined conclusion (61). One of the major drawbacks of narrative reviews is the selection bias in regard to the included studies that could lead to misleading conclusions. In the present paper, aiming to limit the effect of this innate limitation, we chose to include only the results of the available relevant randomized control trials when the comparison of the techniques was the actual challenge. On the contrary, studies of lower level of evidence were only used for presenting the timeline of the surgical trends in regard to the technical aspects of PD. Finally, the fact that causes other than the adopted surgical technique alone might be implemented in the etiology of certain complications, such as the incidence of DGE, should be taken into account when interpreting the results of this study.

Conclusions

The preservation of the pylorus has been established as the mostly utilized approach during PD among specialized, in the surgical treatment of pancreatic cancer, centers worldwide. Factors that influenced this phenomenon are the shorter operation times, the less intraoperative blood loss, the decreased technical difficulty, and the similar short- and long-term outcomes compared to the classic Whipple. However, there is a

notable trend in the literature highlighting the increasing incidence of DGE following PPPD. Among other factors, pylorus dysfunction attributable to the surgical maneuvers has been implemented in the etiology of DGE. In an attempt to overcome this limitation of the PPPD, PRPD with the preservation of the stomach had been proposed. In theory, PRPD could maintain the advantages of organ sparing surgery and at the same time guarantee a more seamless gastric emptying. Only three RCTs to date aimed to evaluate the approach with only one reporting results in favor of PRPD in regard to DGE incidence. The PyloResPres trial, a multicenter German trial comparing PPPD and PRPD, is currently enrolling patients and could provide adequate evidence in regard to the optimal approach during PD.

Authors' Contributions

Study conception and design: D.S, K.T, D.Z; acquisition of data: A.S, L.K, E.P; analysis and interpretation of data: A.S, L.K; drafting the manuscript: D.S, D.Z; critical revision: L.K, A.S, E.P, K.T; All authors reviewed the manuscript.

Competing Interests

Authors declare that there are no conflicts of interest.

Funding

This research received no external funding.

References

1. Wagner M, Redaelli C, Lietz M, Seiler CA, Friess H, Büchler MW. Curative resection is the single most important factor determining outcome in patients with pancreatic adenocarcinoma. Br J Surg. 2004;91(5):586-9.
2. Bassi C, Falconi M, Salvia R, Mascetta G, Molinari E, Pederzoli P. Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients. Dig Surg. 2001; 18(6):453-7; discussion 458.
3. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg. 2015;220(4):530-6.
4. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lee Lucas F, Batista I, et al. Hospital volume and surgical mortality in the United States. N Engl J Med. 2002;346(15):1128-37.
5. Harnoss JC, Ulrich AB, Harnoss JM, Diener MK, Büchler MW, Welsch T. Use and results of consensus definitions in pancreatic surgery: a systematic review. Surgery. 2014;155(1):47-57.
6. Kausch W. Das Carcinom der Papilla duodeni und seine radikale Entfernung. Beitr klin Chir 1912;78:439-86.
7. Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. Ann Surg. 1935;102(4):763-79.
8. Whipple AO. The rationale of radical surgery for cancer of the pancreas and ampullary region. Ann Surg. 1941;114(4):612-5.
9. Trimble IR, Parsons WB, Sherman CP. A one-stage operation for the cure of carcinoma of the ampulla of Vater and the head of the pancreas. Surg Gynecol Obstet. 1941;73:711–722.
10. Watson K. Carcinoma of ampulla of vater successful radical resection. Br J Surg 1944;31:368-73.
11. Traverso LW, Longmire WP Jr. Preservation of the pylorus in pancreaticoduodenectomy. Surg Gynecol Obstet. 1978;146(6):959-62.
12. Traverso LW, Longmire WP Jr. Preservation of the pylorus in pancreaticoduodenectomy a follow-up evaluation. Ann Surg. 1980;192(3):306-10.
13. Roder JD, Stein HJ, Hüttl W, Siewert JR. Pylorus-preserving versus standard pancreatico-duodenectomy: an analysis of 110 pancreatic and periampullary carcinomas. Br J Surg. 1992;79(2):152-5.
14. Keck T, Wellner UF, Bahra M, Klein F, Sick O, Niedergethmann M, et al. Pancreatogastrostomy versus pancreatojejunostomy for reconstruction after pancreatoduodenectomy (RECOPANC, DRKS 00000767): Perioperative and Long-term Results of a Multicenter Randomized Controlled Trial. Ann Surg. 2016;263(3):440-9.
15. Lin PW, Lin YJ. Prospective randomized comparison between pylorus-preserving and standard pancreaticoduodenectomy. Br J Surg. 1999; 86(5): 603-7.
16. Lin PW, Shan YS, Lin YJ, Hung CJ. Pancreaticoduodenectomy for pancreatic head cancer: PPPD versus Whipple procedure. Hepatogastroenterology. 2005;52(65):1601-4.
17. Paquet KJ. Comparison of Whipple's pancreaticoduodenectomy with the pylorus-preserving pancreaticoduodenectomy - a prospectively controlled, randomized long-term trial (Vergleich der partiellen Duodenopankreatektomie (Whipple-Operation) mit der pyloruserhaltenden Zephaloduodenopankreatektomie - eine prospektive kontrollierte, randomisierte Langzeitstudie). Chirurgische Gastroenterologie. 1998;14:54-8.
18. Seiler CA, Wagner M, Bachmann T, Redaelli CA, Schmied B, Uhl W, et al. Randomized clinical trial of pylorus-preserving duodenopancreatectomy versus classical Whipple resection - long term results. Br J Surg. 2005; 92(5):547-56.
19. Tran KT, Smeenk HG, Eijck CH, Kazemier G, Hop WC, Greve JW, et al. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. Ann Surg. 2004;240(5):738-45.
20. Hüttner FJ, Fitzmaurice C, Schwarzer G, Seiler CM, Antes G, Büchler MW, et al. Pylorus-preserving pancreaticoduodenectomy (pp Whipple) versus pancreaticoduodenectomy (classic Whipple) for surgical treatment of periampullary and pancreatic carcinoma. Cochrane Database Syst Rev. 2016;2(2):CD006053.
21. Karanicolas PJ, Davies E, Kunz R, Briel M, Koka HP, Payne DM, et al. The pylorus: take it or leave it? Systematic review and meta-analysis of pylorus-preserving versus standard whipple pancreaticoduodenectomy for pancreatic or periampullary cancer. Ann Surg Oncol. 2007;14(6):1825-34.
22. Probst P, Hüttner FJ, Meydan Ö, Hilal MA, Adham M, Barreto SG, Besselink MG, et al. Evidence Map of Pancreatic Surgery – a living systematic review with meta-analyses by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2021;170(5):1517-1524.
23. Eshuis WJ, van Eijck CH, Gerhards MF, Coene PP, de Hingh IHJT, Karsten TM, et al. Antecolic versus retrocolic route of the gastroenteric anastomosis after pancreatoduodenectomy: a randomized controlled trial. Ann Surg. 2014;259(1):45-51.
24. Kim DK, Hindenburg AA, Sharma SK, Suk CH, Gress FG, Staszewski H, et al. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? Ann Surg Oncol. 2005;12(3):222-7.
25. Kawai M, Yamaue H. Pancreaticoduodenectomy versus pylorus-preserving

pancreaticoduodenectomy: the clinical impact of a new surgical procedure; pylorus-resecting pancreaticoduodenectomy. J Hepatobiliary Pancreat Sci. 2011;18(6):755-61.
26. van Berge Henegouwen MI, van Gulik TM, DeWit LT, Allema JH, Rauws EA, Obertop H, et al. Delayed gastric emptying after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: an analysis of 200 consecutive patients. J Am Coll Surg. 1997;185(4):373-9.
27. Büchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Z'graggen K. Changes in morbidity after pancreatic resection: toward the end of completion pancreatectomy. Arch Surg. 2003;138(12):1310-4; discussion 1315.
28. Schmidt CM, Turrini O, Parikh P, House MG, Zyromski NJ, Nakeeb A, et al. Effect of hospital volume, surgeon experience, and surgeon volume on patient outcomes after pancreaticoduodenectomy: a single-institution experience. Arch Surg. 2010;145(7):634-40.
29. Hu HL, Zhou XD, Zhang Q, Shi X. Factors influencing delayed gastric emptying after pancreaticoduodenectomy - a meta-analysis. Hepatogastroenterology. 2014;61(134):1539-45.
30. Grossi S, Lin A, Wong A, Namm J, Senthil M, Gomez N, et al. Costs and Complications: Delayed Gastric Emptying after Pancreaticoduodenectomy. Am Surg. 2019;85(12):1423-1428.
31. Wobith M, Weimann A. Oral Nutritional Supplements and Enteral Nutrition in Patients with Gastrointestinal Surgery. Nutrients. 2021;13(8):2655.
32. Martignoni ME, Friess H, Sell F, Ricken L, Shrikhande S, Kulli C, et al. Enteral nutrition prolongs delayed gastric emptying in patients after Whipple resection. Am J Surg. 2000;180(1):18-23.
33. Parmar AD, Sheffield KM, Vargas GM, Pitt HA, Kilbane EM, Hall BL, et al. Factors associated with delayed gastric emptying after pancreaticoduodenectomy. HPB (Oxford). 2013;15(10):763-72.
34. Lermite E, Sommacale D, Piardi T, Arnaud JP, Sauvanet A, Dejong CH, et al. Complications after pancreatic resection: diagnosis, prevention and management. Clin Res Hepatol Gastroenterol. 2013;37(3):230-9.
35. Dong K, Yu XJ, Li B, Wen EG, Xiong W, Guan QL. Advances in mechanisms of postsurgical gastroparesis syndrome and its diagnosis and treatment. Chin J Dig Dis. 2006;7(2):76-82.
36. Strömmer L, Räty S, Hennig R, Adrian TE, Friess H, Böttiger Y, et al. Delayed gastric emptying and intestinal hormones following pancreatoduodenectomy. Pancreatology. 2005;5(6):537-44.
37. Yeo CJ, Barry MK, Sauter PK, Sostre S, Lillemoe KD, Pitt HA, et al. Erythromycin accelerates gastric emptying after pancreaticoduodenectomy. A prospective, randomized, placebo-controlled trial. Ann Surg. 1993; 218(3):229-37; discussion 237-8.
38. 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(6):771-9.
39. Kawamoto M, Konomi H, Kobayashi K, Shimizu S, Yamaguchi K, Tanaka M. Type of gastrointestinal reconstruction affects postoperative recovery after pancreatic head resection. J Hepatobiliary Pancreat Surg. 2006;13(4):336-43.
40. Tani M, Terasawa H, Kawai M, Ina S, Hirono S, Uchiyama K, et al. Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy: results of a prospective, randomized, controlled trial. Ann Surg. 2006;243(3):316-20.
41. Grover M, Farrugia G, Stanghellini V. Gastroparesis: a turning point in understanding and treatment. Gut. 2019;68(12):2238-2250.
42. Schorn S, Demir IE, Vogel T, Schirren R, Reim D, Wilhelm D, et al. Mortality and postoperative complications after different types of surgical reconstruction following pancreaticoduodenectomy-a systematic review with meta-analysis. Langenbecks Arch Surg. 2019;404(2):141-157.
43. Yekebas EF, Wolfram L, Cataldegirmen G, Habermann CR, Bogoevski D, Koenig AM, et al. Postpancreatectomy hemorrhage: diagnosis and treatment: an analysis in 1669 consecutive pancreatic resections. Ann Surg. 2007;246(2):269-80.
44. Malgras B, Dokmak S, Aussilhou B, Pocard M, Sauvanet A. Management of postoperative pancreatic fistula after pancreaticoduodenectomy. J Visc Surg. 2023;160(1):39-51.
45. PARANOIA Study Group; Writing group; Halle-Smith JM, Pande R, Hall L, Hodson J, Roberts KJ; Steering committee; et al. Perioperative interventions to reduce pancreatic fistula following pancreatoduodenectomy: meta-analysis. Br J Surg. 2022;109(9):812-821.
46. Kawaida H, Kono H, Hosomura N, Amemiya H, Itakura J, Fujii H, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery. World J Gastroenterol. 2019; 25(28):3722-3737.
47. Xiang C, Chen Y, Liu X, Zheng Z, Zhang H, Tan C. Prevention and Treatment of Grade C Postoperative Pancreatic Fistula. J Clin Med. 2022; 11(24):7516.
48. Dai M, Liu Q, Xing C, Tian X, Cao F, Tang W, et al. Early Drain Removal is Safe in Patients With Low or Intermediate Risk of Pancreatic Fistula After Pancreaticoduodenectomy: A Multicenter, Randomized Controlled Trial. Ann Surg. 2022;275(2):e307-e314.
49. Kuemmerli C, Tschuor C, Kasai M, Alseidi AA, Balzano G, Bouwense S, et al. Impact of enhanced recovery protocols after pancreatoduodenectomy: meta-analysis. Br J Surg. 2022;109(3):256-266.
50. Miedema BW, Sarr MG, van Heerden JA, Nagorney DM, McIlrath DC, Ilstrup D. Complications following pancreati coduodenectomy. Current management. Arch Surg 1992;127:945-9.
51. Patel AG, Toyama MT, Kusske AM, Alexander P, Ashley SW, Reber HA. Pylorus-preserving Whipple resection for pancre atic cancer. Is it any better? Arch Surg 1995;130:838-4
52. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007;142(5):761-8.
53. Paquet KJ. Vergleich der partiellen Duodenopankreat- mit der pyloruserhaltenden Zephaloduo- denopankreatektomie ± eine prospektiv kontrollierte, randomi - sierte Langzeitstudie. Chir Gastroenterol. 1998;14:54–8
54. Wenger FA, Jacobi CA, Haubold K, Zieren HU, Müller JM. Gastrointestinale Lebensqualität nach Duodenopankreatektomie beim Pankreascarcinom. Vorläufige Ergebnisse einer prospektiv-randomisierten Studie: PD vs PPPD (Gastrointestinal quality of life after duodenopancreatectomy in pancreatic carcinoma. Preliminary results of a prospective randomized study: pancreatoduodenectomy or pylorus-preserving pancreatoduodenectomy). Chirurg. 1999;70(12):1454-1459. German.
55. Lin PW, Lin YJ. Prospective randomized comparison between pylorus-preserving and standard pancreaticoduodenectomy. Br J Surg. 1999; 86(5):603-7.
56. Tran KT, Smeenk HG, van Eijck CH, Kazemier G, Hop WC, Greve JW et al. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. Ann Surg. 2004;240(5): 738–745.
57. Seiler CA, Wagner M, Bachmann T, Redaelli CA, Schmied B, Uhl W et al. Randomized clinical trial of pylorus-preserving duodenopancreatectomy versus classical Whipple resection - long term results. Br J Surg. 2005; 92(5):547–556
58. Srinarmwong C, Luechakiettisak P, Prasitvilai W. Standard Whipple's operation versus pylorus preserving pancreaticoduodenectomy: a randomized controlled trial study. J Med Assoc Thail. 2008;91(5):693–698
59. Taher M, Khan Z, Chowdhury M, Nur-E-Elahi M, Chowdhury A, Faruque M et al. Pylorus preserving pancreaticoduodenectomy vs. standard Whipple's procedure in case of carcinoma head of the pancreas and periampullary carcinoma. Mymensingh Med J. 2015;24(2):319-25.
60. Diener MK, Knaebel H-P, Heukaufer C, Antes G, Büchler MW, Seiler CM. A systematic review and meta-analysis of pylorus-preserving versus classical pancreaticoduodenectomy for surgical treatment of periampullary and pancreatic carcinoma. Ann Surg. 2007;245:187-200
61. Hanna M, Gadde R, Allen C, Meizoso J, Sleeman D, Livingstone AS et al. Delayed gastric emptying after pancreaticoduodenectomy. J Surg Res. 2016; 202(2):380–388
62. Busquets J, Martín S, Secanella L, Sorribas M, Cornellà N, Altet J, et al. Delayed gastric emptying after classical Whipple or pylorus-preserving pancreatoduodenectomy: a randomized clinical trial (QUANUPAD). Langenbecks Arch Surg. 2022;407(6):2247-2258.

63. Hayashibe A, Kameyama M, Shinbo M, Makimoto S. The surgical procedure and clinical results of subtotal stomach preserving pancreaticoduodenectomy (SSPPD) in comparison with pylorus preserving pancreaticoduodenectomy (PPPD). J Surg Oncol. 2007;95(2):106-9.
64. Kawai M, Tani M, Hirono S, Miyazawa M, Shimizu A, Uchiyama K, et al. Pylorus ring resection reduces delayed gastric emptying in patients undergoing pancreatoduodenectomy: a prospective, randomized, controlled trial of pylorus-resecting versus pylorus-preserving pancreatoduodenectomy. Ann Surg. 2011;253(3):495-501.
65. Kawai M, Tani M, Hirono S, Okada K, Miyazawa M, Yamaue H. Pylorus-resecting pancreaticoduodenectomy offers long-term outcomes similar to those of pylorus-preserving pancreaticoduodenectomy: results of a prospective study. World J Surg. 2014;38(6):1476-83.
66. Matsumoto I, Shinzeki M, Asari S, Goto T, Shirakawa S, Ajiki T, et al. A prospective randomized comparison between pylorus- and subtotal stomach-preserving pancreatoduodenectomy on postoperative delayed gastric emptying occurrence and long-term nutritional status. J Surg Oncol. 2014;109(7):690-6.
67. Hackert T, Probst P, Knebel P, Doerr-Harim C, Bruckner T, Klaiber U, et al. Pylorus Resection Does Not Reduce Delayed Gastric Emptying After Partial Pancreatoduodenectomy: A Blinded Randomized Controlled Trial (PROPP Study, DRKS00004191). Ann Surg. 2018;267(6):1021-1027.
68. Klaiber U, Probst P, Hüttner FJ, Bruckner T, Strobel O, Diener MK, et al. Randomized Trial of Pylorus-Preserving vs. Pylorus-Resecting Pancreatoduodenectomy: Long-Term Morbidity and Quality of Life. J Gastrointest Surg. 2020;24(2):341-352.
69. Klaiber U, Probst P, Strobel O, Michalski CW, Dörr-Harim C, Diener MK, et al. Meta-analysis of delayed gastric emptying after pylorus-preserving versus pylorus-resecting pancreatoduodenectomy. Br J Surg. 2018; 105(4):339-349.
70. Varghese C, Bhat S, Wang TH, O'Grady G, Pandanaboyana S. Impact of gastric resection and enteric anastomotic configuration on delayed gastric emptying after pancreaticoduodenectomy: a network meta-analysis of randomized trials. BJS Open. 2021;5(3):zrab035.
71. Fahlbusch T, Luu AM, Höhn P, Klinger C, Werner J, Keck T, et al. Impact of pylorus preservation on delayed gastric emptying after pancreaticoduodenectomy-analysis of 5,000 patients based on the German StuDoQ|Pancreas-Registry. Gland Surg. 2022;11(1):67-76.
72. Werba G, Sparks AD, Lin PP, Johnson LB, Vaziri K. The PrEDICT-DGE score as a simple preoperative screening tool identifies patients at increased risk for delayed gastric emptying after pancreaticoduodenectomy. HPB (Oxford). 2022;24(1):30-39.
73. Renz BW, Adrion C, Klinger C, Ilmer M, D'Haese JG, Buhr HJ, et al. Pylorus resection versus pylorus preservation in pancreatoduodenectomy (PyloResPres): study protocol and statistical analysis plan for a German multicentre, single-blind, surgical, registry-based randomised controlled trial. BMJ Open. 2021;11(11):e056191.
74. Zureikat AH, Postlewait LM, Liu Y, et al. A Multi-institutional Comparison of Perioperative Outcomes of Robotic and Open Pancreaticoduodenectomy. Ann Surg 2016;264:640-9.