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Research Article

Results of Combined Closure of Pancreatic Duct Stump with Pancreatico-Jejunostomy (Invaginating Type) after Whipple's Operation an "Assessment of a New Modality"

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Abstract

Introduction: Pancreaticoduodenectomy is technically demanding procedure with high morbidity rate approaching 30 - 50%, as risk of leakage or failure of healing, resulting in pancreatic fistula (PF). More than 80 different methods of pancreatico-enteric reconstruction have been proposed. Many factors were responsible for the increased incidence of complications have been identified, as small pancreatic duct size with a soft pancreas is known to be a risk factor for major leakage.

Aim of Work: Evaluation of end to end pancreatico-jejunostomy (Invagination technique) with closure of pancreatic duct stump after Whipple's operation in accordance to, safety, incidences of associated operative complications Pancreatic Fistula (PF), and anastomosis operative time.

Methodology: Fifty seven patients underwent an elective pancreatico-duodenectomy (Whipple's procedure) between January 2014 and June 2017. All patients did end-to-end invagination pancreatico-jejunostomy (PJ) with pancreatic duct stump closure. The diameter of the main pancreatic duct, the texture of the remnant pancreas, estimated blood loss and transfusion, total operative and anastomotic procedure times, as well as histopathological examination and postoperative complications, specially the fistula formation were determined and studied.

Results: 57 patients underwent Whipple's procedure (Pancreatico-Duodenectomy). The mean operative time was 371 minutes (+/- 50 minutes), while the mean anastomotic time was 12 minutes (+/-2). Mean blood loss intra-operatively was 375.37 ml, Regarding the incidence of pancreatic fistula, the fistula was recorded in 4 patients (7%). There was no significant change in S. amylase, lipase and CT scan pre and post-operative, confirming the absence of pancreatitis due to pancreatic duct closure.

Discussion: We modified a new technique combining both pancreatic duct (Wirsung) closure together with end to end pancreatico-jejunostomy (invagination) anastomosis, aiming to reduce incidence of POPF, as well as shortening the time of the anastomosis. This technique was rarely used because of the risk of postoperative pancreatitis, permanent exocrine and endocrine insufficiency. Pancreatic remnant occlusion is a safe, less complicated alternative management of the pancreatic stump during Whipple's procedure.

Conclusion: Pancreatic remnant occlusion is a safe, less time consuming and less complicated alternative management of the pancreatic stump during Whipple's procedure.

Keywords: *Pancreatic Duct; Pancreatico-Jejunostomy; Whipple's Operation*

Introduction

Pancreaticoduodenectomy is technically demanding procedure with postoperative mortality less than 5% and morbidity 30 - 50% [1,2]. Mainly measurable risk of leakage or failure of healing, resulting in pancreatic fistula (PF), which leads to other surgical complications including intra-abdominal infection, hemorrhage, the occasional need for re-operation, and possible death [3]. The dramatic consequences of a technical reconstructive failure suggested a number of methods for reducing the incidence of pancreatic fistula, as the site of reconstruction, anastomotic techniques, sutures, biologic adhesives and trans-anastomotic stents [4]. Many studies have attempted to examine prognostic risk factors for anastomotic leaks after duodeno-pancreatectomy. However, until now all different pancreatico-jejunal reconstructions failed to give clear evidence of specific superiority [4]. The choice of an anastomotic method from the technical point of view, for an "ideal" pancreatico-jejunal anastomosis would meet the following criteria: easy to teach, associated with a low rate of pancreatic failure-related complications, and applicable to all patients [5]. No gold standard for pancreatico-enteric reconstruction illustrating the complexity of surgical techniques [5]. Many factors were responsible, among which was small pancreatic duct size with soft pancreas, which is known to be a risk factor for major leakage [3]. In the present study we reported the results of 57 retro and prospectively duodeno-pancreatectomies performed in three Hepato-Biliary-Pancreatic centers, in an attempt to study the management of pancreatic remnant. We did end-to-end invagination pancreatico-jejunostomy (PJ) together with pancreatic duct stump closure in all these patients, aiming to decrease the rate of PF.

Aim of Work

Evaluation of end to end pancreatico-jejunostomy (Invagination technique) with closure of pancreatic duct stump after Whipple's operation in accordance to, safety, incidences of associated operative complications Pancreatic Fistula (PF), and anastomosis operative time.

Methodology

The present study is a retro and prospective study, in which Fifty seven patients underwent an elective pancreatico-duodenectomy (Whipple's procedure) in three Hepato-Bilio-Pancreatic centers (National Hepatology and Tropical Medicine Research Institute "NHTMRI"*, Theodore Bilharz Research Institute (TBRI) and Mokkatum Insurance Hospital between January 2014 and June 2017. All patients did end-to-end invagination pancreatico-jejunostomy (PJ) with pancreatic duct stump closure whenever possible. Sixty two patients were enrolled for Whipple's procedure, from these only fifty seven patients were eligible for our technique. The cross-sectional diameter of the pancreas and intestines, were the main anatomical landmark for our anastomosis. In the remaining cases, other techniques were performed instead and excluded from the study. The total operative, and anastomotic procedure times, diameter of the main pancreatic duct, the texture of the remnant pancreas, estimated blood loss and transfusion, postoperative complications as well as histopathological examination and specially the fistula formation were studied.

Preoperative investigations

A complete preoperative diagnostic assessment, including, CBC, liver, renal, coagulation profile, serum albumin, minerals, CRP and serum Amylase and Lipase. Chest X ray, abdominal U/S, abdominal CT scan (Dynamic-multislice) with pancreatic protocol, for assessment of the lesion size (mean 3.4 cm) and its relation to portal vein and SMV and SMA together with assessment of pancreatic duct diameter. EUS with biopsy, ERCP and stenting of the CBD either by pre-cut or by fistula technique, done in 44 patients (77.2%) and failed in 13 (22.8%). Only three patients (5.2%) underwent percutaneous trans-hepatic biliary drainage with stent (PTD). Antibiotic and antithrombotic prophylaxis was routinely given. After tumor resectability, the texture of pancreatic parenchyma (soft/fragile or hard/fibrotic), were intraoperatively obtained. Pathological evaluation of the absence of fibrosis (pancreatitis) denotes soft/fragile parenchyma.

PJ operative procedure

The pancreas will be transected with an electro-cautery and/or the Harmonic scalpel on the scheduled line after intra-operative U/S assessment for the pancreas, the tumor and the related vascular structures. Hemostasis, during the transaction of the pancreas identification of the main pancreatic duct was done and the duct was cut (neither by the harmonic scalpel nor by the electro-cautery) by a scalpel. The duct then after identification and completion of pancreatic resection is well identified and bared for around 1 to 2 mm

from the pancreatic edge to facilitate the closure safely. The pancreatic remnant is mobilized for approximately 3 - 5 cm to allow its intussusception into the intestine (proximal jejunal loop). The proximal pancreatic duct stump is closed using prolene 4 - 5/0 in either a continuous or interrupted manner according to the size of the pancreatic duct. In some cases, we used mechanical stapler during the pancreatic transaction (Figure 1) (with four stay sutures at 3, 6, 9, 12 o" clock of the pancreatic cut surface [6,7].

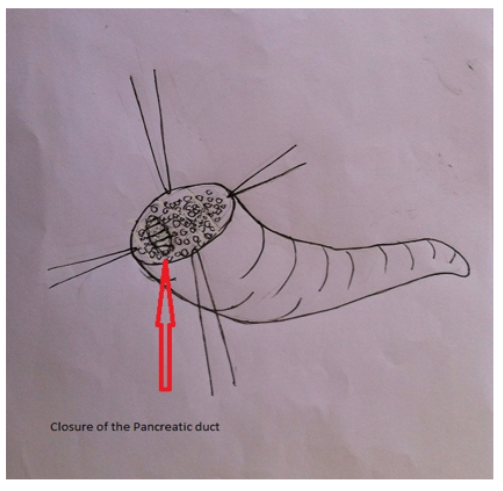


Figure 1

The Jejunal free limb is moved through trans-mesocolic route to the pancreatic cut end (through an opening in the transverse mesocolon).

Proximal jejunal loop is prepared for anastomosis, by eversion (intussusceptum)creating the intestinal cuff through which the pancreas is intussuscepted (Figure 2).

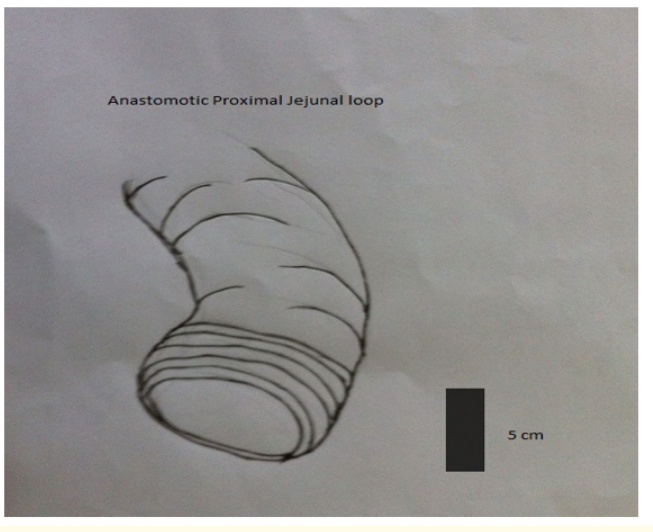


Figure 2

Insertion of two to four stitches one on each of the upper and lower border of the pancreatic stump (one on each of 3, 6, 9, 12 o" clock of the cut surface of the pancreas in case of four stitches- as in figure 1) and the summit of the jejunal cuff. These sutures are put 5 - 6 cm away from the edge of the intestine (at the summit of the everted edge of the proximal jejunal loop) and at the cut surface of the pancreas, so that the cuff is 3 - 5 cm completely invaginated inside the jejunal loop, using synthetic long-term non-absorbable suture, Prolene (size 3/0), then the everted distal end of the jejunal loop is re-positioned over the dissected cuff of the pancreatic edge and sutured over the pancreas either by continuous or interrupted manner, starting by the posterior wall, then the anterior wall of the pancreatico-jejunal anastomosis, using non absorbable prolene suture (3/0) as in figure 3. Figure 4 shows complete invagination of the pancreatic stump (3 - 5 cm) into the proximal jejunal loop (so a pancreatic distal end completely invaginated into the jejunal loop with a cuff of a 5 cm long and the pancreatic duct closed as mentioned before).

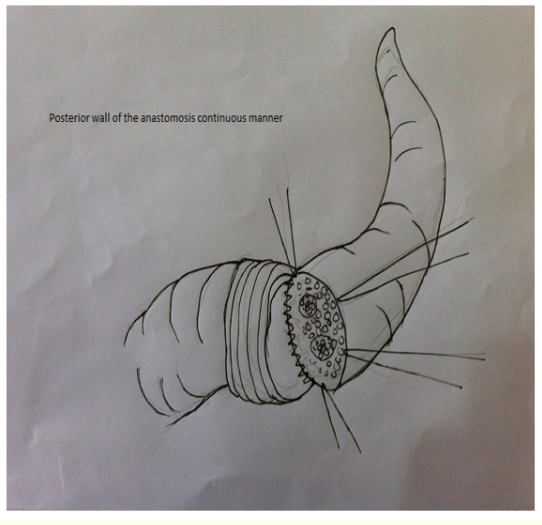


Figure 3

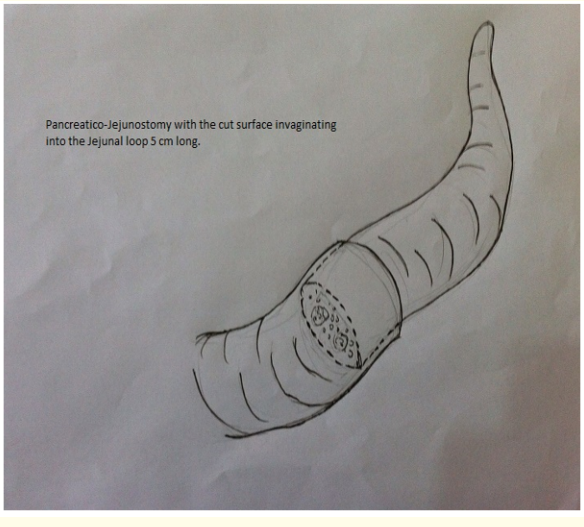


Figure 4

All patients had two drains (one on each side of the midline incision), close to the pancreatic anastomosis.

Follow-up

The follow-up of patients was divided into early and late.

Early follow-up (D0-D15): From the end of the operation (D0) up to two weeks postoperative (D15).

We use both laboratory and radiological investigations.

Laboratory investigations: Daily from D0 up to D7, then every three days up to D14 or discharge (the nearest) or on demand starting from D7 if the patient hospitalization is prolonged than D14, as liver, renal, coagulation profile, serum albumin, minerals, CRP.

Serum amylase and lipase were done routinely for the three successive postoperative days (D1 to D3) then at D7 and D15, to be compared with the results pre-operatively.

Amylase and Lipase in body fluids from the drain were done routinely starting from D3 postoperative up to D7 then on D10 and D14 if the drains were still in place.

Radiological investigations: Chest X ray on the first postoperative day, repeated every two days or on demand. Repeated abdominal U/S starting from D3 post.op., then every three days, or on demand. Abdominal CT scan was asked on demand if the U/S was susceptible.

The peri-operative mortality, complications particularly, major pancreatic leakage and PF, re-operation, histo-pathological examination, need of blood transfusion, start of oral feeding, drain removal, as well as postoperative hospital stay were documented.

Late follow-up (D15-up to 6 months)

The late follow-up started from D15, or discharge up to six months postoperative, by both laboratory and abdominal U/S on regular bases every two weeks, starting from 2nd week up to three months, then every month up to 6 months, the laboratory investigations include the serum Amylase and serum Lipase, during the follow-up. Routine CT scan of the abdomen and pelvis was asked for all patients 6 weeks postoperatively, for assessment of the postoperative field, and the pancreatic duct with a comparison of the size pre-operatively.

Complications:

1. **Pancreatic fistula:** Defined as measurable pancreatic fluid secretion output after the third postoperative day (D3), either isolated pancreatic secretion content or mixed pancreatic secretion content with post-operative serous discharge.

   The drain output tested starting from D3 for pancreatic enzymes (amylase and lipase in body fluids), pancreatic fistula (PF)when the drain is more than three times the normal serum range.

   ISGPF: (The ISGPF is a classification for pancreatic fistula based on clinical parameters) [8].

   Grade A: Fistula without clinical symptoms.

   Grade B: Fistula with clinical symptoms or need any intervention.

   Grade C: Fistula with severe clinical symptoms.

   The pancreatic fistula is also measured and classified according to the outcome every twenty-four hours; classified as minor, moderate and major pancreatic fistula.

   In our study we used both classifications for evaluation of the pancreatic fistula postoperatively.

2. **Fluid collection (abscess):** Fever, leukocytosis, tachycardia, and local abdominal tenderness with collection of fluid at least 5 cm in diameter associated with pus on aspiration diagnosed with ultrasound or CT, for clinical [9].
3. **Delayed gastric emptying:** Persistent of vomiting postoperative day 3 [9].
4. **Postoperative pulmonary complications:** Pneumonia which is diagnosed by either, pulmonary infiltrates with pulmonary CT, sputum culture with pathogenic bacteria, and prolonged ventilator support [9].

Statistical analysis

The minimum and maximum values are expressed as mean ± standard deviation (SD), expressing the quantitative data analysis, while the qualitative data analysis are presented as percentages. The Shapiro-Wilk test checks quantitative data normality. The Student parametric test were used in case of normal distribution, and nonparametric Mann-Whitney test in the case of non-normal distribution. The qualitative data nonparametric tests used depends on the size of the group as, Chi-square, Yates corrected Chi-square, and -square test. All data were analysed using statistical software statistical 10.0 (StatSoft, Inc.).

Ethical consideration

The present study is a retro and prospective study, concerning patients operated in three centers' of Hepato-Biliary-Pancreatic surgery in Cairo. Due to difficulties to communicate with patients after discharge from the hospitals we could not collect correct consent for data retrieval from our patients enrolled in this study, but I do assure that the data was collected in a very ethical manner from these departments through an intermediate without announcements for the names or the personal details of enrolled patients. All personal data of our enrolled patients were preserved and kept away from data retrieving personnel and advise these departments for enrolling a blank data retrieval consent to be signed by all patients admitted to enable the researcher for retrospective data retrieval ethically corrected.

Results

Throughout the 22 monthsduration 57 patients with pancreatic tumor in three Hepato-Bilio-Pancreatic surgery Unites, were examined and evaluated for operability and resectability [pancreatico-duodenectomy (Whipple's procedure)]. From these 57 patients, 44 males (77.2%), and 13 females (22.8%). The mean age of our patients were 63.18 years. 44 patients had Pancreatic head cancer (77.2%), 8 patients (14%) peri-ampullary carcinoma, 4 patients (7%) cholangiocarcinoma, and only one patient (1.8%) had pancreatic body mass (Table 1 and Chart 1).

All patients underwent Whipple's procedure (Pancreatico-Duodenectomy).

The mean operative time was 371 minutes (+/-50 minutes), while the mean anastomotic time was 12 minutes (+/-2) (Chart 2).

The pancreas was normal in consistency in 2 patients (3.5%), soft in 6 patients (10.5%), while the pancreas was firm with obvious pancreatitis in 49 patients (85%).The pancreatic duct was closed by continuous 5/0 prolene sutures in 56 patients (98.2%) and by interrupted sutures in one patient (1.8%). Mean blood loss intra-operatively was 375.37 ml and the amount of transferred packs whether blood or fresh frozen plasma in relation to the number of patients are shown in table 2. Two drains are always placed in all patients (Table 2).

	All patients (n = 57)	
Gender N (%)		
Male	44	(77.2)
Female	13	(22.8)
Age mean (SD) years	63.18	(7.82)
Lesion N (%)		
Head of pancreas	44	(77.2)
Cholangio-carcinoma	4	(7)
Periampullary carcinoma	8	(14)
Mass in the body of pancreas	1	(1.8)
Tumor size mean (SD) cm	3.4	(0.93)

Table 1: *Data of patients enrolled in the study.*

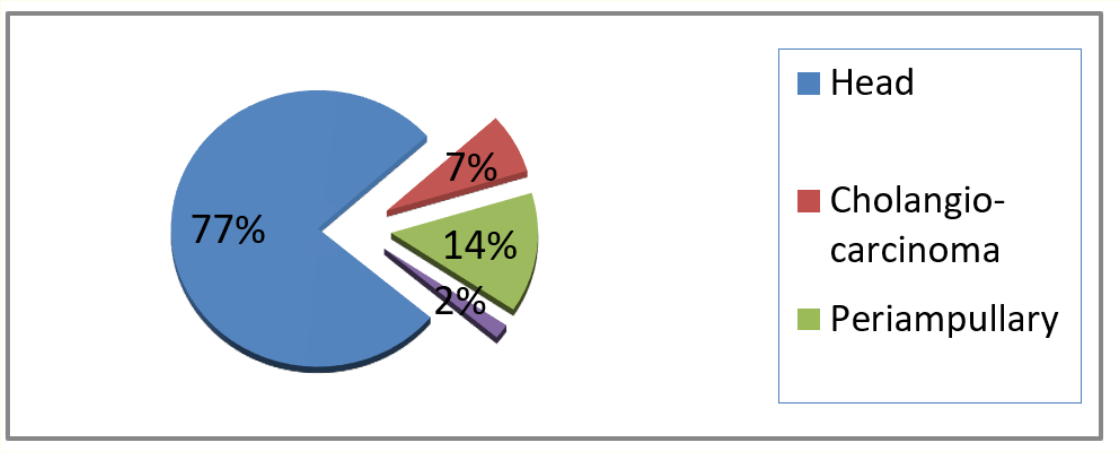


Chart 1: *Distribution of patients according to the site of lesion.*

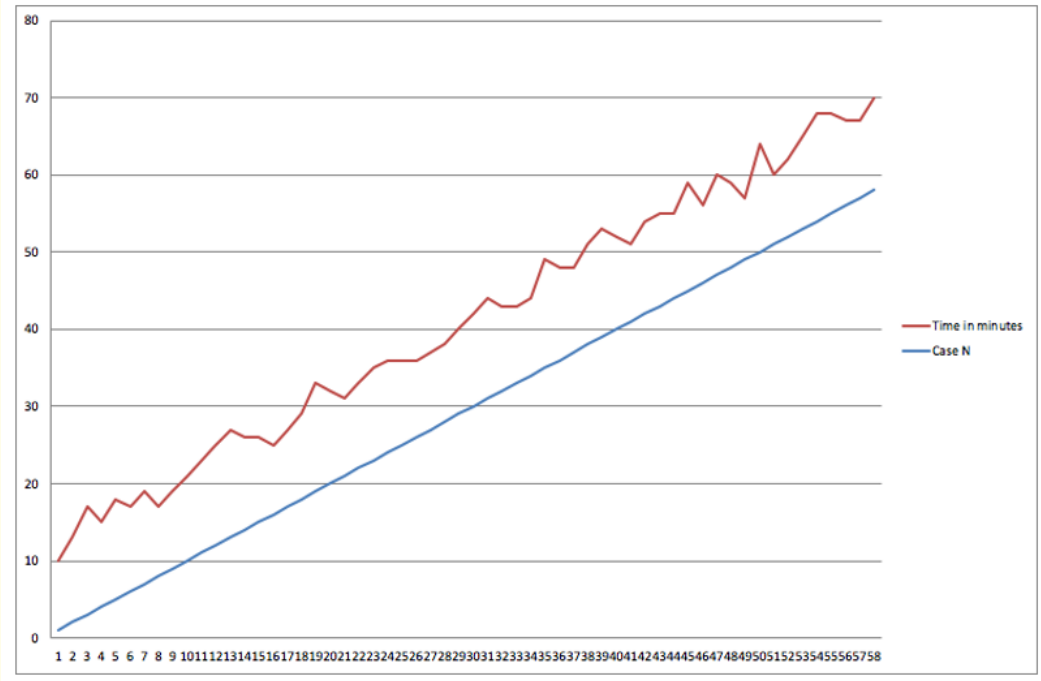


Chart 2: *Time for the pancreatic anastomosis.*

	All patients (n = 57)	
Blood loss mean (SD) cc	357.37	(118.28)
State of the pancreas N (%)		
Normal	2	(3.5)
Pancreatitis	49	(86)
Soft pancreas	6	(10.5)
Type of surgery N (%)		(100)
Whipple's procedure	57	
Duration of operation mean (SD) min	371.1	(50.18)
Blood transfusion N (%)		
No	2	(3.5)
One pack	18	(31.6)
Two packs	25	(43.9)
Three packs	11	(19.3)
Four packs	1	(1.8)
Plasma transfusion N (%)		
No	45	(78.9)
One pack	1	(1.8)
Two packs	2	(3.5)
Three packs	3	(5.3)
Four packs	5	(8.8)
Six packs	1	(1.8)
Type of closure N (%)		
Continuous	56	(98.2)
interrupted	1	(1.8)
Drains N (%)		
Two	57	(100)

Table 2: *Intra-operative assessment of studied patients.*

All patients started partial parenteral nutrition from D1 postoperatively, and continued till patients had complete oral feeding, to preserve the GIT mucosal integrity and improve immunity, with mean duration of 4.3 days (ranging from 3 - 6 days post-op.). The hospital stay was 8.42 days (ranging from 6 - 19 days). Regarding the incidence of pancreatic fistula, the fistula was recorded in 4 patients (7%), from those four patients only three patients had pre-operative neo-adjuvant chemotherapy together with pancreatitis (firm in consistency). All the fistulae were low output fistula, Grade A, lasting for approximately 8.5 days (from 6 - 22 days). PF with elevated s.amylase and s.lipase in drains ranging more than three times the normal serum range will be considered pancreatic fistula, patients were followed up by serial U/S for assessment for all fistula patients together with daily CBC, CRP(quantitative type).

Serum amylase and serum lipase were done for all patient started from D2 post operatively and every 3 days till removal of the drains then once weekly up to 6 weeks. There were no significant change in S. amylase and lipase pre and post-operative, confirming the absence of pancreatitis due to pancreatic duct closure (Chart 3).

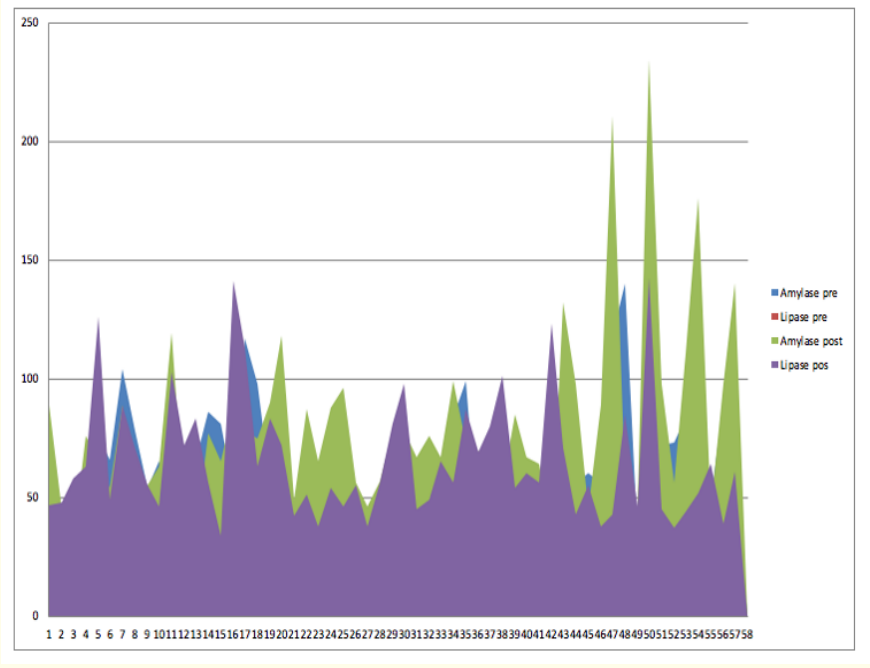


Chart 3: *Comparison between serum Amylase (28-100) and Lipase (up to 60).*

All patients underwent C.T scan study at 6 weeks post-operatively with pancreatic protocol to confirm pancreatic ductal dilatation in comparison with the previous C.T pre-operatively. There were no significant change in pancreatic duct size pre and post-operative (Chart 4 and Figure 5 and 6).

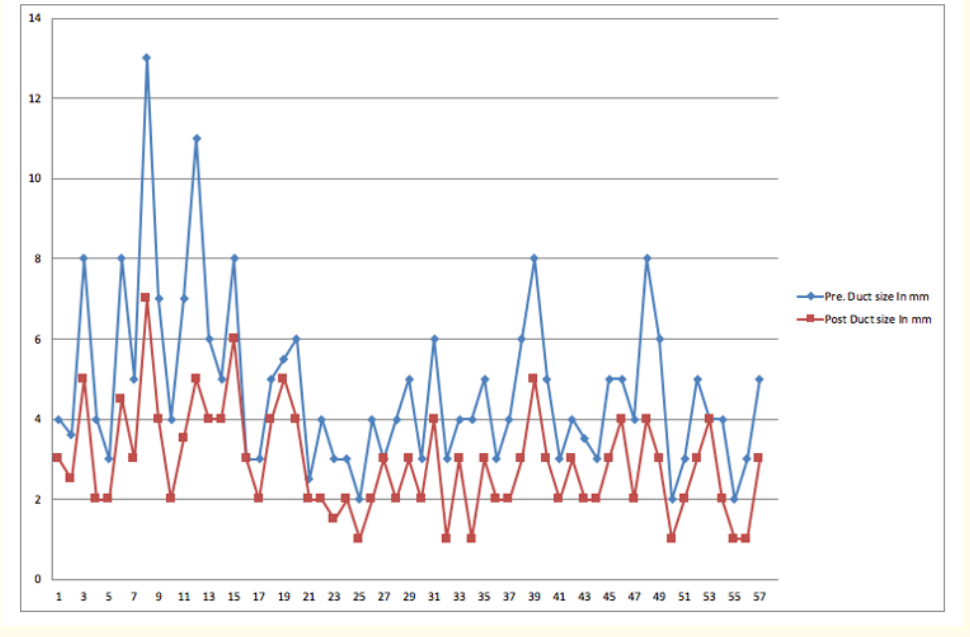


Chart 4: *Comparison between the Pancreatic duct size preoperative and postoperative by C.T study at 6 weeks postoperatively.*

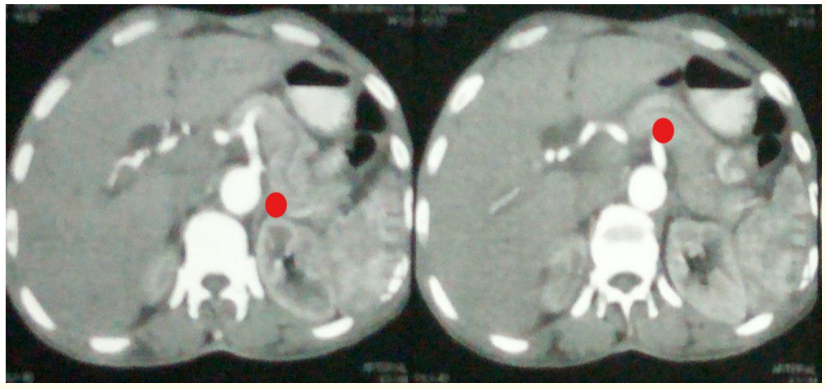


Figure 5: *CT pre-operative with red tag on the dilated pancreatic duct.*

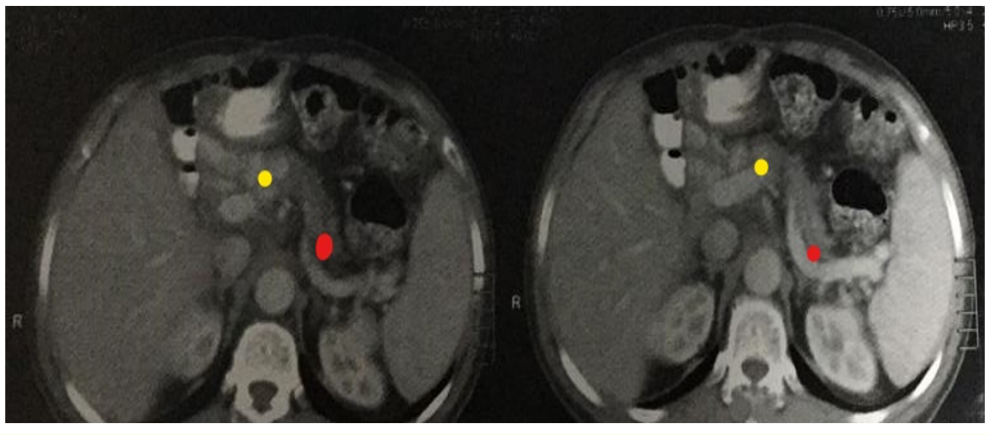
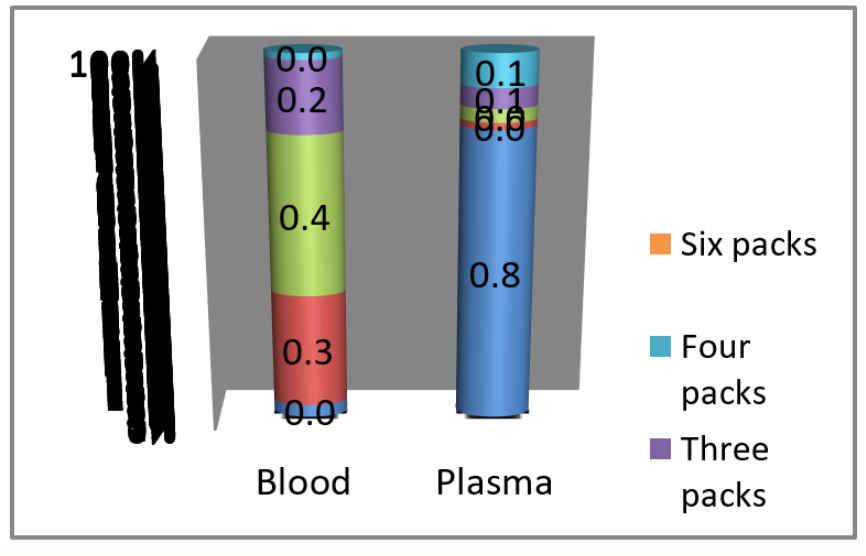


Figure 6: *Post-operative CT with red tag on the pancreatic duct showing no further dilatation and yellow tag on the invaginated loop.*

	All patients (n = 57)	
Drain out I*	6.8	(2.6) (4 - 19)
Drain out II*	8.5	(3.14) (6 - 22)
Oral feeding*	4.33	(0.55) (3 - 6)
Hospital stay*	8.42	(1.7) (6 - 17)
TPN N (%) Partial from D1	57	(100)
Fistula N (%)	4	(7)
CT 6 weeks later N (%) No PD dilatation	57	(100)

Table 3: *Post-operative assessment of patients.*



Graph 1: *Distribution of patients according to post-operative blood transfusion.*

Discussion

Many attempts were made to decrease the incidence of POPF and therefore morbidity and mortality post pancreatico-jejunostomy [10]. We modified a new technique combining both pancreatic duct (Wirsung) closure together with end to end pancreatico-jejunostomy (invagination) anastomosis, aiming to reduce incidence of POPF. Katarzyna Kusnierz., *et al.* assumed that placing smaller number of stitches between the pancreas and the intestine shortens the time of the anastomosis (pancreatico-jejunostomy) (+/-14.2 minutes) and reduces trauma to the pancreas. In this study the median operative time was 12 +/- 2 minutes. Post-operative pancreatic leak or fistula is due to leak out of digestive pancreatic enzymes from the pancreatic ductal system into the peritoneal cavity and the peri-pancreatic space leading to morbidity such as, ileus, abdominal pain, abscess, sepsis, and hemorrhage [11]. Pancreatic fistula is less dangerous from over-sewn of the pancreatic remnant than from a pancreatico-jejunal anastomosis because no activation of leaking pancreatic enzymes as there is no defect of the small bowel [11].

In the past, ligation of the pancreatic duct without creating continuity to the GI tract is a means of fistula prevention as creating pancreatico-enteric anastomosis after pancreaticoduodenectomy was associated with complications and leak [12]. Brunschwig 1952, reported no pancreatic fistula following pancreatic duct ligation of three cases, larger reports by Goldsmith and colleague, found that POPF rate was equal between patients with pancreatic duct ligation and that with anastomosis to the jejunum [14]. Several studies was comparing different techniques of pancreatic anastomoses, post PD and without any pancreatic anastomosis, found significant decreased in morbidity and mortality without pancreatic anastomosis especially in elder people [15]. The best management for the pancreatic stump after PD remains a challenge, an interesting option is the occlusion technique by various methods [10].

The invagination technique in small ducts or soft friable pancreas is much safer in those high risk as stated by some authors, but still it is difficult to state the superiority of the invagination technique over others [16]. Also, as stated by Yang., *et al.* Chinese authors, postulated an interesting modification for the end-to-end anastomosis invagination pancreatico-jejunostomy by trans-pancreatic U-sutures, with postoperative pancreatic fistulas 2.2% [18,19]. In the present study we used the end-to-end invaginated pancreatico-jejunostomy with closure of the pancreatic duct (Wirsung) to lower morbidity as stated by Bilimoria., *et al*. Because of the risk of postoperative pancreatitis, fear of severe hemorrhagic complications, permanent exocrine and endocrine insufficiency, this technique was rarely used [20] that is why it was abandoned or reserved to selected cases [21]. In this study we followed up s. amylase and lipase post-operative with no

significant changes together with abdominal CT to monitor the change in size of the pancreatic duct diameter, no significant change indicating no postoperative pancreatitis. Dilated ducts with gush of the pancreatic fluid when opening the pancreatic duct within fibrotic pancreas means, an already occluded duct, which we occludes again by over-sewing or stapling after pancreatectomy [22]. Pancreatic duct occlusion during Whipple's procedure is safe with less complication, an alternative management of the pancreatic duct stump [23].

Katarzyna., *et al*. state that, methods of intussusceptions allow a tension-free adhesion of the intestinal wall to the pancreas by placing a few number of sutures between the pancreas and the intestine. In the present study we placed two to four stitches one on each of the upper and lower border of the pancreatic stump (one on each upper and lower border of the pancreas) and the summit of the Jejunal cuff. These sutures are put 5 - 6 cm away from the edge of the intestine and at the cut surface of the pancreas, so that the cuff is 3 - 5 cm to avoid parenchymal ischemia and parenchymal fibrosis [24]. Katarzyna., *et al.* stated that many sutures may damage the pancreatic parenchyma (especially in soft pancreas) causing scarring in the line of anastomosis, parenchymal ischemia and parenchymal fibrosis.

To determine the safety of types of anastomosis and its modifications is difficult without prospective randomized trials [24]. Anastomoses performed, independently of any other technique, with a small amount of complications, should be considered safe [24]. The consistency of the pancreatic parenchyma is the only reproducible factor to significantly reduce morbidity and mortality post pancreaticoduodenectomy for which the surgeon has very little control [25].

The rates of mortality and morbidity of pancreatoduodenectomy perioperative are reported at 1% - 3% and 30% - 40%, respectively now days, at high-volume centers [25]. In the present study the perioperative mortality and morbidity are 1.75% and 33.34% respectively.

Comparing the traditional end-to-end invagination anastomosis, our technique bears the following advantages: few numbers of sutures are less traumatizing to the pancreas, safe because the intestine cuff adheres any gaps between the jejunum and the pancreas remnant. Closure of the pancreatic duct minimize pancreatic leak. Limitations of our study may be due to small size sample. Anastomoses by the intussusception technique were performed when the sizes of pancreas and intestine were appropriate and matched each other.

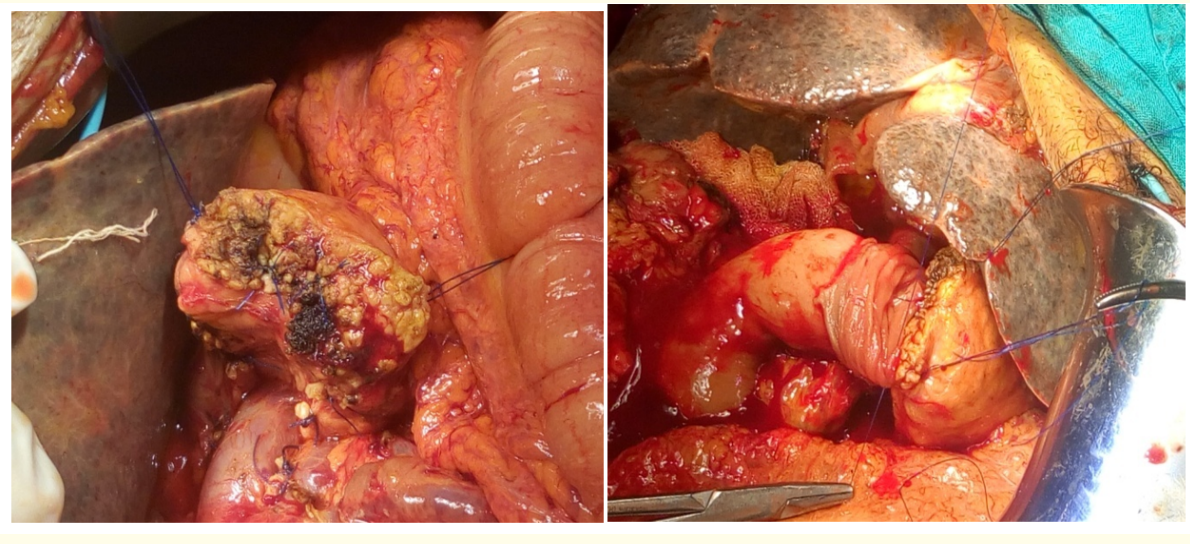


Figure 7: *Cut surface of pancreas with duct closure and stay sutures Fixation of the pancreas to the summit of the everted J. loop.*

Figure 8: *The Pancreatico-jejunal anastomosis- end to end- Pancreas invaginated into the Jejunal loop.*

Conclusion

PF following duct occlusion was nearly always reported, even if subclinical but not negligible sequelae. Pancreatic remnant occlusion is a safe, less time consuming and less complicated alternative management of the pancreatic stump during Whipple's procedure. It does not affect the long-term survival of patients treated for cancer of the head of the pancreas, can be a useful tool in the surgical treatment of pancreatic cancer.

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