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Original Article

OPTIMIZED DRAINAGE OF PANCREATIC-DIGESTIVE ANASTOMOSIS IN PATIENTS WITH PANCREATODUODENAL RESECTION

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Summary

The study compared early post-surgical complications between two groups of patients with pancreatoduodenal resection for pancreatic head carcinoma: patients with pancreatic-gastric anastomosis with mixed drainage and controls with pancreatic jejunal anastomosis with external drainage. The present study was a cohort study. The patient group was selected prospectively, and the control group – retrospectively. Patients were randomized by sex, age, primary tumor location, pancreatic parenchyma density, clinical symptoms, tumor–node–metastasis (TNM), and grade (G). We used the IBM SPSS Statistics software with the following tests: Fisher's exact test, Pearson's chi-squared test, Mann–Whitney U test. The optimized reconstruction approach with mixed drainage reduced early complications: early mortality - by 2.5%, overall morbidity - by 7.5%; pancreatic-digestive anastomosis insufficiency - by 2.5%; intra-abdominal bleeding - by 2.5%; intra-abdominal infection - by 2.5%; gastroparesis - by 5.0%; wound infection - by 2.5%; biliary leakage - by 2.5%. There were no cases of clinically significant pancreatic fistula. The control group was associated with an average of 9-fold higher relative risk of early complications. The passage was restored between the 4th and 7th day. Patients had a shorter average hospital stay (11 days) compared to controls (22 days). Digestive anastomoses reconstruction on a single loop and mixed intraluminal drainage through a modified nasogastric tube led to a 7-fold reduction in early post-surgical complications and a 2-fold shorter hospital stay.

Keywords: pancreaticojejunostomy, pancreatico-gastrostomy, pancreatic fistula, mixed drainage

Introduction

Pancreatic cancer is the fourth leading oncological cause of death. Overall, 5-year survival is from 5.0% to 8.0% [1]. The modern surgical treatment method is proximal pancreatoduodenal resection (PDR), also known as classical Whipple (CW), developed by Whipple AO et al. in 1935. The biggest advantage of this surgical procedure is radical treatment. The main disadvantage is that,

regardless of the type of pancreatic-digestive anastomosis, it remains physiologically burdened, leading to a high incidence of pancreatic insufficiency and fistula, PF (9.0-14.0%) [2], and the rate of early complications remains high for modern radical treatment standards (up to 60.0%).

In CW, newly created digestive anastomoses disrupt the physiological "horseshoe-shaped" anatomical configuration between the stomach and small intestine.

Newly constructed digestive anastomoses (T-L PJA and T-L GJA) are dual-loop and have blind-ended post-resection stumps: a small intestinal stump next to T-L PJA and a gastric stump next to T-L GJA. When combined with gastric and intestinal post-resection paresis, the result significantly burdens the digestive anastomoses. The incidence of clinically significant fistulas (grades B and C, according to ISGPF) is 16.00% for pancreatoduodenectomy [3]. A retrospective study from 2015 with 532 PDR confirmed these results: PF (grades B + C) was 10.2% [4].

The Fistula Risk Score Group (FRSG) identified four factors associated with high pancreatic fistula (PF) risk: soft parenchyma, a diameter of pancreas <3.0 - 4.0 mm, cystic pathology (lack of fibrosis, fatty degeneration), and intraoperative blood loss (>1000 ml - 1500 ml) [5]. Choledochal-jejunal anastomosis (CJA) insufficiency was rarely observed (5.0-8.0%) [6], with bile leakage in the abdominal cavity and development of intra-abdominal infection (IAI) – biliary peritonitis, and pancreatic stump necrosis (0.5-9%) [7]. The IAI incidence was from 17.0% [8] to 25.5% [6]. The intra-abdominal hemorrhage (IAH) values ranged from 7.1% [9], 13.0% [10], to 17.5% [11] were observed. Delayed gastric emptying (DGE) is a common complication: 8.0% – 45.0% [10]. Among pulmonary complications (9.9%) [6], the most common were pneumonia (5.0%), pleural effusion (3.0%), respiratory failure (2.0%), pleural empyema (0.5%), and pulmonary embolism (0.5%). Revision for early complications was applied in 10.0% of the operated patients. In a 7-year study from 2015 involving 70 CW cases [9], 37.0% were re-admitted, with nausea and vomiting being the most common reason for admission (24.2%) and pneumonia (19.24%) being the second most common. In the same study, the most common cause for reoperation was the presence of intra-abdominal abscess [9].

Mechanical unloading of the anastomosis is a prerequisite for better clinical results. The new concept of the present study aims to reduce the mechanical burden on the pancreatic-digestive anastomosis by applying an optimized reconstruction approach (replacement of T-L PJA with T-L PGA; replacement of T-L GJA with T-T GJA) and an optimized drainage method (application of modified double lumen nasogastric tube) after PDR.

Material and Methods

The present study was a cohort study. The patient group was selected prospectively. We performed 40 proximal PDR with PGA Mix drainage for ten years (2007-2017) on a random basis at the Saint Anna Hospital, Varna, Bulgaria. The control group was selected retrospectively using the Oncologic Dispensary register for the Varna Region for the same period.

We studied 710 patients with pancreatic cancer: 371 men and 339 women. We randomly sampled 80 patients with PDR and T-L PJA Ext drainage (simple random sampling without replacement) from 275 surgically treated patients. We randomized them according to the epidemiological indicators of the patient group (Table 1). Exclusion criteria were: localization of carcinoma in the body and tail of the pancreas, total/subtotal pancreatectomy, and distal pancreatoduodenal resection. Data were processed and analyzed using IBM SPSS Statistics Version 19.00 for Windows. The following statistical tests were used: Fisher's exact test, Pearson's chi-squared test, Mann–Whitney U test.

Surgical procedure

The resection was performed according to the Whipple method, and the sequence of resected organs was as follows: antrectomy, 5-7 cm from the pylorus; pancreas head and neck resection; cholecystectomy with resection of the distal choledochus; resection of the distal duodenum and jejunum, 5 cm from the ligament of Treitz. Compared to the Whipple procedure, the

optimized reconstruction approach included the replacement of T-L PJA with T-L PGA, and T-L GJA with T-T GJA. Reconstruction ended with a truncal vagotomy. The optimized drainage method included mixed drainage (internal and external) (Figures 1, 4), internal drainage of the common pancreatic duct with a stent, and external drainage using a double lumen nasogastric tube that drained (actively and passively) all three digestive anastomoses. The double lumen nasogastric tube exited through the gastric stump, passed through the small intestine, and reached the choledochus; the end of the tube entered 2-3 cm into the choledochus and was fixed to the posterior wall of the HJA with a single fast-absorbing suture. A stent drained the pancreatic duct into the tube (actively and passively). There was no drainage through the anterior abdominal wall.

Results

The effectiveness of the surgical procedure was determined by comparing the early post-surgical complications in the patient and control groups (Table 2). The lack of post-surgical resection stumps, reconstruction of digestive anastomoses on a single loop, and their mixed intraluminal unloading (internal and external) through active and passive aspiration led to substantial (6 to 7 times), statistically significant ($p < 0.05$) reduction in early post-surgical complications: early mortality by 2.5%, total morbidity by 7.5%; pancreatic-digestive anastomosis insufficiency by 2.5%; intra-abdominal bleeding by 2.5%; intra-abdominal infection by 2.5%; gastroparesis by 5.0%; wound infection by 2.5%, biliary leakage by 2.5% and no clinically significant cases of pancreatic fistula (Table 2). The control group (PJA Ext drainage) was found to be with an average of 9-fold higher relative risk (OR) for early post-surgical complications (Table 2), 7-fold higher risk for early mortality, 11-fold higher risk for overall morbidity, 15-fold higher risk for insufficiency of the pancreatic-digestive anastomosis, and an 8-fold higher risk for intra-abdominal bleeding. The risk was 9-fold higher for intra-abdominal infection, 4-fold higher for gastroparesis, 7-fold higher for wound infection, and 9-fold higher for a biliary leak (Figures 2, 3). The nasogastric tube was removed within 24 to 36 hours after the passage restoration. The passage was most often restored between the 4th and 7th day. The patient group had a shorter average hospital stay (11 days) than the control group with CW (22 days).

Discussion

PDR was developed by Whipple A.O. et al. in 1935. Over the years, various methods have been proposed to optimize pancreatic-digestive anastomosis: classic Whipple (CW) PDR was replaced by pyloric-preserving (PPPD) or pylorus-resecting with gastric preservation (PRPD, GPPD). Optimized anastomotic surgical techniques were offered to enhance anatomical strength and ensure optimal blood supply to pancreatic-digestive anastomoses (PJA or PGA), and optimized drainage of digestive anastomoses was proposed. Stent placement through the pancreatic-digestive anastomosis after PDR may help divert pancreatic juice from the anastomosis site, decompressing the residual pancreas and maintaining patency of the common pancreatic duct. However, the benefits remain controversial. External stent complications are associated with the timing of its removal and internal stent complications with the high incidence of migration to an atypical location. External and internal stents show comparable clinical results in the short and long term, and the type of pancreatic stent is a subjective choice of the surgeon [17-21]. The use of external stents may be associated with a significant reduction in PF incidence, substantial post-surgical complications incidence (IAA, DGE, WI), and length of hospital stay [17-20, 22-26]. The use of internal stents in patients with soft parenchyma and narrow pancreatic duct (<3.0 mm) is associated with a higher PF risk and morbidity [18, 27], and the benefits of its use compared to no-stent drainage are controversial [17-20, 27]. Timing of drainage removal is an independent PF risk factor. Early drainage removal on days 3-4 is associated with reduced PF incidence, abdominal and lung complications, and a shorter average hospital stay. Drainage removal within 72 hours is recommended for patients at low PF risk (firm parenchyma, pancreatic duct width >3.0 mm, drainage amylase content ≤5000 U/L) [12-15].

Longer drainage retention is reasonable in patients at high PF risk (soft parenchyma, narrow pancreas <3.0 mm, drainage amylase content > 5000 U/L). Persistence of drainage over three weeks is an independent risk factor for PF, according to the International Study Group of Pancreatic Fistula [16]. In the present study, drains were placed in the pancreatic duct. Percutaneous extravertebral drains were replaced with a specifically designed double lumen nasogastric tube, allowing intraluminal drainage of all three digestive anastomoses: T-L PGA; T-L HJA, T-T GJA. We developed a procedure for measuring the volume and pressure of gastrointestinal contents, which determined the frequency and volume of active aspiration. The nasogastric tube was removed within 24 to 36 hours after the passage restoration. The passage was most often restored between days 4 and 7, and the average hospital stay was 11 days, twice shorter than in the CW group.

Conclusions

The absence of post-surgical stumps, digestive anastomoses reconstruction on a single loop, and their mixed intraluminal unloading (internal and

Table 1. Epidemiological characteristics of patient and control groups

Variable	Total n (%)	PJA Ext drainage %	PGA Mix drainage %	P Value
n	120	80	40	
Gender				[1]0.697
male	67 (55.8%)	46 (57.5%)	21 (52.5%)	
female	53 (44.2%)	34 (42.5%)	19 (47.5%)	
Age,				[3]0.674
Mean ± SD	66 ± 10	67 ± 1	66 ± 2	
Median	67	68	66	
Primary tumor origin				[2]0.951
Pancr. head adenocarcinoma	43 (35.8%)	27 (33.8%)	16 (40.0%)	
Ampullary adenocarcinoma	36 (30.0%)	25 (31.3%)	11 (27.5%)	
Distal CBD adenocarcinoma	12 (10.0%)	8 (10.0%)	4 (10.0%)	
Duodenal adenocarcinoma	5 (4.2%)	3 (3.8%)	2 (5.0%)	
Others	24 (20.0%)	17 (21.3%)	7 (17.5%)	
Pancreas parenchyma				[1]0.692
Firm	74 (61.7%)	48 (60.0%)	26 (65.0%)	
Soft	46 (38.3%)	32 (40.0%)	14 (35.0%)	
Symptom				
with jaundice	90 (100.0%)	55 (68.8%)	35 (87.5%)	[1]0.027
with epigastric pain	80 (100.0%)	52 (65.0%)	28 (70.0%)	[1]0.683
with body weight loss	85 (100.0%)	53 (66.3%)	32 (80.0%)	[1]0.139
with nausea/vomiting	70 (100.0%)	45 (56.3%)	25 (62.5%)	[1]0.560
with gastrointestinal bleeding	4 (100.0%)	3 (3.8%)	1 (2.5%)	[1]1.000
with diabetes mellitus	17 (100.0%)	15 (15.0%)	5 (12.5%)	[1]0.788
with ERCP	16 (100.0%)	10 (12.5%)	6 (15.0%)	[1]0778
TNM				[1]1.000
T1	23 (19.2%)	15 (18.8%)	8 (20.0%)	
T2	97 (80.8%)	65 (81.3%)	32 (80.0%)	
G				[2]0.773
G1	7 (5.8%)	5 (6.3%)	2 (5.0%)	
G2	80 (66.7%)	54 (67.5%)	26 (65.0%)	
G3	25 (20.8%)	17 (21.3%)	8 (20.0%)	
G4	8 (6.7%)	4 (5.0%)	4 (10.0%)	

PD – pancreatoduodenectomy; CBD - common bile duct, SD - standard deviation; PJA – pancreaticojejunostomy; PGA – pancreaticogastrostomy; Ext - external; Mix- mixed; ERCP - endoscopic retrograde cholangiopancreatography; [1]Fisher's Exact Test; [2]Pearson Chi-Square Test; [3]Mann-Whitney Test

external) through active and passive aspiration lead to a substantial (7-fold) statistically significant reduction in early post-surgical complications and 2-fold shorter hospital stay.

Table 2: Early post-surgical complications in the patient and control groups

Variable	PJA Ext drainage % (n=80)	PGA Mix drainage % (n=40)	OR	P Value
Surgical mortality to 1 month	12 (15.0%)	1 (2.5%)	6.8	[1]0.058
Surgical morbidity	38 (47.5%)	3 (7.5%)	11.2	[1]0.000
Pancreatic insufficiency	23 (28.8%)	1 (2.5%)	15.7	[1]0.000
Pancreatic fistula grade (B+C)	15 (18.8%)	0 (0.0%)	x	[1]0.002
Intra-abdominal hemorrhage	14 (17.5%)	1 (2.5%)	8.2	[1]0.019
Intra-abdominal infection	15 (18.8%)	1 (2.5%)	9.0	[1]0.020
Delayed gastric emptying	14 (17.5%)	2 (5.0%)	4.0	[1]0.086
Wound infection	12 (15.0%)	1 (2.5%)	6.9	[1]0.058
Bile leak	15 (18.8%)	1 (2.5%)	9.0	[1]0.020
Hospital stay	22 d	11 d	x	[3]0.000

PD – pancreatoduodenectomy; PJA – pancreaticojejunostomy; PGA – pancreaticogastrostomy Ext - external; Mix - mixed; OR - odds ratio; [1]Fisher's Exact Test; [2]Pearson Chi-Square Test; [3]Mann-Whitney *U* Test

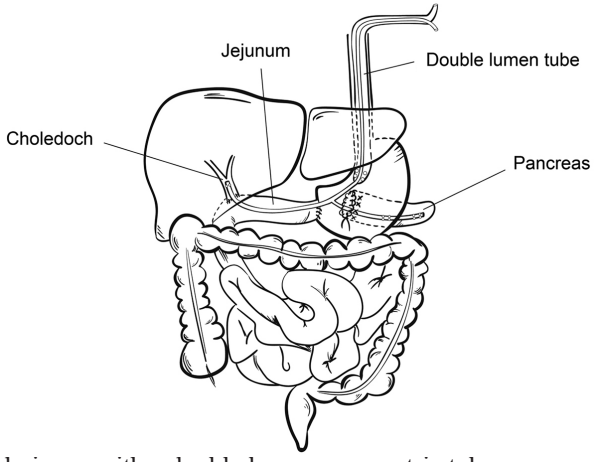

Figure 1. Diagram of PDA drainage with a double lumen nasogastric tube

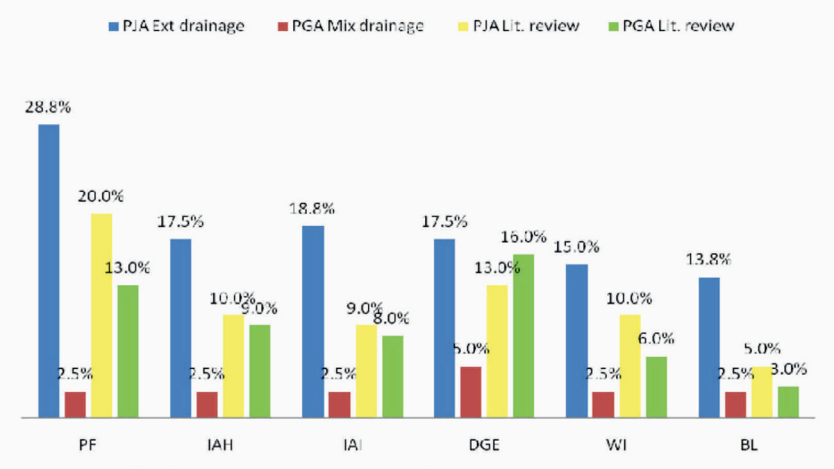

Figure 2. Distribution of early (up to 1 month) post-surgical complications cases. PI - Pancreatic insufficiency, IAH - Intra-abdominal hemorrhage, IAI - Intra-abdominal infection, DGE - Delayed gastric emptying, WI - Wound infection, BL - Bile leak

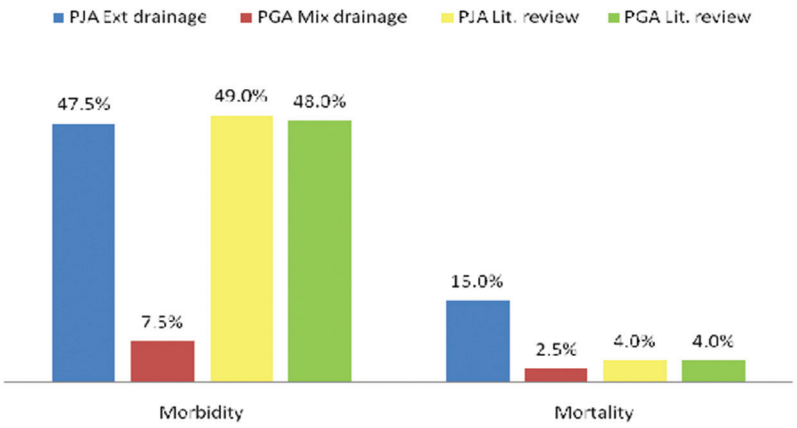

Figure 3. Distribution of total early morbidity and mortality cases.

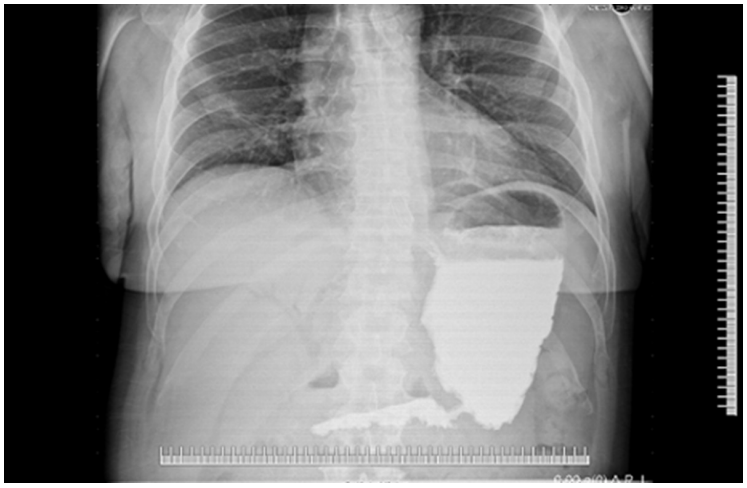

Figure 4. Post-surgical contrast radiography of the PGA

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