



Isolated loop vs. single loop pancreatojejunostomy after pancreaticoduodenectomy: A comparative study in Zagazig University

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Abstract

Summary &Background: Postoperative pancreatic fistula (POPF) is considered to be one of the most serious complications after Pancreaticoduodenectomy increasing costs and hospital stay. Many factors influence pancreatic leakage after PD, including sex, age, jaundice, operative time, intraoperative blood loss, pancreatojejunal anastomotic technique, texture of the remnant pancreas, pancreatic duct size, use of somatostatin, and surgeons experience. Pancreatojejunostomy is commonly used in the reconstruction after Pancreaticoduodenectomy, but the incidence of Postoperative pancreatic fistula remains high. Many centers started using an isolated Roux loop of jejunum for PJ to decrease the incidence of POPF. Proponents of this technique believe that diversion of bile away from the PJ minimizes pancreatic enzyme activation and reduces the risk of pancreatic fistula. Another argument in favor of using an isolated loop in PJ relies on the belief that if a pancreatic fistula forms, it will be a pure pancreatic fistula and these fistulae cause less complication when compared with a complex pancreatic fistula in which bile activates pancreatic juice with more morbidity and mortality. **Objectives:** to compare outcomes of isolated Roux loop pancreatojejunostomy and single loop pancreato jejunostomy including the primary outcomes such as the rate of POPF and the secondary outcomes such as hospital stay, time to oral feeding, associated morbidity and mortality. **Patients and methods:** This non-randomized controlled clinical trial was carried out in General Surgery Department of Zagazig university hospitals during the period from May 2019 to January 2022, and included 36 patients who underwent Pancreaticoduodenectomy for pancreatic head cancer and, periampullary and duodenal carcinoma. Patients were divided non-randomly into two equal groups each is 18 patients. In both groups pancreatojejunal anastomosis was done using invagination (Dunking) method but one group of them was reconstructed by isolated loop technique (ILPJ) and the other group was reconstructed by single loop technique (SLPJ). The data were recorded including demographic data, intraoperative and postoperative data. **Results:** there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regarding age, sex, smoking and preoperative comorbidities ($p>0.05$). The current study showed that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard operative time (274.4 ± 33.3 min. Vs 270.6 ± 22.9 min) ($p>0.05$), intraoperative blood loss (1450 ± 314.9 ml Vs 1444.4 ± 285.4 ml) ($p>0.05$) and the need for blood transfusion (4.5 ± 1.8 units Vs 4.5 ± 1.1 units) ($p>0.05$). The incidence of pancreatic leak was comparable in both groups with no significant difference between them (11.1% in ILPJ Vs 33.3% in SLPJ) ($p>0.05$). Mortality related to POPF was also comparable in both groups with no fistula-related deaths in ILPJ and two fistula-related deaths in SLPJ (0% in ILPJ Vs 11.1% in SLPJ) ($p>0.05$).

Conclusion: this study showed no significant reduction of pancreatic anastomosis leak when the isolated loop technique is performed for the construction of pancreatojejunal anastomosis instead of the single loop technique, but there is slight improvement in fistula-related morbidity and mortality and the need for re-exploration. Also due to wide use of surgical staplers in reconstruction there is no more prolonged operative time in ILPG, so we recommend it as a safe technique for pancreatojejunal anastomosis in patients undergoing PD. However, further randomized controlled trials should be undertaken to ascertain these findings.

Key Words: pancreatic fistula, Pancreaticoduodenectomy, isolated loop, single loop

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Introduction

Pancreaticoduodenectomy is considered as one of the most challenging and complex intra-abdominal operations. Although postoperative mortality has decreased to less than 5% in major centers, the rate of postoperative complications remains high and is largely due to disruption of the pancreatic anastomosis [1]. The incidence of Postoperative pancreatic fistula ranges from 5% to 25% in most series when pancreatojejunostomy is the method of reconstruction [2]. Postoperative pancreatic fistula is considered to be one of the most serious complications after Pancreaticoduodenectomy increasing costs and hospital stay. Severe Postoperative pancreatic fistula can even cause intra-abdominal abscesses, sepsis and life-threatening hemorrhage [3]. Many factors influence pancreatic leakage after PD, including sex, age, jaundice, operative time, intraoperative blood loss, pancreatojejunal anastomotic technique, texture of the remnant pancreas, pancreatic duct size, use of somatostatin, and surgeons experience [4]. Numerous methods to deal with the pancreatic remnant have been proposed, including use of fibrin glue to occlude the main pancreatic duct, suture ligation of the pancreatic duct, pancreatic duct stenting, modification of the jejunal anastomosis (end-to-end versus end-to-side, invagination versus duct-to-mucosa isolated loop versus single loop) and pancreaticogastrostomy [5]. An isolated loop pancreatojejunostomy (ILPJ) for the drainage of the pancreatic stump was first described by Machado et al. in 1976 with an attempt to reduce the activation of pancreatic juice by biliary secretion thereby reducing the incidence of anastomotic breakdown [6]. The benefit of this technique is that the diversion of bile away from the pancreatojejunostomy site minimizes the pancreatic enzyme activation and thus reduces the risk of Postoperative pancreatic fistula [7]. However, most literatures showed that this technique failed to demonstrate any significant reduction of pancreatic anastomosis leakage. The data showed that complication rates; POPF rates, grade and duration of spontaneous closure; morbidity and mortality

were of the same in the ILPJ group when compared to Conventional SLPJ. The explanation given was healing of pancreaticoenteric anastomosis is dependent on many factors and diversion of bile is only one of them. Even activation of leaking pancreatic juice is not solely dependent on the presence of bile: intestinal juices can also activate pancreatic secretions. [8].

Patients and Methods

Study Design

This non-randomized controlled clinical trial was carried out in General Surgery Department of Zagazig university hospitals during the period from May 2019 to January 2022. This study was approved by the Institutional Review Board (IRB) and informed consent was obtained from all patients.

Patients

Patients were divided non-randomly into two equal groups based on the type of management of the pancreatic remnant. Each group included 18 [2361](#) patients. In both groups pancreatojejunal anastomosis was done using invagination (Dunking) method but one group of them was reconstructed by isolated loop technique (ILPJ) and the other group was reconstructed by single loop technique (SLPJ). The data were recorded including demographic data, intraoperative and postoperative data. The data included patient age, sex, pre operative associated co-morbidity, pathological diagnosis, duration of operation, operative blood loss, need for blood transfusion, postoperative pancreatic leak and its management, bile leak and other postoperative complications, length of hospital stay, and fistula-related mortality.

The patients were also evaluated preoperatively with base-line laboratory tests (CBC, Liver and kidney functions, Coagulation profile), Blood group matching, random blood sugar and hepatitis B and C markers Abdominal Ultrasonography, Pelvi-abdominal CT with contrast, antithrombotic prophylaxis was given.

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Inclusion criteria

Patients with operable and resectable pancreatic head cancer, periampullary and duodenal carcinoma.

Exclusion criteria

Patients who aren't fit for general anesthesia due to sever comorbidity and Patients with irresectable or inoperable pancreatic head cancer, periampullary and duodenal carcinoma.

Operative techniques

Patients were subjected to general anesthesia. All patients underwent classic Whipple PD. Pancreaticojejunostomy was performed with invagination (Dunking) method. All patients were assessed as regards to pancreatic duct diameter following resection but without pancreatic duct stenting. All pancreaticojejunal anastomoses were hand sewn and constructed in two layers; 2/0 polypropylene for the inner layer mucosa to mucosa and 0 polypropylene for the outer layer seromuscular to the pancreatic capsule and parenchyma in continuous manner. In the first group who underwent isolated loop PJ anastomosis, reconstruction was begun using the transected

jejunum, brought up through the mesocolon, which was anastomosed in an end to end to the pancreatic remnant using dunking method. A separate loop was fashioned for the hepaticojejunal anastomosis by dividing the jejunum about 60 cm beyond the pancreatic anastomosis. This was anastomosed end to side to the hepatic duct. The gastrojejunal anastomosis was performed 25 cm downstream to the hepaticojejunostomy. The PJ loop was then sutured to the main loop as jejunojejunostomy. In the second group of patients who underwent a single loop PJ reconstruction, the retained jejunum was brought through a rent in the right transverse mesocolon with the PJ anastomosis performed first as before, to the end of the jejunum, following sequentially by a standard end to side hepaticojejunostomy and lastly gastrojejunostomy and enteroenterostomy. Two drains were placed, one close to the pancreaticojejunal anastomosis and other in the right subhepatic space. Pancreatic drain fluid amylase was measured in the postoperative period when there is suspicion of pancreatic fistula. In the absence of a pancreatic fistula, the pancreatic drain was removed after day 7. All patients received proton pump inhibitor prophylaxis during the postoperative course.

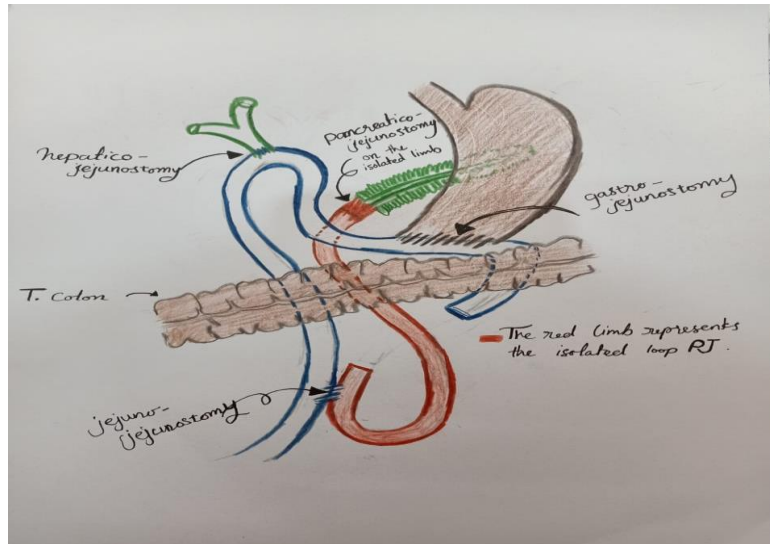


Figure 1: Diagram showing the isolated loop pancreaticojejunostomy technique

Study Definitions

Postoperative pancreatic fistula was defined according to the International Study Group on Pancreatic Fistula (ISGPF) definition: drainage of any measurable volume of fluid with fluid amylase more than or equal to three times the upper limit of normal serum value on postoperative day 3 or later.

Pancreatic fistulae were graded according to ISGPF criteria into Grades A, B and C according to their clinical course [9]. All cases of postoperative PF were identified as representative of either pure or complex fistulae depending on the nature of the draining fluid. The presence of bile or enteric contents suggested a complex fistula, whereas the presence of clear, water like fluid suggested a pure



PF. In case of suspicion of intra-abdominal sepsis, CT scans were performed. Delayed gastric emptying (DGE) was defined as the need for nasogastric intubation for more than 10 days postoperatively, inability to resume enteral feeding at 14 days after surgery, need of prokinetics for more than 10 days or re-insertion of the nasogastric tube [10]. Length of hospital stay was defined as the period from the first postoperative day until discharge from hospital. Death within the same hospital admission or within 30 days of surgery was considered as operative mortality.

Postoperative Outcomes

The primary outcome assessed was the presence or absence of a pancreatic fistula, demonstrated clinically, radiologically or at reoperation. Other features evaluated included differences in operative times, blood loss and requirements, postoperative complications and length of hospital stay.

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using

Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance:

- Chi square Test (χ^2) and fisher exact: was used to study comparison and association between two qualitative variables.
- t-test: was used for comparison between two groups having quantitative variables with normal distribution (for parametric data).
- A P-value of < 0.05 was considered statistically significant &<0.001 for high significant result for two tailed tests.

Statistical analysis




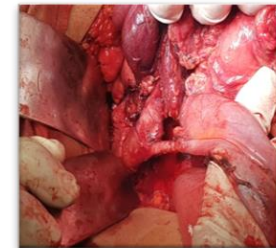
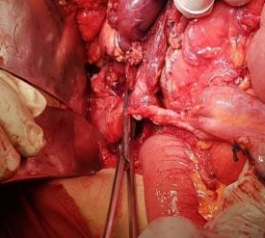
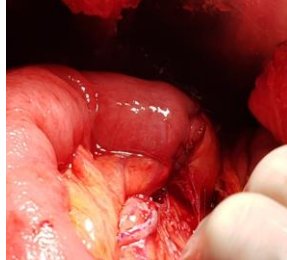
 <p>Figure 2: the specimen of PD in patient with periampullary mass</p>	 <p>Figure 3: specimen of PD in patient with duodenal carcinoma</p>
 <p>Figure 4: portal vein dissection and division of neck of pancreas</p>	 <p>Figure 5: CBD dissection</p>
 <p>Figure 6: transection of CHD</p>	 <p>Figure 7: Invagination pancreaticojejunostomy</p>



Figure 8: creation of GJ

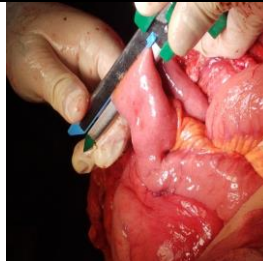


Figure 9: isolation of the PJ limb

Results

The current study showed that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard

operative time (274.4± 33.3 min. Vs 270.6± 22.9 min) (p>0.05), intra-operative blood loss (1450± 314.9 ml Vs 1444.4± 285.4 ml) (p>0.05) and the need for blood transfusion (4.5± 1.8 units Vs 4.5± 1.1 units) (p>0.05).

Table 1: Intra-operative data among the studied groups

Variable	Isolated loop PJ group N=18	Single loop PJ group N=18	t-test	P-value
Operative time (min): Mean ± SD Range	274.4± 33.3 220-330	270.6± 22.9 230-300	0.408	0.686
Intraoperative blood loss (ml): Mean ± SD Range	1450± 314.9 1000-2000	1444.4± 285.4 1000-2000	0.055	0.986
Blood transfusion (units): Mean ± SD Range	4.5± 1.8 2-10	4.5± 1.1 3-7	----	1

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Postoperatively, the present study showed that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard Postoperative bleeding (two cases in each group), Wound infection (1case in ILPJ Vs 2 cases in SLPJ), Pulmonary complication (2 cases in

ILPJ Vs 3 cases in SLPJ), Biliary leakage (only 2 cases in SLPJ managed conservatively) (p>0.05), also, there was no statistically significant difference between groups as regard Gastrojejunostomy leakage, Delayed gastric emptying & Pancreatitis (p>0.05).

Table 2: Post-operative data among the studied groups

Variable	Isolated loop PJ group N=18		Single loop PJ group N=18		χ ²	P-value
	N	%	N	%		
Postoperative bleeding:					-----	1
No	16	88.9	16	88.9		
Yes	2	11.1	2	11.1		
Wound infection:					fisher	1
No	17	94.4	16	88.9		
Yes	1	5.5	2	11.1		
Pulmonary complication:	16	88.9	15	83.3	fisher	1



No	2	11.1	3	16.7		
Yes						
Biliary leakage:					fisher	0.486
No	18	100	16	88.9		
Yes	0	0	2	11.1		
Management of biliary leak:					fisher	0.486
Null	18	100	16	88.9		
Conservative	0	0	2	11.1		
Gastrojejunostomy leakage:	18	100	18	100	---	1
No						
Delayed gastric emptying:	16	88.9	17	94.4	fisher	1
No	2	11.1	1	5.6		
Yes						
Pancreatitis:					fisher	1
Null	17	94.4	16	88.9		
Conservative	1	5.6	2	11.1		

Regarding POPF, it occurred in 8 patients out of total 36 patients (2 patients in ILPJ Vs 6 patients in SLPJ). In ILPJ one patient developed grade A fistula managed conservatively and recovered and the second case was grade C fistula required surgical intervention and recovered well also with no mortality related to fistula. Whereas in SLPJ 3 patients developed grade A fistula managed conservatively and recovered well, the 4th patient developed grade B fistula with collection required

percutaneous drainage and recovered well, the 5th patient developed grade B fistula required percutaneous drainage but died due to fistula and the 6th patient developed grade C fistula underwent re-exploration and died. there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard Re-exploration and overall mortality (2 deaths in ILPJ not related to POPF due to hemorrhage and pulmonary complications Vs 3 deaths in SLPJ of which two are related to POPF) (p>0.05).

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Table 3: POPF among the studied groups

Variable	Isolated loop PJ group N=18		Single loop PJ group N=18		χ ²	P-value
	N	%	N	%		
Pancreatic leakage:						
No	16	88.9	12	66.7	3.6	0.312
Grade A	1	5.6	3	16.7		
Grade B	0	0	2	11.1		
Grade C	1	5.6	1	5.6		
Total Pancreatic leakage:						
No	16	88.9	12	66.7	fisher	0.229
Yes	2	11.1	6	33.3		
Management of POPF:						
No	16	88.9	12	66.7	3.6	0.312
Conservative	1	5.6	3	16.7		
Re-exploration	1	5.6	1	5.6		
Percut. Drainage	0	0	2	11.1		



Result of management:						
Null	16	88.9	12	66.7	4.2	0.212
Recovery	2	11.1	4	22.2		
Fistula related Death	0	0	2	11.1		
Re-exploration:						
No	17	94.4	17	94.4		
Yes	1	5.6	1	5.6	-----	1
Overall Mortality:						
No	16	88.9	15	83.3	fisher	1
Yes	2	11.1	3	16.7		

Discussion

Pancreaticoduodenectomy (PD), one of the most complex intra-abdominal operations, is widely used for benign and malignant disease located in the pancreatic head or perampullary region [11]. Despite developments in surgical techniques, pancreaticoduodenectomy is still accompanied by a high postoperative complication rate of 40–50% [12]. Previous studies demonstrated that the most common complications after pancreaticoduodenectomy were postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE) [12,13]. Several methods of digestive tract reconstruction have been proposed to reduce the main postoperative complications, mainly conventional single loop pancreatojejunostomy, isolated loop pancreatojejunostomy [14], and pancreaticogastrostomy [15]. Isolated pancreatojejunostomy, first described in 1976, was proposed to reduce complications such as POPF, based on the theory of separating bile and pancreatic enzymes. However, the debate regarding these two reconstructions is still present. Some studies demonstrated that isolated pancreatojejunostomy may be associated with less postoperative complications, such as POPF and delayed gastric emptying (DGE) [16,17]. Kaman et al. suggested that morbidity and mortality could be reduced using isolated pancreatojejunostomy to separate the bile from pancreatic secretions [18]. However, other studies reached different conclusions [19]. The aim of this study is to assess the use of isolated loop pancreatojejunostomy technique as a preventive approach for

postoperative pancreatic fistula and also to identify the best management protocol of it with early diagnosis. This study was conducted in General Surgery department in Zagazig University Hospitals. It was carried out on 36 patients with pancreatic head cancer and patients with perampullary and duodenal carcinoma. Patients were divided into 2 equal groups (18 patients each): the first group who underwent Isolated loop PJ and the second group who underwent Single loop PJ.

The current study showed that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard intra-operative data ($p > 0.05$). In agreement with our results Chhaidar et al. [20] reported that Median operative time was not significantly longer in the single loop PJ group (5.5 h [range, 4–9.16 hours]) compared with the isolated loop PJ group (5.4 h [range, 4–8 hours]) ($p = 0.84$). Also, in agreement with our results Li et al. [21] reported that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard operative time, intraoperative blood loss and blood transfusion. As well, Tani et al. [22] reported that the duration of operation was non-significantly longer for Isolated loop PJ group than single loop PJ procedures. Also, there was no statistically significant difference between the studied groups as regard intraoperative blood loss and blood transfusion.

However, in disagreement with our results Ballas et al. [23] reported that the duration of operation was significantly longer for Isolated loop PJ group than Single loop PJ procedures. This may be due to the higher incidence of intraoperative complications in the loop PJ group than single loop PJ procedure and

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time needed for anastomosis. But Now due to wide use of staplers there is no more prolonged operative time in both groups. Similarly, Kaman et al. [18] reported that duration of operation was significantly longer and Blood transfusion was significantly higher in loop PJ group than single loop PJ procedures. The meta-analysis by Deng et al. [24] investigated the advantage between isolated Roux loop pancreatojejunostomy (IPJ) and conventional pancreatojejunostomy (CPJ) after pancreaticoduodenectomy (PD), the pooled results revealed that ILPJ had longer operation time (WMD = 36.55, 95% CI 6.98 to 66.11, P = 0.02). the study revealed that both procedures are comparable as regard intraoperative blood loss and blood transfusion. Also, a systematic review and meta-analysis by Lyu et al. [19] aimed to compare the safety and effectiveness of the following procedures after pancreaticoduodenectomy: isolated pancreatojejunostomy, isolated gastrojejunostomy, and conventional pancreatojejunostomy. Pooled analysis showed that isolated pancreatojejunostomy required longer operation time vs conventional pancreatojejunostomy (WMD = 43.61, 95% CI: 21.64–65.58, P = 0.00). Postoperatively, the present study showed that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard Postoperative bleeding, Wound infection, Pulmonary complication, Biliary leakage & Pancreatic leakage (p>0.05). also, there was no statistically significant difference between groups as regard Gastrojejunostomy leakage, Delayed gastric emptying & Pancreatitis (p>0.05). In agreement with our results the meta-analysis by Deng et al. [24] revealed that there were no significant differences between both groups in postoperative pancreatic fistula, delayed gastric emptying, postoperative bleeding, intra-abdominal abscess, bile leakage, wound infection, and morbidity. Also, the systematic review and meta-analysis by Lyu et al. [19] revealed that Regarding postoperative pancreatic fistula, clinically-relevant postoperative pancreatic fistula, delayed gastric emptying, clinically-relevant delayed gastric emptying, bile leakage, hemorrhage, major complications and overall complications, , the meta-analysis reported that there were no significant differences for either isolated pancreatojejunostomy versus conventional pancreatojejunostomy or isolated gastrojejunostomy versus conventional pancreatojejunostomy. Furthermore, in

agreement with our results Chhaidar et al. [20] reported that Overall morbidity did not differ significantly between IPJ and CPJ groups (57.1% versus 52.1%; p = 0,7). Pancreatic fistula (PF) occurred in three patients of IPJ group (8.6%) and in 10 (28.6%) patients of CPJ group (p = 0.031). The clinical PF (grade B or C) was also significantly higher in the CPJ groups (25.7% versus 2.8%; p = 0.006). No statistical differences were found between the two groups with regard to other postoperative complications, including delayed gastric emptying, bile leakage and pulmonary complications. As well, Li et al. [21] reported that Overall morbidity did not differ significantly between RYR and CR groups (51.2% versus 58.1%; P = 0.51). Pancreatic fistula (PF) occurred in 10 patients of RYR group (23.3%) and in 11 patients of CR group (25.6%) (P = 0.80). The clinical PF was also similar in the two groups (9.7% versus 4.3%; P = 0.39). No statistical differences were found between the two groups with regard to other postoperative complications, including delayed gastric emptying, bile leakage, wound infection, intra-abdominal abscess, haemorrhage, ileus, re-exploration, and pneumonia. Also, Tani et al. [22] reported that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard Postoperative complications. Similarly, Ballas et al. [23] reported that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard major and minor complications. The same result was reported by Kaman et al. [18]. Finally, we found that that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard Re-explanation and overall mortality (p>0.05). In agreement with our results the meta-analysis by Deng et al. [24] revealed that there were no significant differences between both groups in overall mortality. Furthermore, the systematic review and meta-analysis by Lyu et al. [19] revealed that regarding reoperation, and mortality, the meta-analysis reported that there were no significant differences for either isolated pancreatojejunostomy versus conventional pancreatojejunostomy or isolated gastrojejunostomy versus conventional pancreatojejunostomy. Also, in agreement with our results Chhaidar et al. [20] reported that Re-laparotomy due to severe Pancreatic fistula (PF) was significantly more often in the CPJ group. Analysis of postoperative mortality revealed no significant difference between the two groups. As well, Li et al.



[21] reported that One patient died in either of the two groups, accounting for a mortality of 2.3% in our series. Both deaths resulted from intra-abdominal bleeding secondary to PF. Also, Tani et al. [22] reported that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard reexploration and mortality ($p>0.05$). Similarly, Ballas et al. [23] reported that there was no statistically significant difference between isolated loop PJ group and single loop PJ group as regard mortality rate. The same result was reported by Kaman et al. [18].

Conclusion

this study showed no significant reduction of pancreatic anastomosis leak when the isolated loop technique is performed for the construction of pancreatojejunal anastomosis instead of the single loop technique. But there is slight improvement in fistula-related morbidity and mortality and the need for re-exploration. Also due to wide use of surgical staplers in reconstruction there is no more prolonged operative time in ILPG, so we recommend it as a safe technique for pancreatojejunal anastomosis in patients undergoing PD. However, further randomized controlled trials should be undertaken to ascertain these findings.

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