Reconstruction methods after pancreaticoduodenectomy for pancreatic carcinoma: better method to prevent serious complications

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Purposes
The of aim of this study was to assess the safety of pancreatic anastomosis after pancreaticoduodenectomy (PD) and to compare the results of pancreaticogastrostomy (PG) versus pancreaticojejunostomy (PJ) following PD in a prospective and randomized setting.

Background
Pancreatic fistula after PD represents a critical trigger of potentially life-threatening complications and is also associated with markedly prolonged hospitalization. The best method for dealing with the pancreatic stump after PD remains in question.

Patients and methods
The study included 50 patients, 33 (64%) men and 18 (36%) women with a mean age of 66.3 ± 4 years. All patients underwent clinical evaluation, laboratory assessment, and computed tomography or MRI examination. All patients undergoing PD with soft residual tissue were randomized to receive either pancreaticogastrostomy (group PG) or end-to-side pancreaticojejunostomy (group PJ). The postoperative follow-up ranged from 6 to 12 months.

Results
No mortality was recorded. The mean ICU stay duration was 2.4 ± 0.8 days. The duration of hospital and ICU stay was shorter in group PG ($P = 0.03$). The mortality because of surgical causes was higher in group PJ ($P = 0.02$). The frequency of postoperative complications — that is, pancreatic fistula ($P = 0.0343$), intra-abdominal bleeding and collection ($P = 0.0376$) — was higher in group PJ; however, there was no significance between both groups in the frequency of abdominal wall abscess and biliary leakage ($P = 0.39$). The patients with intra-abdominal collection were treated well by conservative measures in group PG ($P = 0.023$); however, patients who needed open drainage were less ($P = 0.0376$) and there was no significance between both groups in computed tomography-guided drainage ($P = 0.56$).

Conclusion
Pancreaticogastrostomy could be considered better as a reconstruction method; with shorter hospital stay, No Necrosis of pancreatic remnant, Less frequency of post operative complications & so Re-do with its complication is less.

Keywords:
morbidity, pancreatic carcinoma, pancreaticoduodenectomy, pancreaticogastrostomy, pancreaticojejunostomy

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Introduction

Pancreatic cancer is the fourth leading cause of cancer death in men and the fifth in women, accounting for 4.8 and 5.5% of cancer deaths in men and women, respectively. The aggressive biology of these tumors and the high local recurrence rate in combination with the early metastatic spread lead to 5-year survival rates between 11 and 21% after resection [1,2].

Pancreaticoduodenectomy (PD) is the standard surgical procedure for various malignant and benign disease of the pancreas and the periampullary region. During the recent years, the mortality rate of PD has decreased to 5% in specialized centers [3].

Surgical resection by means of PD provides the only chance of cure for patients with periampullary and pancreatic carcinoma. Advances in the surgical technique have reduced the operative mortality rate to below 5% in high-volume centers. Nevertheless, operative morbidity remains high, occasionally approaching 30–40%, most often including pancreatic and biliary fistula, intra-abdominal bleeding or collection, and abdominal wall abscesses [3].

However, this procedure still carries considerable morbidity up to 40%, depending on the definition of complications. Pancreatic fistula remains a common complication and the main cause of other morbidities and mortality [4,5].

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The classic Whipple operation is the standard basic surgical procedure performed predominantly for the treatment of periampullary and pancreatic head cancer. The classic Whipple operation consists of an en-bloc removal of the pancreatic head, the duodenum, the common bile duct (CBD), the gall bladder, and the distal portion of the stomach together with the adjacent lymph nodes [6,7].

The safe reconstruction of pancreatic–gastrointestinal continuity after PD continues to be a challenge for the pancreatic surgeon. Despite a reduction in the mortality rate to 3–5%, postoperative complications are still high [8–11].

There are many reconstruction methods after PD; pancreaticojejunal (PJ) anastomosis with external drainage of pancreatic duct is the most often used method of reconstruction after PD. Several technique modifications such as placement of the stents, pancreatic duct occlusion, and pancreaticogastrostomy (PG) type of anastomosis are used to decrease pancreatic fistula rate. Nevertheless, anastomosing the pancreatic remnant to a hollow viscous after PD is still the weak link of the operation and leakage of the pancreatic anastomosis remains a problem [8].

Considerable attention has been focused on refinements in the operative technique for PD, especially on the management of the pancreatic remnant, with the intent to decrease the incidence of pancreatic fistula. These efforts include technical modifications such as the pancreaticogastric anastomosis and external drainage of the pancreatic duct [1].

PG could be considered better; some retrospective studies have reported lower pancreatic fistula rate with PG instead of PJ, and a recent meta-analysis suggested that the safer means of pancreatic reconstruction after PD was PG [5–7].

The present study aimed to assess the safety of pancreatic anastomosis after PD and to compare the results of PG versus pancreaticojejunostomy (PJ) following PD in patient having pancreatic carcinoma.

Patients and methods

The current study was conducted at General surgery Department, Benha University Hospital and Hepatobiliary Surgery Department, National liver institute, Menoufiya University from January 2011 to December 2013 so as to allow 12 months follow-up period for the last patient operated upon. After obtaining written fully informed patients consent, all patients presenting were admitted to General Surgery ward for clinical evaluation, laboratory assessment, and underwent computed tomography (CT) or MRI examination for assuring the diagnosis.

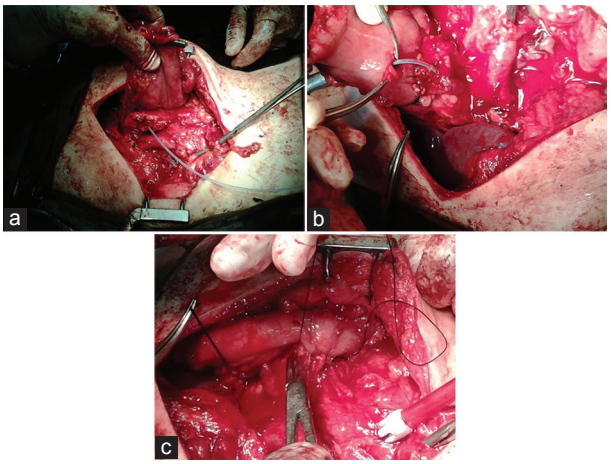
Operative procedure

Upon opening of the abdomen, liver was carefully inspected and palpated for any metastatic disease. Pancreatic tumor was palpated and its mobility was assessed; if it was resectable, the duodenum and head of pancreas were mobilized and the tumor was then bimanually palpated. Then, mobilization of the second and third parts of the duodenum was commenced and continued until the superior mesenteric vein comes into view as it crosses the duodenum. The stomach was mobilized and the right gastroepiploic vein was meticulously dissected and ligated between ligatures just before its termination in the superior mesenteric vein below the neck of the pancreas. All tributaries passing from the head of pancreas and uncinate process to the superior mesenteric vein were divided between ligatures. Cholecystectomy was performed and CBD and lower hepatic ducts were mobilized then CBD was divided just above the entry of the cystic duct. The jejunum was mobilized and the ligament of Treitz was incised to free the duodenojejunal flexure, and proximal jejunum was divided. The neck of the pancreas was divided; pancreatic duct was cannulated with fine catheter, then passed into stomach before end-to-side pancreaticogastrostomy [group PG; $n = 25$ (50%)]. Here, the catheter was divided inside the stomach and fixed in place by one stitch of the first layer of closure (PG was carried out on the posterior wall of the stomach by a double-layer closure: the first layer with nonabsorbable interrupted stitches through the layer of the stomach including its mucosa and pancreatic duct and the second layer through the seromuscular layer of the stomach and full thickness of pancreas, both anteriorly and posteriorly) (Fig. 1) or passed to the jejunum before end-to-side pancreaticojejunal anastomosis [group PJ; $n = 25$ (50%)]. The catheter was brought out through separate jejunal stab (PJ was carried out using the same maneuver applied to PG, double-layer closure except the catheter to outside) (Fig. 2). Then, CBD was anastomosed end-to-side to the jejunum and proximal jejunum was anastomosed to the stomach. After assuring hemostasis, the abdominal cavity was drained and the abdomen was closed [12–14].

Outcome items

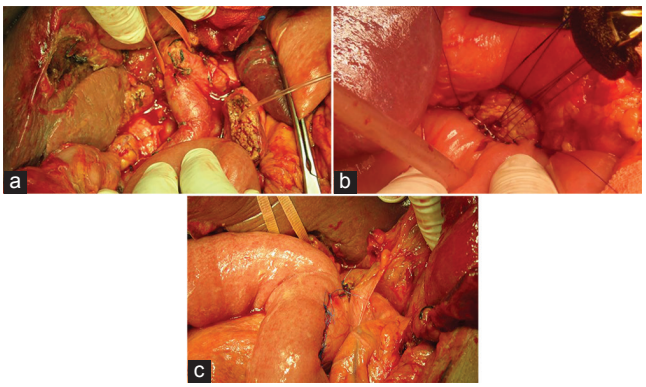
Postoperative pancreatic-associated morbidities (disease specific) included leakage of pancreatic anastomosis/pancreatic fistula (confirmed by fistulogram, CT examination, and by increased amylase level in this fluid leak), biliary leakage (confirmed by bile in the drain fluid from the subhepatic drain or

Figure 1



(a) Stent inside the pancreatic duct. (b) Stent inside stomach and pancreatic duct. (c) Complete pancreaticogastrostomy.

Figure 2



(a) Stent inside the pancreatic duct. (b) Posterior layer of pancreaticojejunostomy. (c) Complete pancreaticojejunostomy.

a subsequently placed percutaneous drain with the level of total bilirubin exceeding the upper limit of normal), intra-abdominal fluid collection/abscess, and/or postoperative bleeding (all can be confirmed by CT examination and clinical course).

Other outcome measures included operation time, blood loss, required blood replacement, status of resection margins, number and status of removed lymph nodes, duration of ICU stay, duration of hospital stay, and postoperative overall mortality.

All deaths that occurred during this study because of nonsurgical cause — that is, pulmonary embolism, myocardial infarction, stroke, etc — were excluded.

Statistical analysis

Analysis of some data was performed using SPSS version 16 (Bristol university; in United Kingdom). Quantitative data were presented as mean and SD and were analyzed using one-way analysis of variance test. Qualitative data were presented as numbers and percentages and were analyzed using the χ^2 and Fisher exact tests. *P*-value less than 0.05 was considered significant, whereas *P*-value less than 0.01 was considered highly significant. However, *P*-value greater than 0.05 was considered insignificant.

However, some other data are presented as mean ± SD and number; ranges and percentages are in parentheses.

Results

The study included 50 patients, 33 (64%) men and 18 (36%) women with a mean age of 66.3 ± 4 years. Indications for surgery were resectable pancreatic cancer [*n* = 37 (74%)], ampullary cancer [*n* = 7 (14%)], cancer of distal bile ducts [*n* = 5 (10%)], and cancer of the duodenum [*n* = 1 (2%)]. All patients were fit for surgery as confirmed by American Society of Anesthesiologists grade (ASA): ASA I [*n* = 29 (58%)], ASA II [*n* = 14 (28%)], and ASA III [*n* = 7 (14%)]. Patients of this study were divided into two groups according to the method of anastmosis after surgery: pancreaticogastrostomy (group PG) [*n* = 25 (50%)] and pancreaticojejunostomy (group PJ) [*n* = 25 (50%)] (Table 1).

All patients underwent PD with a mean operative time of 4 ± 0.8 h (range: 3–5 h). The mean blood loss was 640 ± 115 ml (range: 400–800 ml). All patients required blood transfusion with a mean number of used units of 2.8 ± 0.7 U (range: 2–3 U) (Table 2). No intraoperative complication or mortality was recorded.

The site of tumor origin was described as indications of surgery mentioned in patients and methods. The mean tumor diameter was 2.4 ± 0.4 (range: 1.5–3.5 cm). Nineteen tumors were poorly differentiated (38%). Surgical margin showed microscopic infiltration in four patients (8%); two patients had carcinoma involving the margin at the level of the uncinate process adjacent to the superior mesenteric vein and the other two patients had a positive microscopic margin at the pancreatic neck–body transection site. Twenty-eight patients (56%) showed perineural invasion and three patients (6%) showed vascular invasion. Thirty-four patients (68%) had histologically positive lymph node metastases in the resection specimen and the mean total number of resected lymph nodes was 18 ± 1.8 (range: 16–21 nodes) (Table 3).

Patients passed the immediate postoperative during the immediate postoperative period at surgical ICU for a mean duration of 2.4 ± 0.8 days (range: 1–4 days) were less in group PG [*n* = 8 (0.16 ± 0.47); *P* = 0.03]. The

Table 1 Preoperative data

Age (years)	
Strata	
60	8 (16)
60-70	5 (1)
>70	37 (74)
Total	66.3 ± 4 (52–74)
Sex	
Men	33 (64)
Women	18 (36)
American Society of Anesthesiologists grade (ASA)	
ASAI	29 (58)
ASAII	14 (28)
ASAIII	7 (14)
Indications for operation	
Pancreatic cancer	37 (74)
Ampullary cancer	7 (14)
Cancer of distal bile ducts	5 (10)
Cancer of the duodenum	1 (2)
Method of anastmosis after surgery	
Pancreaticogastrostomy (PG)	25 (50)
Pancreaticojejunostomy (PJ)	25 (50)

Data are presented as means ± SD and number; ranges and percentages are in parenthesis.

Table 3 Pathological data of excised specimens

Data	Findings
Site	
Pancreatic cancer	37 (74)
Ampullary cancer	8 (16)
Cancer of distal bile ducts	4 (8)
Cancer of the duodenum	1 (2)
Size (cm)	
Diameter in its longest axis	2.4 ± 0.4 (1.5–3.5)
Differentiation	
Well	31 (62)
Poorly	19 (38)
Surgical margin invasion	
Yes	4 (8)
No	46 (92)
Perineural invasion	
Yes	28 (56)
No	22 (44)
Perivascular invasion	
Yes	3 (6)
No	47 (94)
Lymph node status	
Positive	34 (68)
Negative	16 (32)
Total number of resected lymph nodes	18 ± 1.8 (15–20)

Data are presented as mean ± SD and number; ranges and percentages are in parentheses.

mortality because of surgical causes was higher in group PJ [n = 3 (0.75 ± 0.5); P = 0.04]; mortality was because of intra-abdominal bleeding and necrosis of pancreatic remnant. Three patients developed intra-abdominal bleeding: two patients were saved, but unfortunately the other one died at the night of operation. However,

Table 2 Operative data

Operative time (h)	
Strata	
3	13 (26)
>3–4	18 (36)
>4–5	19 (38)
Total	4 ± 0.8 (3–5)
Blood loss (ml)	640 ± 115 (400–1500)
Replacement of red cells (U)	
Strata	
2	17 (34)
3	21 (42)
4	12 (24)
Total	2.8 ± 0.7 (2–4)

Data are presented as means ± SD and number; ranges and percentages are in parenthesis.

with respect to necrosis of pancreatic remnant, three patients were explored, but unfortunately these patients died on the fourth postoperative day because of development of septicemic shock and multiorgan failure that failed to respond to treatment (Table 4).

During the hospital stay, the frequency of postoperative complications — that is, pancreatic fistula — (10 patients) was higher in group PJ [in group PG, N = 3 (0.09 ± 0.29) and in group PJ, N = 7 (0.32 ± 0.47)] (P = 0.0343). However, there was no significance between both groups in the frequency of abdominal wall abscess and biliary leakage: six patients [in group PG, N = 2 (0.08 ± 0.27) and in group PJ, N = 4 (0.16 ± 0.37)] (P = 0.39). The patients with intra-abdominal collection were treated well by conservative measures in group PG [N = 2 (0.28 ± 0.45)] as compared with group PJ [N = 4 (0.04 ± 0.2)] (P = 0.023). However, patients who needed open drainage were less in group PG [N = 0 (0)] as compared with group PJ [N = 1 (0.16 ± 0.37)] (P = 0.0376), and there was no significance between both groups in CT-guided drainage (P = 0.56). Finally, patients with abdominal wall abscess were treated well by conservative measures in group PG [N = 2 (0.05 ± 0.3)] as compared with group PJ [N = 1 (0.28 ± 0.45)] (P = 0.023), and there was no need for open drainage in group PG [N = 0 (0)] as compared with group PJ [N = 1 (0.16 ± 0.37)] (P = 0.0376) (Table 5).

Discussion

The safe reconstruction of pancreatic–gastrointestinal continuity after PD continues to be a challenge for the pancreatic surgeon. Patients who stayed during the immediate postoperative period at surgical ICU for a mean duration of 2.4 ± 0.8 (range: 1–4 days) were less in group PG [n = 8 (0.16 ± 0.47); P = 0.03]. The mortality because of surgical causes was higher in group PJ [n = 3 (0.75 ± 0.5); P = 0.02]; mortality was because of intra-

abdominal bleeding and necrosis of pancreatic remnant. In agreement with these results, Kim *et al*. [15] found a significantly less immediate postoperative mortality using PG compared with using PJ. These results were approved in another nonrandomized study by Takano *et al*. [16]. This can be explained by the gastric acid environment that is thought to inhibit the activation of pancreatic enzymes. This consideration, together with the lower tendency for ischemia due to the rich gastric vascular supply, probably justifies the trend toward a lower rate of pancreatic necrosis and intra-abdominal bleeding in the PG group [n = 1 (2%) (0.04 ± 0.2) vs. n = 3 (6%) (0.75 ± 0.5)] (P = 0.04). In contrast to this study, Oussoultzoglou *et al*. [17] found no differences in mortality, but a significant reduction in the rate of pancreatic fistula (and related reoperations) and the duration of hospital stay was found in PG reconstruction in 250 patients analyzed retrospectively.

During the hospital stay, the frequency of postoperative complications — that is, pancreatic fistula, intra-abdominal collection — was less in patients of the PG group [N = 2 (0.08 ± 0.27) vs. N = 7 (0.32 ± 0.47)] (P = 0.0343) in the study published by Yeo *et al*.[18], which is comparable with the present one, revealing the same result. This may be related to the smaller postsurgical anatomic perianastomotic space remaining compared with PJ; the intimate proximity of the stump to the posterior wall of the stomach allows a tension-free, wide, and well-suitable anastomosis with adequate tissue to 'telescope' the stump into the gastric cavity. In addition, the gastric acid environment is thought to inhibit the activation of pancreatic enzymes. In contrast with PJ, the activation of pancreatic exocrine secretions can occur more easily in the presence of intestinal enterokinase and bile. Moreover, Shen and Jin [19] explained the same result; PG avoids the long jejunal loop where pancreatobiliary secretions accumulate during the early postoperative period, and postoperative gastric decompression can provide constant removal of pancreatic and gastric secretions avoiding accumulation, and thus tension on the anastomosis. PG anastomosis reduces the number of anastomoses in a single loop of retained jejunum, which potentially decreases the likelihood of loop kinking.

With respect to postoperative biliary leakage, there was no significance between both groups in the frequency of biliary leakage: six patients [in group PG, N = 2 (0.08 ± 0.27) and in group PJ, N = 4 (0.16 ± 0.37)] (P = 0.39). This result was reported by McKay *et al*. [20] and is partly similar with the result of Wente *et al*. [21].

PG group revealed significant results in the management of intra-abdominal complications, that easily was treated conservatively, and there was no need for open drainage. However, in patients of the PJ group, CT-guided and open drainage were needed, resulting in increased length of hospital stay and increased incidence of related complications of redo operations.

Conclusion

Pancreaticogastrostomy (PG) could be considered better as a reconstruction method; With shorter hospital stay, No Necrosis of pancreatic remnant, Less frequency of post operative complications & So Re-do with its complication is also less.

Table 4 Postoperative ICU data

Variables	Group PG		Group PJ		*F*	*P*-value
Duration of stay (1-4 days); 2.4 ± 0.8 (1.9)	*N* = 8	0.16 ± 0.47	*N* = 11	0.44 ± 0.5	4.94	0.03
Mortality due to surgery: 3 (6%)						
Necrosis of pancreatic remnant	*N* = 1	—	*N* = 2	—	—	—
Intra abdominal bleeding	*N* = 0	—	*N* = 1	—	—	—
Total	*N* = 1	0.04 ± 0.2	*N* = 3	0.75 ± 0.5	9	0.04

PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy.

Table 5 Postoperative morbidity during hospital stay

Variables	Group PG		Group PJ		*F*	*P*-value
Pancreatic leakage	*N* = 3	0.09 ± 0.29	*N* = 7	0.32 ± 0.47	4.7	0.0343
Biliary leakage	*N* = 2	0.08 ± 0.27	*N* = 4	0.16 ± 0.37	0.74	0.39
Intra-abdominal collection						
Conservative treatment	*N* = 2	0.28 ± 0.45	*N* = 4	0.04 ± 0.2	5.7	0.023
C.T guided drainage	*N* = 1	0.04 ± 0.2	*N* = 2	0.08 ± 0.27	0.34	0.56
Open drainage	*N* = 0	0	*N* = 1	0.16 ± 0.37	4.57	0.0376
Abdominal wall abscess						
Conservative treatment	*N* = 2	0.05 ± 0.3	*N* = 1	0.28 ± 0.45	5.7	0.023
Drainage	*N* = 0	0	*N* = 1	0.16 ± 0.37	4.57	0.0376

CT, computed tomography; PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy.

Acknowledgements

Conflicts of interest

None declared.

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