

Delayed gastric emptying after subtotal stomach-preserving pancreatoduodenectomy (SSPPD): pancreatogastrostomy versus pancreatojejunostomy

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Objectives: The relation between type of pancreatic remnant reconstruction and delayed gastric emptying (DGE) following pancreatoduodenectomy (PD) is unclear. We are trying to detect the incidence of DGE following pancreatoduodenectomy and its relation to both types of pancreatic remnant anastomosis, pancreatogastrostomy (PG), and pancreatojejunostomy (PJ).

Methods: This retrospective study includes 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 DGE in both PG and PJ was 27.3%. DGE was strongly associated with IACs, particularly pancreatic fistula (PF). 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. Duration of both NGT and solid diet tolerance were prolonged in DGE patients in comparison to non-DGE patients. Also, prokinetic use, NGT reinsertion, and vomiting were more frequent in DGE patients than non-DGE patients.

Conclusion: DGE was strongly associated with 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, pancreatoduodenectomy, pancreatogastrostomy, pancreatojejunostomy.

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 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 depend on two clinical criteria: (1) duration that NGT is needed, (2) 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 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 due to the disruption of pancreatic anastomosis that may lead to several types of IACs. To reduce the risk of pancreatic reconstruction failure, PG has been used instead

of 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 that revealed 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 the current study, the invagination procedure was done uniformly in PG and PJ for all patients. Thus, in the current study, we are trying to compare the development of clinically evident DGE and its relation with IACs between both types of pancreatic remnant anastomosis.

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 (IHD). 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. 24 patients presented with cancer head of pancreas (14 patients was stage II and 10 patients was stage III), 12 patients presented

with stage II cholangiocarcinoma and 8 patients presented with stage II ampullary carcinoma.

Surgical technique

All patients received venous thrombo-embolic (VTE) prophylaxis at the beginning of surgery in the form of elastic stocking and subcutaneous injection of 5000 IU heparin. Also, a nasogastric tube (NGT) inserted at the beginning of the operation. The operative steps of SSPPD were similar in both groups; the gallbladder, distal common bile duct (CBD), pancreatic head, duodenum, and about 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 the following.

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. Retro-colic 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 limb.

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 to 14 days after surgery. The patients followed for 6 months after surgery.

Classification of DGE and PF

The severity of DGE was identified based on the ISGPS criteria¹⁷ 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 3 grades A, B, and C. Grade A: the patient is asymptomatic and requires no or minimal changes in management and usually is treated conservatively. Grade B: the patient is symptomatic and needs change in the treatment away from the expected normal clinical pathway.

Grade C: the patient has severe symptoms and needs to keep the NGT for a long time. Based on the presence of intra-abdominal complications (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 classify pancreatic fistula into 3 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 (TPN), ultrasound (US) guided drainage of intra-abdominal collection. Finally, grade C, in which the patient has severe symptoms and evidence of sepsis, 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), 65.9% were male, and 34.1% were female. Regarding postoperative staging, cancer head of pancreas (8 patients was stage II and 16 patients was stage III), cholangiocarcinoma (4 patients was stage II and 8 patients was stage III) and ampullary carcinoma (8 patients was stage II). PG was done in 19 (43.2%), while 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, 1 patient (8.3%) had primary DGE, and 11 patients (91.7%) had secondary DGE. Postoperative complications are summarized in **Table 2**.

The NGT was required beyond the second postoperative day in 7 patients (58.3%) Reinsertion of NGT was performed in 5 (41.7%) out 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), while 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 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 3 factors related to the development DGE: PF, IAA, and the type of pancreatic remnant anastomosis **Table 6**.

Table 1: Demographic and clinical features of the patients

Gender	Male	29 (65.9%)
	Female	15 (34.1%)
Age, Mean \pm SD (Range)	56 \pm 13.4 (59-70)	
BMI Mean \pm SD (Range)	20.7 \pm 6.3(17-34)	
Indications of whipple-Kauschprocedure	Cancer head of pancreas	24 (54.5%)
	Lower end cholangiocarcinoma	12 (27.3%)
	Ampullary carcinoma	8 (18.2%)
Types of pancreatic reconstruction	Pancreaticogastrostomy (PG)	19 (43.2%)
	Pancreaticojejunostomy (PJ)	25 (56.8%)
Operative duration (min) Mean \pm SD (Range)	423.6 \pm 10.7(330-710)	
Blood loss (ml) Mean \pm SD (Range)	1050 \pm 20.7(120-2110)	
Hospital stay after surgery (Days)	26 \pm 3.7 (16-124)	

BMI: Body Mass Index.

Table 2: Postoperative complications

Postoperative complications		No (%)	
Total		25 (56.8%)	
Intra-abdominal complications (IACs), No (%)	20 (45.4%)	Pancreatic fistula (PF)	9 (20.5%)
		Intra-abdominal abscess	8 (18.2%)
		Postoperative bleeding	1 (2.3%)
		Chylorrhea	2 (4.5%)
		pancreatitis	1 (2.3%)
		Liver abscess	1 (2.3%)
		Hematemesis	1 (2.3%)
		Primary (without IACs)	1 (8.3%)
		Secondary (with IACs)	11 (91.7%)
		Grade B	2 (4.5%)
	Grade C	10 (22.7 %)	
Delayed gastric empty (DGE) No (%)	12 (27.3%)	SSI	4 (9.1%)
		CRBSI	1 (2.3%)
		Chest infection	1 (2.3%)
Other complications No (%)	6 (13.6%)		

No: Number, SSI: Surgical Site Infection, CRBSI: Catheter-Related Blood Stream Infection.

Table 3: DGE versus Non-DGE patients

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

n: Number, NGT: Nasogastric Tube, DGE: Delayed Gastric Empty.

Table 4: Clinical features of the patients in both groups

Patients data		PG Group No= 19	PJ Group No= 25	P Value
Gender	Male, n (%)	13 (68.4%)	16 (64%)	0.836
	Female, n (%)	5 (26.3%)	10 (40%)	0.811
Age, Mean ± SD (Range)		57 ±12.6 (62-69)	55 ±11.8 (59-70)	0.418
Body mass index (BMI), Mean ± SD (Range)		21.6± 7.2 (17-32)	22.8±7.2 (19-34)	0.692
Cancer head of pancreas, n (%)		5 (26.3%)	19 (76%)	0.349
Indications of PD	Low-end cholangiocarcinoma, n (%)	6 (31.6%)	6 (24%)	0.261
	Ampullary carcinoma, n (%)	5 (26.3%)	3 (12%)	0.193
Previous abdominal surgery, n (%)		4 (21.1%)	6 (24%)	0.427
Preoperative cholangitis, n (%)		11 (57.9%)	18 (72%)	0.146
Preoperative biliary tract drainage, n (%)		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

min: Minutes, SD: Standard Deviation, ml: Milliliters.

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, n (%)	11 (57.9%)	14(56%)	0.514	
Intra-abdominal complications, n (%)	9 (47.4)	11 (44%)	0.604	
Pancreatic Fistula (PF),n (%)	5 (26.3%)	4 (16%)	0.615	
Intra-abdominal abscess (IAA), n (%)	4 (21.1%)	4 (16%)	0.326	
Postoperative bleeding, n (%)	1 (5.3%)	0	0.121	
Chylorrhea, n (%)	0	2 (8%)	0.125	
Pancreatitis, n (%)	0	1 (4%)	0.349	
Liver abscess, n (%)	0	1 (4%)	0.193	
Hematemesis, n (%)	1 (5.3%)	0	0.253	
Delayed gastric empty (DGE), n (%)	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	
SSI, n (%)	1 (5.3%)	3 (12%)	0.368	
Other complications, n (%)	CRBSI, n (%)	0	1 (4%)	0.399
	Chest infection, n (%)	1 (5.3%)	0	0.273

Table 6: Risk factors for DGE

Variables	Odds Ratio	95% CI	P Value
Pancreatic fistula (PF)	29.4	7.2-125.6	< 0.001
Type of pancreatic reconstruction (PG Versus PJ)	5.2	1.6 -13.7	0.001
Intra-abdominal abscess (IAA)	4.7	3.2-49.3	0.06

Discussion

Delayed gastric emptying 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 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 due 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.^{9,12,27,28} DGE is most commonly developed secondary to the IACs, and is extremely rare as an initial incident (primary DGE).^{9,10,26} In the current study, most patients who developed DGE ($n = 11$, 91.7%) had IACs while primary DGE was very rare ($n = 1$, 8.3%), this confirmed the relation between DGE and IACs.

PPPD and retro-colic gastrojejunostomy have been considered typical risk factors for DGE. Hayama et al. and Kawai et al. 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 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 documented 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 technique 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 the current 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 of 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 developing by IACs. Particularly concerning PF, DGE was strongly related to PG than PJ. In the PJ group, 1 out of 4 patients (25%) with PF had DGE, while 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 gastro paresis due 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 sometimes confusing. For example, patients who developed IACs such as a postoperative hemorrhage, chylorrhea, and hematemesis due to the gastric ulcers that may need to withdraw from oral diet despite the absence of gastro paresis. 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 gastro paresis, 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, 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 pancreatic fistula.

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

List of abbreviations:

DGE: Delayed Gastric Emptying.

PD: Pancreaticoduodenectomy.

PG: Pancreaticogastrostomy.

PJ: Pancreaticojejunostomy.

PF: Pancreatic Fistula.

NGT: Nasogastric Tube.

IACs: Intra-abdominal Complications.

IAAs: Intra-abdominal Abscesses.

ISGPS: International Study Group of Pancreatic Surgery.

TPN: Total Parenteral Nutrition.

US: Ultrasound.

SSPPD: Subtotalstomach-preserving pancreatoduodenectomy

BMI: Body Mass Index.

SD: Standard Deviation.

SSI: Surgical Site Infection.

CRBSI: Catheter-Related Blood Stream Infection.

PPPD: Pylorus-preserving pancreaticoduodenectomy.

PrPD: Pylorus-resection pancreaticoduodenectomy.

DM: Diabetes Mellitus.

Declarations.

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Not applicable.

Ethical approval and consent to participate:

This data collection was approved by the Ethical Committee of Faculty of Medicine, Benha University. Written informed consent was obtained from study participants.

Consent for publication:

Not applicable.

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Mohamed S Essa: Study concept, design, literature review.

Ahmad M.F. Salama: Study design, Literature review, writing.

Mohamed E Zayed: data collection, interpretation.

Guarantor:

The corresponding author is the guarantor of submission.

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