Safety and efficacy of isolated pancreatic anastomosis after pancreaticoduodenectomy

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Background
Pancreatic leak after Whipple's pancreaticoduodenectomy is the most serious complication being responsible for most of morbidity and mortality. Different techniques of reconstruction were developed to reduce the incidence of this complication. This study aims to evaluate the technique of isolated loop pancreaticojejunostomy after pancreaticoduodenectomy regarding its safety and efficacy.
Patients and methods
Morbidity and hospital mortality were evaluated in 25 patients underwent Whipple's pancreaticoduodenectomy for malignant tumors followed by isolated loop pancreaticojejunostomy.
Results
Postoperative complications, occurred in nine (36%) patients, three patients developed anastomotic leak, two (8%) pancreatic and one (4%) biliary, the two pancreatic leaks were of grade A. Delayed gastric emptying developed in one (4%) patient. One (4%) patient died due to pulmonary embolism. The mean operative time was 383.4±38.3 min, the mean time of anastomosis was 136.6±20.03 min, the mean intraoperative blood loss was 525.2±225.8 ml and the mean hospital stay was 12.76±3.6 days.
Conclusion
Although isolated loop pancreaticojejunostomy associated with somewhat long operative time due to additional anastomosis, it is associated with low rate and grade of pancreatic fistula and contribute to reducing its severity and subsequent sequelae.

Keywords:
isolated loop pancreaticojejunostomy, Whipple's pancreaticoduodenectomy, pancreatic leak

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Introduction

Pancreaticoduodenectomy (Whipple's operation) is the gold standard treatment of resectable periampullary carcinoma [1], it is a technically demanding procedure associated with high mortality and morbidity [2]. In the last decades the mortality is dramatically decreased to less than 5% in high volume centers while the morbidity is still high [3]. The rate of Whipple's operation is increasing in our community, this is may be due to many causes. Most important, is the wide spread of diagnostic facilities that led to early diagnosis of pancreatic tumors in an early stage, followed by the change of the insight of the disease, its diagnosis, and treatment possibility among health care providers, then the availability of trained surgeons skilled in such surgery. In our institute a fair number of pancreaticoduodenectomy (Whipple's operation) is done yearly, and like other centers, pancreatic leakage is the main cause of morbidity and mortality. In an attempt to refine our results, we started to use the technique of isolated loop pancreaticojejunostomy which was initially introduced by Machado *et al.* [4] in 1976 and based on the theory of preventing pancreatic enzymes activation by intestinal contents and bile and thus protecting the pancreaticojejunal anastomosis from erosion and decreasing the pancreatic leakage.

In the current study we present our experience with the technique of isolated loop pancreaticojejunostomy regarding surgical feasibility, operative and postoperative morbidity, and in-hospital mortality.

Patients and methods

Our patients were recruited from the outpatient's clinic and from the endoscopy unit in our institute where they referred for surgical management or for endoscopic retrograde cholangio-pancreaticography (ERCP), those patients were assessed by:

(1) Ultrasound and high-quality computed tomography.

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(2) ERCP and/or Magnetic resonance cholangio-pancreaticogram (MRCP).
(3) Laboratory investigations in the form of: Complete blood count, bilirubin (total and direct), alkaline phosphatase, urea and creatinine, liver enzymes SGOT and SGPT, blood sugar, prothrombin activity and international normalized ratio (INR), serum albumin, and tumor marker in the form of CEA and CA19-9.
(4) Postoperative histopathological confirmation of the diagnosis.

Patients with liver cirrhosis, portal hypertension, or those who are unfit for surgery as decided by the anesthesia team were excluded.

Patients with distant metastasis, peritoneal deposits, or locally irresectable tumors, as indicated by preoperative workup and/or intraoperative findings, were excluded.

A total of 25 patients in the period from January 2015 to March 2017 were eligible for the study and underwent pancreaticoduodenectomy (Fig. 1).

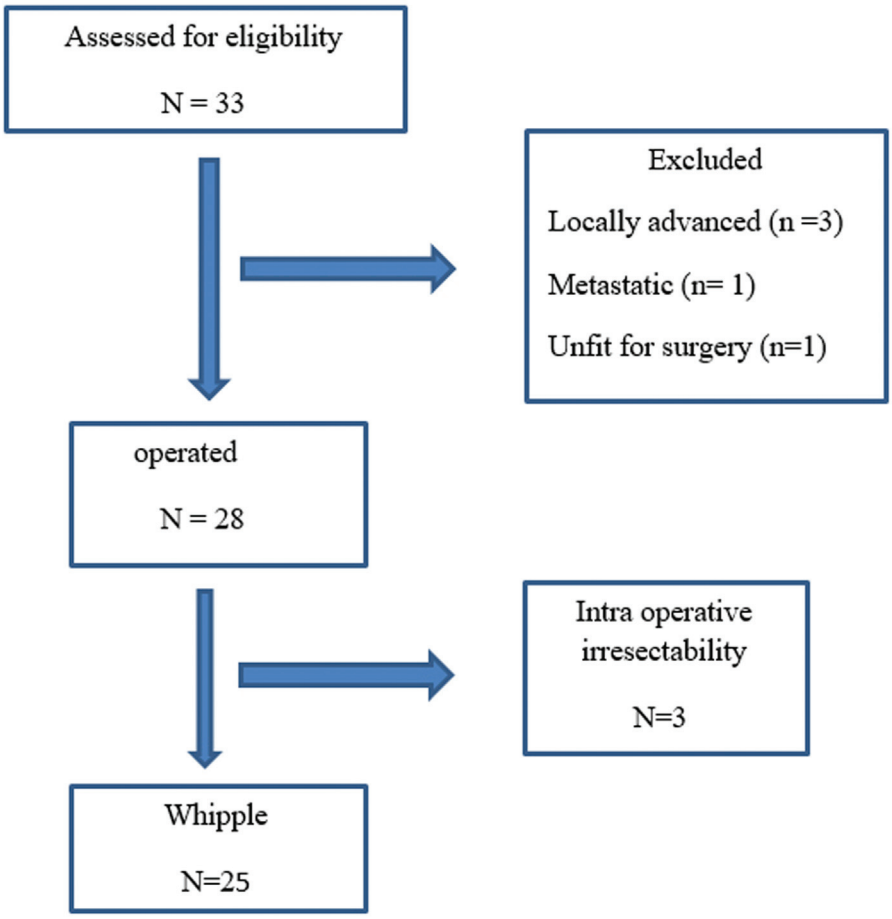
Informed consent was obtained from all patients and the study was approved by the local ethics committee.

Surgical technique

We started with a complete exploration of the abdomen to exclude any peritoneal seedling and/or liver metastasis. Pancreatic respectability was assessed through kocherization of right colon and duodenum medially to the inferior vena cava (IVC) and the abdominal aorta. We continue exploration of pancreatic head by dissection of superior mesenteric vein (SMV) from below and hepatoduodenal ligament above exposing the portal vein, the bile duct and the hepatic artery down to the gastroduodenal artery. Finally, we created a tunnel between the pancreatic neck and the SMV.

Distal gastrectomy was done. Cholecystectomy was done, and the common bile duct is divided. The gastroduodenal artery is divided, and the pancreas is divided at the neck. The jejunum is divided about 20 cm distal to the Treitz ligament then, the uncinate process was dissected from the superior

Figure 1



Flow diagram.

mesenteric vessels and pancreaticoduodenectomy is completed.

After pancreatic head excision, reconstruction was begun using the transected jejunum, brought up through the mesocolon, and an end to side pancreaticojejunostomy was done with duct to mucosa anastomosis using interrupted sutures, pancreatic stents are used in soft glands or if the duct was smaller than 3 mm, another reinforcing layer between the pancreatic capsule and the jejunal seromuscular was done. A separate Roux loop was fashioned for the hepaticojejunal anastomosis by dividing the jejunum about 40 cm beyond the pancreatic anastomosis and delivering the distal loop through another opening in the transverse mesocolon to perform a single layer retro colic end to side hepaticojejunostomy. An end to side double layer ante colic gastrojejunostomy is done about 50 cm from the hepaticojejunostomy.

The pancreatic limb is anastomosed about 20 cm downstream the gastrojejunostomy by double layer end to side anastomosis (Fig. 2). Finally, abdominal drains were inserted at the lesser sac and pouch of Morrison.

All specimens were sent for histopathological assessment.

Postoperative management

Patients were managed in surgical high dependency unit (HDU) till their status allows discharging to the ward. Outputs of drains and nasogastric tube are recorded daily. Oral fluids started once peristalsis were present and regular diet restored regularly as patients could tolerate.

Analysis of drainage for amylase level was done if the amount was more than 50 ml/day from the third day or if it was bile stained.

Drains were removed if the pancreatic leak was excluded by the amylase level and/or the amount of drainage was negligible.

Data collection

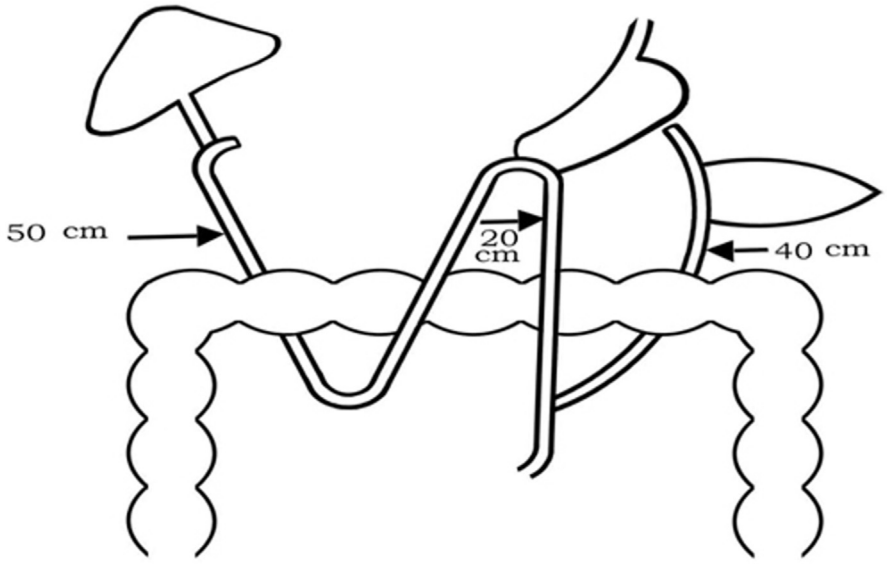
In all patients, total operative time, operative time of reconstruction, day of resuming oral feeding, time of drain removal, postoperative complications, length of postoperative hospital stay, and in-hospital deaths were recorded.

Postoperative pancreatic fistula, was defined according to the International Study Group of Pancreatic Fistula (ISGPF) definition as a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content greater than three times the serum amylase activity [5,6].

Postoperative pancreatic fistulas were classified according to the ISGPF classification as grades A, B, or C according to their clinical course [5,6].

Biliary leak was defined according to ISGPF criteria as the presence of bile in drainage fluid persisting to postoperative day 4.

Figure 2



Schematic drawing of isolated loop anastomosis.

Delayed gastric emptying was defined as output from a nasogastric tube of more than 500 ml/day persisting beyond postoperative day 10, failure to maintain oral intake by postoperative day 14, or need for the reinsertion of a nasogastric tube [5,6].

Results

The study included 25 patients, 16 males and nine females (Table 1), the mean age was 54.8±7.7 years (range, 38–65 years), all patients underwent Whipple's operation with isolated loop pancreaticojejunostomy.

Based on the preoperative work up there were three patients with periampullary lesion, one patient with distal common bile duct (CBD) lesion and the remaining patients were with pancreatic head mass.

The presenting symptoms included: jaundice (22 patients, 88%), abdominal pain, weight loss, pruritus, and cholangitis (Table 2).

The mean bilirubin level was 12.5±35.6 (range, 6–22), the mean albumin level was 3.5±4.34 g (range, 3.2–4.2 g) (Table 3).

Operative and postoperative data

The mean operative time was 383.4±38.3 min (range, 300–465 min), the time of anastomosis was 136.6 ±20.03 min (range, 100–170 min) and the mean estimated blood loss was 525.2±225.8 ml (range, 250–1200 ml) (Table 4).

Among the 24 patients who survived the mean duration of HDU stay was 2.56±1.12 days (range, 1–5 days), the mean time for resuming oral feeding was 5.16±2.8 days (range, 3–12 days), the mean time for drain removal was 10.64±5.46 days (range, 5–19 days) and the mean hospital stay was 12.76 ± 3.6 days (range 7–22 days).

Postoperative complications (Tables 5 and 6), occurred in nine (36%) patients, one (4%) patient died from pulmonary embolism. Three patients developed anastomotic leak, two (8%) patients developed pancreatic leak and one patient developed biliary leak. The two pancreatic leaks were of grade A and managed conservatively. Delayed gastric emptying developed in

Table 1 Demographic data

Age (years)	
Range	38–65
Mean±SD	54.8±7.7
Sex [*n* (%)]	
Males	16 (64)
Females	9 (36)

Table 2 Preoperative clinical data

Presenting symptoms	*n* (%)
Jaundice	22 (88)
Abdominal pain	11 (44)
Weight loss	8 (32)
Pruritus	7 (28)
Cholangitis	3 (12)

Table 3 Preoperative laboratory investigations

Preoperative laboratory values	Mean±SD
Hemoglobin (g %)	11.2±4.35
WBC's (10/mm^3)	7±21.6
Bilirubin (mg/dl)	12.5±35.6
Albumin (mg/dl)	3.5±4.34
Creatinine (mg/dl)	0.76±4.83

WBC, white blood cell.

Table 4 Operative and postoperative data

Total operative time (min) [mean±SD (range)]	383.4±38.3 (300–465)
Duration of anastomosis (min) [mean±SD (range)]	136.6±20.03 (100–170)
Blood loss (ml) [mean±SD (range)]	525.2±225.8 (250–1200)
HDU stay (days) [mean±SD (range)]	2.56±1.2 (1–5)
Time to oral feeding (days) [mean±SD (range)]	5.16±2.85 (3–12)
removal (days) [mean±SD (range)]	10.64±5.46 (5–19)
Hospital stay (days) [mean±SD (range)]	12.76±3.6 (7–22)

Table 5 Postoperative morbidity and mortality

Patients with complications	*n* (%)
Overall complications	9 (36)
Pancreatic leakage grade	
A	2 (8)
B	0 (0)
C	0 (0)
Biliary leakage	1 (4)
Wound infection	2 (8)
Hydropneumothorax	1 (4)
Pulmonary embolism	1 (4)
Delayed gastric emptying	1 (4)
Mortality due to pulmonary embolism	1 (4)

Table 6 Final histopathological diagnosis

Histopathology	*n* (%)
Pancreatic adenocarcinoma	19 (76)
Invasive duct carcinoma derived from IPMN	1 (4)
Malignant mucinous cystic neoplasm	1 (4)
Ampullary adenocarcinoma	2 (8)
Distal end CBD	1 (4)
Duodenal adenocarcinoma	1 (4)

IPMN, intraductal papillary mucinous neoplasm.

one patient (and managed by total parenteral nutrition (TPN) and nasogastric tube).

Two patients had wound infection, and one patient had iatrogenic hydropneumothorax during central venous pressure line (CVP) insertion and managed by intercostal tube.

The final histopathology of the resected lesions was, 19 patients with adenocarcinoma of pancreas, one patient with malignant mucinous cystic neoplasm, one patient with intraductal papillary mucinous neoplasm, two patients with ampullary adenocarcinoma, one patient with adenocarcinoma of distal end of CBD and one patient with duodenal adenocarcinoma on top of villous adenoma.

Discussion

There have been 70 reported variations of reconstruction after pancreaticoduodenectomy. The pancreaticojejunal anastomosis is the source of most reported morbidity and mortality [3]. Separation of the pancreaticojejunal and hepaticojejunal anastomoses has been advocated by several authors to minimize the potential for erosion of anastomotic suture lines by pancreatic juice activated by bile, hoping to reduce the morbidity, and mortality resulting from pancreatic anastomotic failure, this is because the inactive pancreatic enzyme precursors are not associated with 'serious complications' [7–10]. Complete and effective separation can only occur if the pancreatic and hepatic anastomoses are on separate Roux loops [11].

Different studies using the technique of isolated Roux loop pancreatic drainage reported good result with marked drop in anastomotic leak rates ranging from 0 to 5.7% with zero fistula-related mortality [3,11–15]. These results encouraged us to introduce this technique in our institute in an attempt to achieve better results, and actually in our series of 25 pancreaticoduodenectomies, only one (4%) patient died and the cause of death was pulmonary embolism and not related to pancreatic leak, namely the pancreatic leak-related mortality was zero.

The overall morbidity in our study was 39%, in the literature the postoperative morbidity ranging between 30 and 50% [12–16]. Postoperative pancreatic fistula occurred in two (8%) patients and the two cases were of grade A fistula and managed conservatively, this could be considered a relatively good result taking into consideration the study was done in low volume center.

Although the operative time was somewhat prolonged due to additional anastomosis, but this is a small price for the final good results with relatively low rate and low grade of pancreatic fistula that resulted in reasonable hospital stay (12.76±3.6) which in turns decreased the hospital coasts and this may be of value to centers in developing countries that suffer from shortage of resources like our center. These results are partially consistent with the prospective randomized study done by Shan Ke *et al.* [17] who concluded that the incidence of pancreatic fistula after isolated loop reconstruction was not less than that after conventional single loop reconstruction, but the isolated loop was associated with decreased fistula severity, hospital stay, and hospital costs.

Although our study has some limitations, such as the absence of comparison with the other technique, and the small number of patients, still we can conclude that; isolated loop reconstruction is a good technique specially in low volume centers in developing countries, at least it contributes to reducing the severity of pancreatic fistula with its dangerous sequelae, and is associated with shorter hospital stay which is valuable for such centers suffering from shortage of resources, however other comparative studies with larger number of patients are needed to confirm this.

Conflicts of interest

There are no conflicts of interest.

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