Delayed gastric emptying after subtotal stomach-preserving pancreatoduodenectomy: pancreatogastrostomy vs pancreatojejunostomy

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Objective
The relation between type of pancreatic remnant reconstruction and delayed gastric emptying (DGE) following pancreatoduodenectomy (PD) is unclear. The authors are trying to detect the incidence of DGE following PD and its relation to both types of pancreatic remnant anastomosis, pancreaticogastrostomy (PG) and pancreaticojejunostomy (PJ).
Patient and methods
This retrospective study included 44 patients who underwent PD. These patients were classified according to the type of pancreatic anastomosis into two groups: PG group and PJ group. The development of DGE and its combination with intra-abdominal complications (IACs) was compared between both groups. Risk factors responsible for clinically evident DGE were analyzed.
Results
The incidence of GDE in both PG and PJ was 27.3%. DGE was strongly associated with IACs, particularly pancreatic fistula. Furthermore, DGE occurred more commonly with PG than PJ. Although IACs developed at a similar rate in both types of pancreatic reconstruction, DGE in combination with IACs was more frequent with PG. Durations of both nasogastric tube and solid diet tolerance were prolonged in DGE patients in comparison with non-DGE patients. Moreover, prokinetic use, nasogastric tube reinsertion, and vomiting were more frequent in DGE patients than non-DGE patients.
Conclusion
DGE was strongly associated IACs. Regarding the type of pancreatic reconstruction, DGE is more common with PG than PJ. This may be because IACs developed more frequently with PG, resulting in more frequent development of DGE.

Keywords:
gastric emptying, pancreaticogastrostomy, pancreatoduodenectomy, pancreatojejunostomy

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Introduction

Whipple–Kausch operation is the standard surgical treatment for cancer head of the pancreas and periampullary tumors [1]. The procedure is associated with low mortality (0–6%) if it is performed in a specialized center [2–4]. The morbidity rate is still high, ranging from 30% to more than 50% [5]. The most common major postoperative complications are pancreatic fistula (PF) and delayed gastric emptying (DGE). Although it is not a life-threatening complication, DGE is associated with a prolonged postoperative hospital stay, reduced quality of life, and higher costs [6].

In 2006, International Study Group for Pancreatic Surgery (ISGPS) developed a definition for DGE depending on two clinical criteria: first, duration that nasogastric tube (NGT) is needed and second, period until tolerance of solid food. Based on these criteria, several studies about DGE have been reported [5,7–9]. Several theories explain the pathophysiology of DGE, including denervation and ischemia of the antrum and pylorus, in addition to decreased motilin [9,10].

Furthermore, the association between intra-abdominal complications (IACs) and DGE has been documented [8–10]. Because of the relation between IACs and DGE, the type of reconstruction of pancreatic remnants may be an essential factor in the development of DGE. This is owing to the disruption of pancreatic anastomosis that may lead to several types of IACs. To reduce the risk of pancreatic reconstruction failure, pancreaticogastrostomy (PG) has been used instead of pancreaticojejunostomy (PJ) by several surgeons [11,12].

However, there is no definite recommendation showing high efficacy and safety of PG [13]. Despite many recent meta-analyses revealing that the occurrence of DGE was comparable between both types of pancreatic reconstruction, there seemed to be multiple variations in PG's performance in these reports [11,14–16]. In this study, the invagination procedure was done uniformly in PG and PJ for all patients. Thus, in this study, we tried to compare the development of clinically evident DGE and its relation with IACs between both types of pancreatic remnant anastomosis.

Patient and methods

Of 51 patients who underwent elective Whipple–Kausch procedure from August 2017 to December 2019 in the General Surgery Department, Benha University Hospital. All patients underwent subtotal stomach-preserving PD (SSPPD). During our study, seven patients died, and so were excluded from the study. Three patients died from cardiac complications in the form of ischemic heart disease. Two patients died from pulmonary complications in the form of pulmonary embolism. The other two patients died from intra-abdominal sepsis due to anastomotic disruption. The remaining 44 patients who recovered and were discharged from the hospital were retrospectively analyzed. A total of 24 patients presented with cancer head of pancreas (14 patients were stage II and 10 patients were stage III), 12 patients presented with stage II cholangiocarcinoma, and eight patients presented with stage II ampullary carcinoma. This data collection was approved by the Ethical Committee of Faculty of Medicine, Benha University. Written informed consent was obtained from study participants.

Surgical technique

All patients received venous thromboembolic prophylaxis at the beginning of surgery in the form of elastic stocking and subcutaneous injection of 5000 IU heparin. Moreover, a NGT was inserted at the beginning of the operation. The operative steps of SSPPD were similar in both groups; the gallbladder, distal common bile duct, pancreatic head, duodenum, and ~10–15 cm proximal jejunum were resected. The duodenum was dissected by Kocher maneuver till the left renal vein appeared in the field. The antrum stayed excised 1–2 cm proximal to the pyloric sphincter. A Jackson-Pratt drain was inserted close to the sites of anastomosis in both groups. Post-resection reconstruction for both groups was as follows:

PG group

PG was done with invagination of the distal portion of pancreatic remnant into the stomach using absorbable monofilament sutures on the posterior gastric wall (hand-sewn technique) in addition to inserting a pancreatic duct stent. Retrocolic end-to-side hepaticojejunostomy was done using absorbable monofilament sutures in an interrupted fashion. Gastrojejunostomy 45–60 cm distal to biliary-enteric anastomosis was done with Braun entero-enteric anastomosis between afferent and efferent limbs.

PJ group

PJ was performed with end-to-side duct-to-mucosa using absorbable monofilament sutures in interrupted fashion with the insertion of pancreatic duct stent. Biliary-enteric anastomosis and gastrointestinal reconstruction were performed like the PG group.

Postoperative management

There were no differences in the postoperative management between the two groups.

In both groups, NGT was removed when the daily output was less than 500 ml, usually on the first or second postoperative day. Full liquid diet to soft diet was started on the fourth or fifth postoperative day. The regular diet was initiated 10–14 days after surgery. The patients were followed for 6 months after surgery.

Classification of DGE and PF

The severity of DGE was identified based on the ISGPS criteria [17] in both groups. Grades B and C DGE were defined as symptomatic DGE. Symptomatic DGE was further divided into two types (primary and secondary DGE), based on the presence or absence of IACs. An upper gastrointestinal series was performed to confirm the patency of gastrojejunostomy to rule out the mechanical causes of abnormal gastric emptying. According to the ISGPS criteria [18], the grade of PF was identified, and grades B and C PF were defined as clinically relevant PF.

ISGPS classify DGE into three grades: A, B, and C. In grade A, the patient is asymptomatic and requires no or minimal changes in management and usually is treated conservatively. In grade B, the patient is symptomatic and needs change in the treatment away from the expected normal clinical pathway. In grade C, the patient has severe symptoms and needs to keep the NGT for a long time. Based on the presence of IACs, symptomatic DGE (grade B and C) was classified into two types: primary and secondary. Mechanical causes of DGE, such as narrowing at the site of anastomosis, were excluded by upper gastrografin study [5]. ISGPS also classifies PF into three grades: grade A:

biochemical leak, in which the patient has no clinical symptoms with only elevation of amylase in the body fluid and no deviation from the normal postoperative pathway; grade B, the patient has clinical symptoms that need a change in expected postoperative treatment such as octreotide medications, total parenteral nutrition, and ultrasound-guided drainage of intra-abdominal collection, and finally, grade C, in which the patient has severe symptoms and evidence of sepsis and organ failure. The patient needs abdominal reentry to control sepsis, fistula, and their significant sequelae.

Results

This study includes 44 patients who underwent SSPPD. The mean age was 56±13.4 years (range: 59–70 years). Overall, 65.9% were male and 34.1% were female. Postoperative staging revealed cancer head of pancreas (eight patients was stage II and 16 patients was stage III), cholangiocarcinoma (four patients was stage II and eight patients was stage III), and ampullary carcinoma (eight patients was stage II). PG was done in 19 (43.2%), whereas PJ was done in 25 (56.8%). Patients' characteristics are illustrated in Table 1.

The overall mortality rate was 6.8% (n=3). Morbidity was observed in 25 (56.8%), and IACs were noted in 20 (45.5%). The IACs in the present study included PF, IAA, chylorrhea, postoperative hemorrhage, liver abscess, pancreatitis, hematemesis, and postoperative bleeding. Clinically relevant DGE was developed in 12 patients (27.3%), denoting that it was the most frequent complication, classified as grades B [n=2, (4.5%)] and C [n=10, (22.7%)]. Of the 12 clinically relevant DGE patients, one (8.3%) patient had primary DGE and 11 (91.7%) patients had secondary DGE. Postoperative complications are summarized in Table 2.

The NGT was required beyond the second postoperative day in seven (58.3%) patients. Reinsertion of NGT was performed in five (41.7%) of the 12 patients with symptomatic DGE. The mean hospital stay after surgery was 26±3.7 (16–124 days) (Table 3).

There was no statistically significant variation between the two groups regarding age, sex distribution, mean BMI, and preoperative cholangitis with biliary drainage. Intraoperative blood loss tends to be less in the PJ group than the PG group (P=0.086), whereas operative duration was significantly longer in the PJ group than the PG group (P<0.001) (Table 4). The complications after surgery were generally similar between both groups except for DGE, which happened more frequently in the PG

Table 2 Postoperative complications

Postoperative complications	*N* (%)
Total	25 (56.8)
Pancreatic fistula	9 (20.5)
Intra-abdominal abscess	8 (18.2)
Intra-abdominal complications	20 (45.4%)
Postoperative bleeding	1 (2.3)
Chylorrhea	2 (4.5)
Pancreatitis	1 (2.3)
Liver abscess	1 (2.3)
Hematemesis	1 (2.3)
Delayed gastric empty	12 (27.3)
Primary (without IACs)	1 (8.3)
Secondary (with IACs)	11 (91.7)
Grade B	2 (4.5)
Grade C	10 (22.7)
Other complications	6 (13.6)
SSI	4 (9.1)
CRBSI	1 (2.3)
Chest infection	1 (2.3)

CRBSI, catheter-related blood stream infection; IAC, intra-abdominal complication; SSI, surgical site infection.

Table 1 Demographic and clinical features of the patients

Sex [*n* (%)]	
Male	29 (65.9)
Female	15 (34.1)
Age [mean±SD (range)]	56±13.4 (59–70)
BMI [mean±SD (range)]	20.7±6.3 (17–34)
Cancer head of pancreas [*n* (%)]	24 (54.5)
Indications of Whipple–Kausch procedure [*n* (%)]	
Lower end cholangiocarcinoma	12 (27.3)
Ampullary carcinoma	8 (18.2)
Types of pancreatic reconstruction [*n* (%)]	
Pancreaticogastrostomy	19 (43.2)
Pancreaticojejunostomy	25 (56.8)
Operative duration (min) [mean±SD (range)]	423.6±10.7 (330–710)
Blood loss (ml) [mean±SD (range)]	1050±20.7 (120–2110)
Hospital stay after surgery (days)	26±3.7 (16–124)

Table 3 DGE vs non-DGE patients

DGE parameters	DGE patients (*n*=12) [*n* (%)]	Non-DGE patients (*n*=32) [*n* (%)]	*P* value
Solid diet tolerance (days) [mean±SD (range)]	11±2 (8–16)	6±1 (5–7)	<0.001
NGT			
Duration (days)			
Mean±SD (range)	5±1 (4–10)	2±1 (1–4)	<0.001
Reinsertion	5 (41.7)	2 (6.25)	<0.001
Vomiting	9 (75)	6 (18.8)	<0.001
Prokinetics use	12 (100)	7 (21.9)	<0.001
Grade ADGE	0	–	–
Grade B DGE	2 (4.5)	–	–
Grade C DGE	10 (22.7)	–	–

DGE, delayed gastric empty; NGT, nasogastric tube.

Table 4 Clinical features of the patients in both groups

Patients data	PG group (*n*=19) [*n* (%)]	PJ group (*n*=25) [*n* (%)]	*P* value
Sex			
Male	13 (68.4)	16 (64)	0.836
Female	5 (26.3)	10 (40)	0.811
Age [mean±SD (range)]	57±12.6 (62–69)	55±11.8 (59–70)	0.418
BMI [mean±SD (range)]	21.6±7.2 (17–32)	22.8±7.2 (19–34)	0.692
Indications of PD			
Cancer head of pancreas	5 (26.3)	19 (76)	0.349
Lower-end cholangiocarcinoma	6 (31.6)	6 (24)	0.261
Ampullary carcinoma	5 (26.3)	3 (12)	0.193
Previous abdominal surgery	4 (21.1)	6 (24)	0.427
Preoperative cholangitis	11 (57.9)	18 (72)	0.146
Preoperative biliary tract drainage	13 (68.4)	18 (72)	0.761
Operative duration (min) [mean±SD (range)]	423.6±12.9 (330–650)	525.8±13.6 (415–710)	<0.001
Blood loss (ml) [mean±SD (range)]	1150±40.8 (500–2110)	950±30.7 (120–1800)	0.086
Hospital stay after surgery (days) [mean±SD (range)]	30±4.3 (16–120)	25±2.8 (14–124)	0.355

group than in the PJ group (42.1 vs 16%, respectively, *P*=0.017). DGE with IACs tended to be more common with PG, even though IACs developed at a similar rate in both groups (36.8 vs 16%, respectively, *P*=0.015). DGE with PF was more common in PG group (100 vs 25%, respectively, *P*=0.019) (Table 5).

Multivariate analysis using logistic regression was undertaken. There are three factors related to the development of DGE: PF, IAA, and the type of pancreatic remnant anastomosis (Table 6).

Discussion

DGE is the most frequent postoperative complication after PD. The mean incidence of DGE is 17%, although it varies widely among trials [5,19,20]. DGE after PD was initially described by Warshaw in 1985 [21]. Proposed risk factors for DGE may be general such as diabetes mellitus (DM), previous abdominal surgery, and history of cholangitis or factors related to surgery, such as a reduction in plasma motilin level or a result of duodenal resection, denervation, and ischemia of stomach owing to mobilization and lymphadenectomy in addition to postoperative IACs [22–24]. The incidence of DGE does not differ between conventional PD and pylorus-preserving pancreaticoduodenectomy (PPPD) or single loop and Roux-en-Y reconstruction [25].

Recent reports have suggested that DGE is a warning sign of IACs, such as PF or IAA [9,12,26,27]. DGE is most commonly developed secondary to the IACs and is extremely rare as an initial incident (primary DGE) [9,10,28]. In this study, most patients who developed DGE (*n*=11, 91.7%) had IACs, whereas primary DGE was very rare (*n*=1, 8.3%); this confirmed the relation between DGE and IACs.

PPPD and retrocolic gastrojejunostomy have been considered typical risk factors for DGE. Hayama *et al.* [6] and Kawai *et al.* [29] reported that pylorus resection pancreaticoduodenectomy (PrPD) (95% of the stomach was preserved) with antecolic gastrojejunostomy was associated with a very low incidence of DGE [6,29,30]. Furthermore, the type of pancreatic anastomosis is closely related to IACs, which are risk factors for DGE. Considering the

Table 5 Postoperative complications in both groups

Postoperative complications	Type of pancreatic reconstruction [*n* (%)]		*P* value
	PG [19 (43.2%)]	PJ [25 (56.8%)]	
Total	11 (57.9)	14 (56)	0.514
Intra-abdominal complications	9 (47.4)	11 (44)	0.604
Pancreatic fistula	5 (26.3)	4 (16)	0.615
Intra-abdominal abscess	4 (21.1)	4 (16)	0.326
Postoperative bleeding	1 (5.3)	0	0.121
Chylorrhea	0	2 (8)	0.125
Pancreatitis	0	1 (4)	0.349
Liver abscess	0	1 (4)	0.193
Hematemesis	1 (5.3)	0	0.253
Delayed gastric empty	8 (42.1)	4 (16)	0.017
Primary (without IACs) (*n*=10, 14)	1 (5.3)	0	0.146
Secondary (with IACs) (*n*=9, 11)	7 (36.8)	4 (16)	0.015
With PF (*n*=5, 4)	5 (100)	1 (25)	0.019
Without PF (*n*=14, 21)	3 (21.4)	3 (14.3)	0.212
Other complications			
SSI	1 (5.3)	3 (12)	0.368
CRBSI	0	1 (4)	0.399
Chest infection	1 (5.3)	0	0.273

CRBSI, catheter-related blood stream infection; IAC, intra-abdominal complication; SSI, surgical site infection; PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy.

Table 6 Risk factors for DGE

Variables	Odds ratio	95% CI	*P* value
Pancreatic fistula	29.4	7.2–125.6	<0.001
Type of pancreatic reconstruction (PG vs PJ)	5.2	1.6–13.7	0.001
Intra-abdominal abscess	4.7	3.2–49.3	0.06

CI, confidence interval; DGE, delayed gastric emptying; PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy.

relationship between DGE and IACs, an intimate relation between the type of pancreatic anastomosis and the development of DGE is expected [7,9].

In spite of several recent meta-analyses documenting that the development of DGE was comparable between the two types of pancreatic anastomosis, there seemed to be many differences in the technique of PG in these meta-analyses [11,14–16]. In our study, the techniques used for both types of pancreatic remnant reconstruction (invagination technique) were done uniformly for all cases, so any bias that might affect DGE were almost eliminated. There was no bias in the patient selection between both groups, even though the current study was retrospective, which adds to the validity of the analysis. In this study, the DGE was more common in PG group than PJ group. This would suggest that the surgical technique of PG itself influenced DGE development. Likely, the fixation of the posterior gastric wall to the pancreatic remnant affects gastric motility. In particular, PG in this study was done with an invagination technique, which resulted in more anatomical disruption than duct-to-mucosa technique and could result in more affection of gastric motility, PF, or other IACs.

Because some observational studies documented a lower incidence of PF with PG, some surgeons prefer PG over PJ in patients with high risk for PF [11,12]. However, there are no high-quality studies or randomized controlled trials to provide good evidence that PG has greater safety than PJ [13]. Similarly, in the current study, there were no significant variations in the frequency of both PF and IACs between both groups. Still, DGE with IACs developed more frequently in the PG group.

Our data supposed that the PG was more liable than the PJ in the way of DGE development by IACs. Particularly concerning PF, DGE was strongly related to PG than PJ. In the PJ group, one of four patients (25%) with PF had DGE, whereas all PG patients with PF developed DGE. It is possible that, in patients with PJ, the increasing distance from the site of pancreatic anastomosis would decrease gastroparesis owing to PF or per pancreatic inflammation.In spite of the type of pancreatic remnant, anastomosis should not be selected based on avoidance of DGE alone, PG tends to stimulate DGE and thereby leading to patient frustration, delayed hospital discharge, and the need for nutritional support. When PG is recommended, surgeons should take care to inhibit disturbance of gastric motility including the anastomotic technique by avoidance of the incision on the anterior wall of the

stomach or performing a vertical incision rather than horizontal incision [31].

Although most of the investigators use the ISGPS diagnostic criteria for diagnosis of DGE, interpretation of DGE is sometimes confusing. For example, patients who developed IACs, such as a postoperative hemorrhage, chylorrhea, and hematemesis due to the gastric ulcers, may need to withdraw from oral diet despite the absence of gastroparesis. This confusion developed because the ISGPS criteria did not enumerate the presence or absence of co-existing complications, exclusion criteria, and the method for diagnosis of gastroparesis, although the criteria are simple, objective, and clearly measurable. Amendment of the definition is needed for further analysis of the causes of DGE [6,32].

Our study showed long operative duration and hospital stay and increase in amount of blood loss in some cases. This could be explained by many reasons, including previous abdominal surgery, history of cholangitis which make dissection difficult during surgery in these cases, in addition to the operations done by two different teams with different experience and time till closure of PF.

The drawbacks of this study are the small number of patients included in the study. Accumulation of further cases with minimal variations is required to definitively describe the risk for DGE between PG and PJ in the future.

Finally, the development of DGE and its relation with IACs was compared between different types of pancreatic remnant reconstruction. IACs, including PF, were strongly related to DGE. DGE occurred more commonly in the PG than in the PJ. We suggest that PG itself exhibits patients to DGE by the fixation to the posterior gastric wall and IACs were more frequent with PG, and these lead to frequent development of DGE in PG.

Conclusion

Intra-IACs are strongly related to DGE. DGE occurred more commonly in the PG group than in the PJ group. IACs could explain this. There were more common in the PG group, which lead to the development of DGE.

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Conflicts of interest

There are no conflicts of interest.

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