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Incidence of Leakage in Pancreatic Anastomosis with External Stent after Whipple Operation

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Abstract

Background: Pancreaticojejunal anastomotic leakage (PJAL) and subsequent pancreatic fistula are the most serious problems associated with pancreatic remnant. Reoperation as a pancreaticogastrostomy, repeat pancreaticojejunostomy, or total pancreatectomy is necessary in the case of severe PJAL, and it relies on the patient's clinical status.

Aim of Study: To identify the risk factors for pancreatic fistula after pancreaticoduodenectomy (PD), and the incidence and prediction of PJALthrough a comparison between using external pancreatic duct stent and no stent.

Material and Methods: Acomparative cohort studywas conducted on 20 patients who were enrolled and divided into two equal groups, group 1 included 10 patients with pancreatic external stent and group II included 10 patients without pancreatic stent.

Results: No statistically significant differences were noted between study groups regarding all study parameters such as interventions and outcomes. Also, no differences were noted between study groups regarding main study outcomes as the incidence of postoperative pancreatic fistula was 1 case (10.0%) vs. 3 cases (30.0%); p=0.264, bile leak was 1 case (10.0%) vs. 2 cases (20.0%); p=0.531 and there was no mortality in group 1 (0.0%) and only 1 case in group 2 (10.0%); p=0.305.

Conclusions: External pancreatic duct stenting has no significant effect on decreasing the rate of Post-Operative Pancreatic Fistula (POPF) suggests that external stenting of the pancreatic duct to drain pancreatic juice shouldn't be used as a routine in preventing the complications of pancreatic leakage.

Key Words: *Pancreatic anastomosis – Leakage – Stent – Whipple operation.*

Introduction

PANCREATICODUODENECTOMY (PD), or the Whipple procedure, is a complicated risky surgical treatment performed for numerous malignant and benign diseases of the pancreas and periampullary region. The perioperative mortality rate related to a PD has dramatically fallen during the last 80 years, from greater than 25% to much less than 3% **[1]**.

This has been in large part because of centralization with specialization of pancreatic surgery in large volume centers, enhancements in preoperative care, and the advances in interventional radiology and its availability to assist with treating complications when they arise **[2]**.

In Pancreaticoduodenectomy after successful resection, the pancreatic stump is mostly managed by pancreatico-jejunal anastomosis. Many alternatives were introduced to enhance the results: invaginating end-to-end or end-to-side pancreaticojejunostomy with a one- or two- layer suture, duct-to-mucosa anastomosis (without or with internal or external stenting of the duct), simple suture legation of the pancreatic duct without enteric anastomosis and 'glue occlusion' of the duct **[3]**.

Pancreaticojejunal anastomotic leak rate has been observed to occur in 6-24% of patients after pancreaticoduodenectomy, and it's related to a mortality rate of 20% to 80%. Conservative treatment normally yields excellent results in mild PJAL **[4]**.

However, in severe PJAL and in particular the case of anastomotic dehiscence, reoperation becomes inevitable as it constitutes the primary cause of early postoperative mortality because of abdominal sepsis. In such cases, a surgeon should always consider the extent of dehiscence, the clinical status of the patient, and the vitality of the pancreatic remnant to determine the best surgical management. Depending on the severity of leakage, simple wide drainage, creating a new pancreaticojejunal anastomosis, or even completion pancreatectomy can be the treatment of choice **[5]**.

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To date, there has been no consensus regarding which approach gives out a better advantage in the prevention of pancreatic fistula (PF) after pancreaticoduodenectomy (PD) among internal and external drainage. Specifically, few studies have assessed the two approaches in the subgroup of patients with high=risk factors for PF.

Material and Methods

This comparative cohort studies included patients attended department of general surgery for Whipple procedure.

Type of study:

Comparative cohort study.

Randomization:

Random Number Generator Software.

Inclusion criteria:

Patients of both sexesaged ≥18 years old with firm pancreas and wide pancreatic duct >4mm.

Exclusion criteria:

Patients with soft pancreas, pancreatic duct diameter <4mm, locally advanced tumours or metastatic patients.

Patients and Methods:

A comparative cohort study was conducted at Department of General Surgery at Ain Shams University Hospitals from January 2021 until February 2022.

Participating patients signed informed written consent after thorough explanation of the details and purpose of the current study. The study protocol was approved by the Ethical Research Committee of General Surgery Department and Faculty of Medicine, Ain Shams University.

Each patient was subjected to full history taking, clinical presentation and biochemical indicators of pancreatic leak. Intraoperative data as duct size, consistency of pancreas (firm/hard), blood loss, vascular injury (portal vein, splenic vein, hepatic artery, SMV) and operative time were recorded. Postoperative complications either general as shock, hemorrhage, DVT, pulmonary embolism and urinary retention or operation-related (local) as pancreatic fistula, delayed gastric emptying (DGE), biliary anastomotic leak, peri-anastomotic fluid collection and tube-related complications were assessed.

The severity of pancreatic fistula was determined based on clinical criteria and then stratified into 3 levels of impact on the patient: Grades A, B, and C; grade A fistulas are transient, asymptomatic biochemical fistulas, defined by only elevated drain amylase levels, grade B fistulas are clinically apparent, symptomatic fistulas that require diagnostic evaluation and therapeutic intervention and grade C fistulas render patients in a critical condition, with sepsis and/or organ dysfunction and they require more significant interventions, usually in an intensive care setting, or surgical re-exploration for definitive management.

The median length of stay, median time to resume unlimited oral intake, median day of nasogastric tube removal, incidence of readmission, and reoperation and mortality in hospital admission were also recorded. Follow-up was performed for 3 months.

Surgical methods:

In the present study, pancreatic anastomosis was performed with an end-to-side and duct-to-mucosa Pancreatico-jujenostomy. In addition, two-layer suture was used for the PJ anastomosis, and an appropriately sized Nelaton tube was placed in the pancreatic duct.

Suture for the posterior wall of the PJ:

The posterior wall of the pancreatic remnant and the jejunal muscularis was sutured using interrupted suture with a 4/0 absorbable suture (PDS) from the upper edge of the pancreatic remnant to the lower edge of the pancreatic remnant.

Pancreatic stent placement:

After completion of the suture for the posterior wall of the PJ, an appropriately sized Nelaton tube (Fr 6) with multiple side holes was inserted approximately 5cm into the main pancreatic duct and fixed to the pancreatic duct. The other end of the tube was inserted into the jejunum. The other end of the tube was pierced through the jejunum to the outside of the abdominal cavity in the external drainage group (Fig. 1).

Pancreatic duct-jejunal mucosal suture:

The jejunum was cut, and the size of the incision was slightly larger than the diameter of the pancreatic duct. The other end of the Nelaton tube was inserted into the jejunum from the incision. Then, the pancreatic duct was sutured to the jejunal mucosa using interrupted sutures with 4/0 absorbable sutures (PDS).

Suture for the anterior wall of the PJ:

After the pancreatic duct-jejunal mucosal suture, the anterior wall of the pancreatic remnant and the jejunal muscularis was joined using interrupted suture from the lower edge of the pancreatic remnant to the upper edge of the pancreatic remnant (Fig. 2).

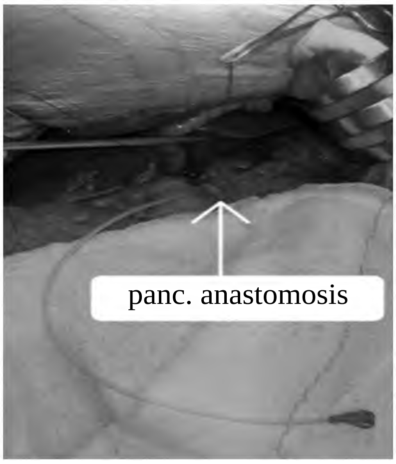

Fig. (1): During insertion of external pancreatic duct stent.

Fig. (2): After complete suturing anterior wall duct to mucosa PJ in the pancreaticoduodenectomy.

Fixation to the external drainage tube:

The other end of the tube was pierced through the jejunum about 15 cm from the anastomosis and embedded into the muscularis of the jejunum, and sutured to the parietal peritoneum, and then to the outside of the abdominal cavity.

Perioperative management:

Patients with a poor status attained an adequate improvement via blood transfusion, supplemental albumin, or pre-operative biliary drainage if the patient had severe concomitant disease (severe anemia, hypoproteinemia, or hyperbilirubinemia). The postoperative treatment included the prophylactic use of antibiotics, acid suppression therapy, nutrition and other treatments.

Patients were also carefully monitored. The external drainage tube was removed 4-6 weeks after pancreaticoduodenectomy.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as mean ± standard deviation and ranges. Also, qualitative variables were presented as numbers and percentages. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test.

Results

In group 1 only one case had POPF grade A which was managed conservatively by close follow up of the drain. The drain content was 200cc on the 5th POD then the content decreased till about less than 50cc on the 12th postoperative day (POD). The patient was discharged after complete oral feeding and guided to follow-up at the out-patient clinic (OPC) to remove the drain after 3 weeks.

In group 2 there was a case that had POPF grade B which was symptomatic but without organ failure. We required drain in situ 3 weeks and this was sufficient in management of the fistula.

In group 2 there was a case that had POPF grade C which developed on the 6th POD and related with severe sepsis and intra-abdominal abscess. The patient was re-admitted to the ICU, started antibiotics and percutaneous drainage (Pig-Tail) was inserted to drain the intra-abdominal abscess and patient resolved after about 10 days without the need of re-operation or further surgical intervention.

There was one case in each group had biliary leakage which was resolved conservatively until being controlled (self-limited) biliary fistulas after 2 weeks.

There was only one case of mortality in group 2 on the 3rd POD caused by hypovolemic shock due to severe bleeding in a hypertensive patient. The patient was hemodynamically unstable and received about 4 units of packed RBCs and 3 units of plasma to maintain circulation stability till re-operation for abdominal exploration but cardiac arrest and death occurred before entering the OR.

Table (1): Comparison between group I and II according to preoperative data.

Baseline characteristics	Group I (n=10)	Group II (n=10)	Test value	*p*-value
Age (years):				
Mean ± SD	63.00±7.26	63.20±6.20	*t*=–0.066	0.948
Range	50-73	50-70		
Sex:				
Female	3 (30.0%)	3 (30.0%)	X^2=0.000	1.000
Male	7 (70.0%)	7 (70.0%)		
ASA classification:				
I	2 (20.0%)	2 (20.0%)	X^2=0.000	1.000
II	8 (80.0%)	8 (80.0%)		
Smoking:				
No	6 (60.0%)	5 (50.0%)	X^2=0.202	0.653
Yes	4 (40.0%)	5 (50.0%)		
Comorbidities:				
No	1 (10.0%)	0 (0.0%)	X^2=1.000	0.317
Yes	9 (90.0%)	10 (100.0%)		
Cardiac	1 (10.0%)	1 (10.0%)	X^2=0.000	1.000
Diabetes	3 (33.3%)	5 (50.0%)	X^2=0.545	0.460
Hypertension	4 (40.0%)	4 (40.0%)	X^2=0.000	1.000
Obesity	1 (10.0%)	2 (20.0%)	X^2=0.373	0.542
Clinical presentation:				
Abdominal pain	3 (30.0%)	4 (40.0%)	X^2=0.209	0.648
Anorexia	5 (50.0%)	7 (70.0%)	X^2=0.792	0.374
Itching	2 (20.0%)	3 (30.0%)	X^2=0.253	0.615
Jaundice	6 (60.0%)	8 (80.0%)	X^2=0.905	0.342
Vomiting	3 (30.0%)	5 (50.0%)	X^2=0.792	0.374
Weight loss	4 (40.0%)	6 (60.0%)	X^2=0.760	0.383

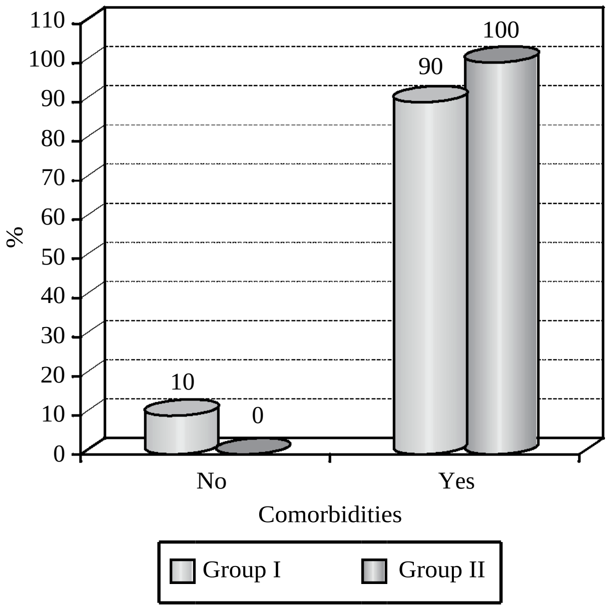

Fig. (3): Comparison between group I and II according to comorbidities.

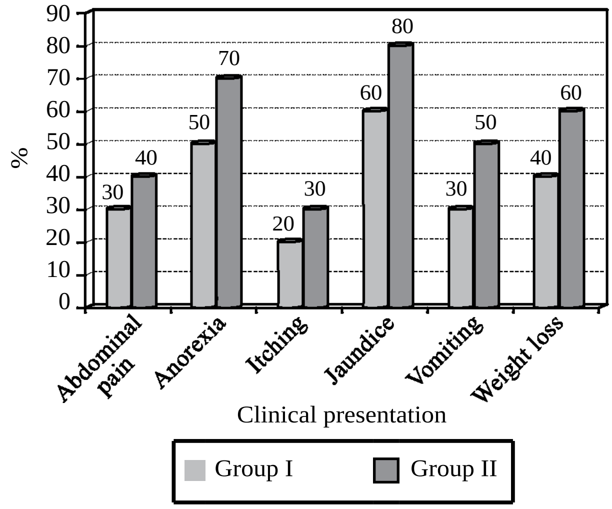

Fig. (4): Comparison between group I and II according to clinical presentation.

Table (2): Comparison between group I and II according to operative data.

	Group I (n=10)	Group II (n=10)	Test value	*p*-value
Operative time (min):				
Mean ± SD	468.10±21.82	451.40±23.76	*t*=1.637	0.119
Range	380-497	349-508		
Tumor location:				
Ampulla Mass	3 (30.0%)	1 (10.0%)	X^2=1.188	0.276
Distal CBD	2 (20.0%)	2 (20.0%)	X^2=0.000	1.000
Duodenal Mass	1 (10.0%)	1 (10.0%)	X^2=0.000	1.000
Pancreatic Head	4 (40.0%)	6 (60.0%)	X^2=0.760	0.383
Estimated blood loss/ml:				
Mean ± SD	568.50±84.85	601.60±132.76	*t*=-0.664	0.515
Range	435-700	350-800		
Transfusion of RBCs:				
No	6 (60.0%)	5 (50.0%)	X^2=0.202	0.653
Yes	4 (40.0%)	5 (50.0%)		
Tumor size (cm):				
Mean ± SD	4.01±0.08	3.94±0.13	*t*=1.450	0.164
Range	3.9-4.4	3.8-4.2		

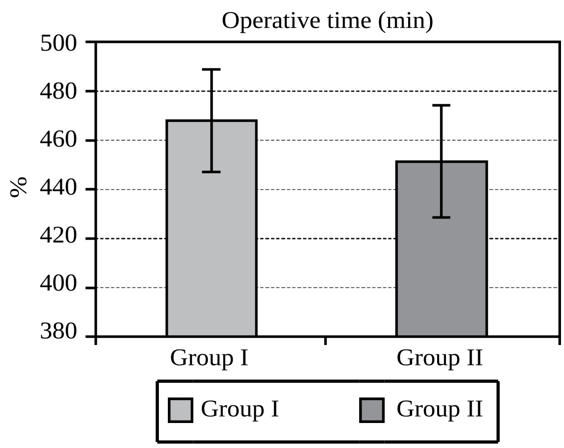

Fig. (5): Comparison between group I and II according to operative time "min".

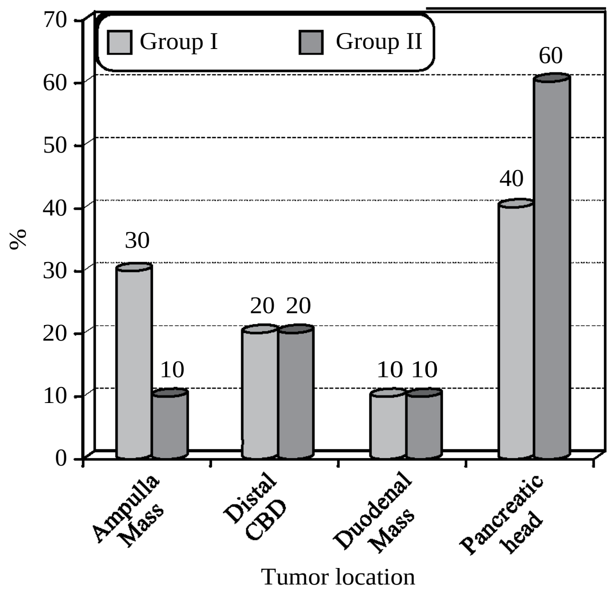

Fig. (6): Comparison between group I and II according to tumor location.

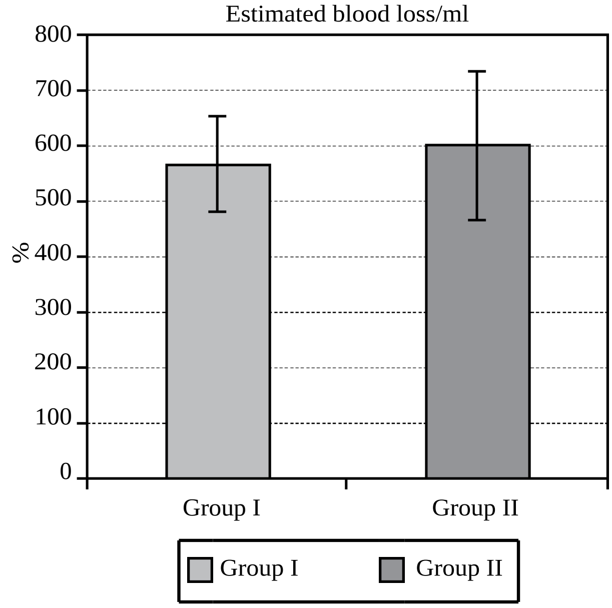

Fig. (7): Comparison between group I and II according to estimated blood loss "ml".

Table (3): Comparison between group I and II according to laboratory data.

Laboratory data	Group I (n=10)	Group II (n=10)	Test value	*p*-value
Total Bilirubin:				
Mean ± SD	5.35±0.38	5.63±0.62	*t*=1.218	0.239
Range	4.5-6.8	5.2-7.2		
ALK Phosphatase:				
Mean ± SD	158.10±10.16	153.00±4.97	*t*=1.426	0.171
Range	145-183	145-159		
GGT:				
Mean ± SD	73.40±2.91	75.10±3.57	*t*=1.167	0.258
Range	68-77	65-81		
TLC:				
Mean ± SD	7.54±0.42	7.73±0.44	*t*=0.988	0.336
Range	6.8-8	5.9-10		
Hemoglobin:				
Mean ± SD	10.54±0.82	10.24±0.80	*t*=0.828	0.419
Range	9-13	8-11		
Albumin:				
Mean ± SD	3.74±0.28	3.92±0.36	*t*=1.248	0.228
Range	3.2-4.5	2.9-4.7		
ALT:				
Mean ± SD	67.24±6.10	72.60±8.79	*t*=1.584	0.131
Range	47-88	40-92		
AST:				
Mean ± SD	73.60±6.38	77.80±7.41	*t*=1.358	0.191
Range	60-80	64-87		
CA 19-9:				
Mean ± SD	196.90±48.74	203.70±11.04	U=0.430	0.672
Range	109-276	145-268		

Table (4): Comparison between group I and II according to post-operative data.

Rate of Postoperative Pancreatic Fistula	Group I (n=10)	Group II (n=10)	X2	*p*-value
No	9 (90.0%)	7 (70.0%)	X^2=1.250	0.264
Yes	1 (10.0%)	3 (30.0%)		
POPF Grade:				
A	1 (10.0%)	1 (10.0%)	X^2=2.25	0.522
B	0 (0.0%)	1 (10.0%)		
C	0 (0.0%)	1 (10.0%)		
No	9 (90.0%)	7 (70.0%)		
Time until unlimited oral intake/day:				
Mean ± SD	6.40±1.43	7.00±1.63	*t*=–0.874	0.394
Range	4-9	5-9		
NG tube removal/day:				
Mean ± SD	3.90±0.99	3.20±0.92	U=1.635	0.119
Range	3-6	2-5		
DGE:				
No	8 (80.0%)	6 (60.0%)	X^2=0.952	0.329
Yes	2 (20.0%)	4 (40.0%)		
DGE Grade:				
A	2 (20.0%)	2 (20.0%)	X^2=2.286	0.319
B	0 (0.0%)	2 (20.0%)		
No	8 (80.0%)	6 (60.0%)		
Complications:				
Bile leak	1 (10.0%)	2 (20.0%)	X^2=0.392	0.531
Intra-abdominal abscess	0 (0.0%)	1 (10.0%)	X^2=1.053	0.305
Percutaneous drainage	1 (10.0%)	2 (20.0%)	X^2=0.392	0.531
Intra-abdominal bleeding	0 (0.0%)	1 (10.0%)	X^2=1.053	0.305
Re-operation	0 (0%)	0 (0%)	X^2=0.000	1.000
Post-Operative ICU stay:				
Mean ± SD	5.00±0.67	5.10±1.60	U=–0.183	0.857
Range	4-6	3-9		
Post-Operative Hospital stay:				
Mean ± SD	9.90±1.66	11.10±3.67	U=–0.943	0.358
Range	8-13	3-18		
Post-operative Mortality:				
No	10 (100.0%)	9 (90.0%)	X^2=1.053	0.305
Yes	0 (0.0%)	1 (10.0%)		

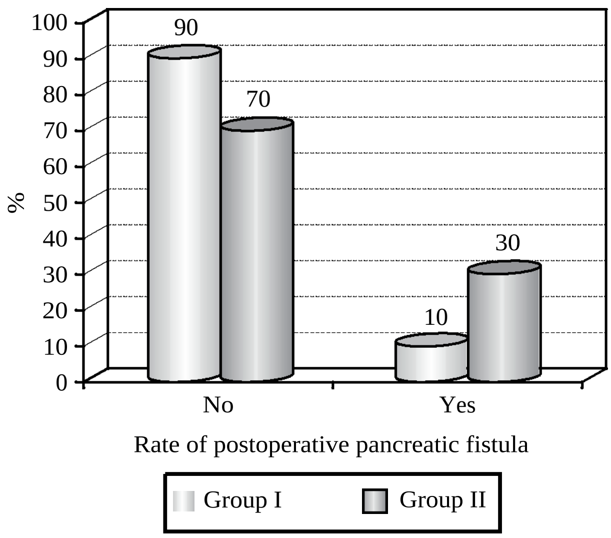

Fig. (8): Comparison between group I and II according to rate of postoperative pancreatic fistula.

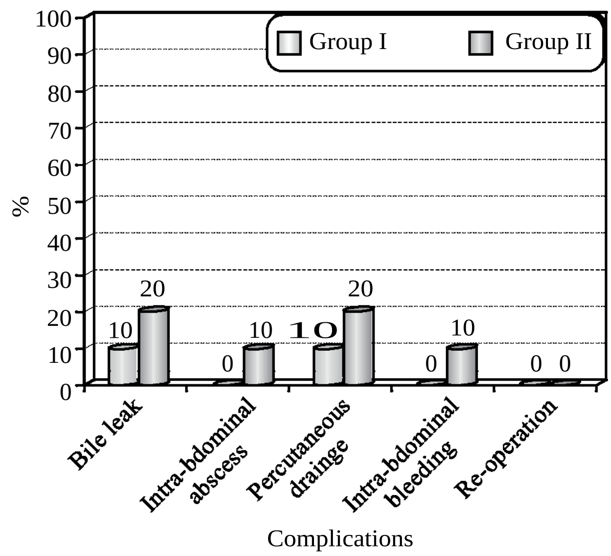

Fig. (9): Comparison between group I and II according to complications.

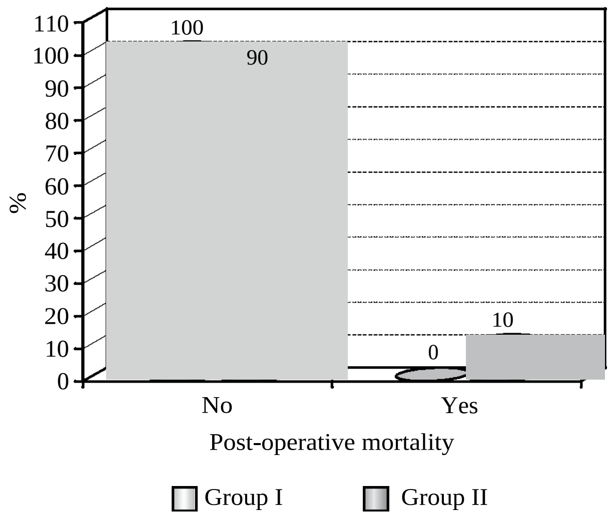

Fig. (10): Comparison between group I and II according to post-operative mortality.

Discussion

Pancreatic anastomosis has been discussed in many literatures for decreasing the incidence of POPF. Current study disagreed with Gu and colleagues who reported that the external drainage method was associated with a higher incidence of clinically relevant postoperative pancreatic fistula (CR-POPF). That study compared the effect of external and internal drainage and without stent on the incidence of CR-POPF to provide evidence to select a better drainage scheme in clinical practice. Overall, 520 patients undergoing pancreatic operation, including panreaticojuojenostomy were included in this single-centre study and were divided into two groups according to drainage methods. The incidence rate of CR-POPF between two groups was significantly different (23.3% vs. 13.6%, $p<0.05$). There was a statistically significant difference in postoperative hospitalization (11.00 vs. 10.00, $p<0.001$) and hospitalization expense (RMB 86733.28 vs. 84085.89 $p<0.05$) between the two groups.

On the other hand, current study agreed with Bin and colleagues who evaluated the clinical effect of different pancreaticojejunostomy techniques in the treatment of pancreaticoduodenectomy and investigated the applicability of pancreaticojejunostomy without pancreatic duct stenting. They found that Pancreaticoduodenectomy without pancreatic duct stenting is safe and reliable and can reduce the operative time and hospital stay. No significant differences were observed in the incidence of postoperative complications. A total of 87 patients who underwent pancreaticoduodenectomy were randomly assigned to either group A (duct-to-mucosa anastomosis with pancreatic duct stenting, n=43) or group B (pancreas-jejunum end-to-side anastomosis without stenting (n=44). The differences in the incidence of postoperative complications such as pancreatic fistula, abdominal bleeding, abdominal infection and delayed gastric emptying were not significantly different between the two groups. However, in that study they found that the operative duration of pancreaticojejunostomy without use of the pancreatic duct stent was significantly shorter in group B than in group A (t=7.137). The postoperative hospital stay was significantly shorter in Group B than in Group A (t= 2.408) [7].

Also, current study agreed with a meta-analysis conducted by Zhao and colleagues who showed that there were no differences in the rates of post-operative complications between Pancreaticoduodenectomy (PD) using internal stents and PD using external stents; internal stents may be more favorable during postoperative management of drainage tube. What is more, internal stents could reduce the digestive fluid loss and benefit the digestive function. The results showed that there is no difference between internal and external drainage in the rate of POPF (p=0.44) [8].

On the same line, current study corresponded with a meta-analysis conducted by Shrikhande and colleagues who showed that there is no clear evidence on the benefit of internal or external stenting after pancreaticoenteric anastomosis [9].

The role of stenting across the PA has been investigated as much for its potential to decrease the rate of POPF as to mitigate the severity of the POPF. The rationale is to divert pancreatic secretions away from the anastomosis as well as allegedly to guide more precise placement of sutures for duct-to mucosa anastomosis.

Against our findings, in an RCT involving 120 patients conducted by Poon and colleagues, the patients who had external stenting had a significantly lower rate of POPF when compared to the nonstented group (3% vs 15%, p=.027), but despite this finding, there were no statistically significant differences found in overall morbidity or hospital mortality [10].

Might be due to different population criteria, current study disagreed with another French RCT conducted by Pessaux and colleaguesinvolving 158 patients with high-risk prognostic factors for CR-POPF including soft pancreatic texture and a main pancreatic duct size <3mm who stated that external stenting was found to decrease CR-POPF and overall morbidity. The CR-POPF rate was 25% in the stented group vs 36% in the no-stent group **[11]**.

In another RCT from Japan conducted by Motoi and colleagues involving 93 patients, among the patients with nondilated ducts, CR-POPFs were shown to occur significantly less often with external stenting versus no stenting (10% vs 40%; *p*=.03), while in those patients with a dilated duct, there were no statistically significant differences found (4% vs 8%) **[12]**.

A recent RCT conducted by Jang and colleagues, involving 328 patients powered for equivalence between internal and external stenting showed that CR-POPF rates were 18.9% and 24.4%, respectively, with a conclusion tending to favor internal stenting but with wide confidence limits; the study, however, failed to stratify by fistula risk **[13]**.

A study conducted by Adham and colleagues stated that the benefit of prophylactic drainage after PD has remained highly controversial with some retrospective evidence showing no benefit [15].

Although a study conducted by Shrikhande and colleagues stated that drains often aid in the detection of complications after pancreatic resections [16].

In an early randomized trial involving 179 patients conducted by Conlon and colleagues, the presence of prophylactic drain failed to reduce the complications after pancreatic resection **[17]**.

However, in a recent, multicenter RCT conducted by George and colleagues involving 137 patients randomized to no drain versus drain, PD without drainage was associated with greater morbidity; the study was terminated early in view of an unacceptable increase in mortality from 3% to 12%, thereby concluding that elimination of drainage in PD increased the severity of complications **[18]**.

The concept of selective drainage in high-risk cases has been brought forward by many experts, and the controversy was reappraised **[19,20]**.

In an RCT assessing early drain removal in patients at low risk of CR-POPF conducted by Bassi and colleagues, 114 patients were randomized to early [postoperative day (POD) 3] versus late (POD5 or beyond) and concluded that prolonged retention of a drain was associated with an increase in complications, hospital stay, and cost **[21]**.

In a post hoc reappraisal of the same trial with risk stratification, moderate/high-risk patients with POD1 drain amylase <5,000U/L had lesser rates of CR-POPF with early drain removal on POD3 (4.2% vs 38.5%, *p*=.003) **[22]**.

That protocol of selective drain placement and early removal was studied in a prospective study conducted by McMillan and colleagues, involving 260 patients by the same authors in the United States and Italy and found that overall CR-POPF rates were less after implementation of this protocol (11.2% vs 20.6%, *p*=.001) **[23]**.

Finally, a recent RCT from Germany conducted by Witzigmann and colleagues compared rates of re-intervention in 438 patients randomized to drainage versus no drainage; the overall re-intervention rates were not found to differ significantly between the groups (drain 21.3% vs no-drain 16.6%; *p*= .0004), and there were no differences in morbidity and mortality; the rate of CR-POPF, however, was found to be significantly less in the no drain group (drain 11.9% vs no-drain 5.7%; *p*=.030) **[24]**.

Conclusions:

External pancreatic duct stenting has no significant effect on decreasing the rate of Post-operative Pancreatic Fistula (POPF) suggests that external stenting of the pancreatic duct to drain pancreatic juice shouldn't be used as a routine in preventing the complications of pancreatic leakage.

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Conflict of interest: The authors declared no conflicts of interest.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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معدلات حدوث تسريب فى قنوات البنكرياس بعد عملية ويبل مع استخدام الدعامة الخارجية

المقدمة : بالنسبة للأورام الخبيثة حول الأمبولة وكذلك الحالات الحميدة مثل التهاب البنكرياس المزمن أو الرتج أو الأورام الغدية الضخمة فى المنطقة المحيطة بالأمبولة، فقد أصبح استئصال البنكرياس والإثنى عشر جراحة ويبل إجراءاً قاسياً.

على الرغم من أن الاستئصال لم يعد مصدر قلق إلا أن إعادة توصيل بقايا البنكرياس لا تزال مشكلة.

يعتبر تسرب البنكرياس وناسور البنكرياس اللاحق من أخطر المشاكل المرتبطة ببقايا البنكرياس. إعادة الجراحة مثل فغر البنكرياس المعدى أو استئصال البنكرياس الكلى أمر ضرورى فى حالة التسرب التفاغرى الشديد للبنكرياس الصائغى ويعتمد ذلك على الحالة السريرية للمريض.

النتائج : لم يلاحظ أى فروق بين مجموعات الدراسة فيما يتعلق بنتائج الدراسة الرئيسية كمعدل ناسور البنكرياس ١ بعد الجراحة (١٠٪) مقابل ٣ (٣٠٪)، تسرب الصفراء ١ (١٠٪) مقابل ٢ (٢٠٪) والوفيات بعد الجراحة ٠ (٠.٠٪) مقابل ١ (١٠٪).

الاستنتاج : فى الختام ليس للدعامة الخارجية لقناة البنكرياس تأثير كبير على تقليل معدل الإصابة بناسور البنكرياس بعد الجراحة مما يشير إلى أنه لا ينبغى استخدامها كإجراء روتينى فى منع مضاعفات البنكرياس والتسريب، لذلك هناك حاجة إلى مزيد من التجارب السريرية ذات أحجام أكبر للعينات لمزيد من التقييم.