Risk factors for postoperative pancreatic fistula following non-traumatic, pancreatic surgery.

Retrospective observational study

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Pancreatic surgery e pancreatic fistula (POPF) is a potentially fatal sequela with substantial morbidity and mortality. POPF incidence and risk factors vary. This study aimed to evaluate the incidence and risk factors of patients with pancreatic fistula (PF) from patients undergoing various pancreatic surgeries for different pancreatic diseases.
MATERIAL AND METHODS: *A retrospective observational study was conducted in the surgical unit of our university hospitals from July 2014 to July 2019. Three hundred forty-seven patients were admitted with* a clinical *diagnosis of pancreatic fistula following both open and laparoscopic approaches for pancreatic benign and malignant tumors.*
RESULTS: *The most prevalent age was >60 years (67%), with a male predominance (83%). The most common diagnosis before surgery was pancreatic head adenocarcinoma (32%), followed by duodenal* neoplasm (19%) *and true epithelial pancreatic cystic neoplasms (18%), ampullary neoplasms (15%), bile duct neoplasms (12%), neuroendocrine neoplasms (2%), and chronic pancreatitis (2%). The most prevalent site of the pancreatic tumor was the head (87%), while accompanied Jaundice (47%) and epigastric discomfort (37%) were the commonest presentations before surgery. Pancreatic duct diameter greater than 3 mm was present in 208 patients (60%), tumor size greater than 3 cm in 63%, hard pancreatic texture in 67%, and preoperative ERCP with a stent in 37% of cases. Tumor in the tail of the pancreas was found in 5% (17 patients) of cases. The commonest operations performed were open pylorus-preserving pancreaticoduodenectomy, open pancreaticoduodenectomy without pylorus-preserving, and open distal pancreatectomy with splenic preservation. Postoperative pancreatic fistula occurred in 8% of cases (27), with ISPGF grade A (biochemical leak) occurring in 17 patients (17/27) and clinically significant POPF occurring in 10 patients (10/27). POPF occurred in 13 patients after distal pancreatectomy, 11 patients after pancreaticoduodenectomy, two cases followed central pancreatectomy, and one. Grade B after pancreaticoduodenectomy and two after distal pancreatectomy. Grade C POPF occurred in four patients after pancreaticoduodenectomy but not after distal pancreatectomy. Age >55 (p=0.00), male (p=0.03), presence of symptom (p=0.0008), location at Head of the pancreas (p=0.0004), elevated CA19-9 (p=0.0004), jaundice (p=0.0001) and pancreatic texture (p=0.00**).*
CONCLUSION: *Pancreatic fistula occurred in 27 patients (8%), a comparatively low incidence. POPF was linked to age, Jaundice, gender, pancreatic head cancer, symptoms, high CA 19-9, jaundice, and a soft pancreas. POPF incidence was higher after distal pancreatectomy, whereas POPF severity was higher after pancreaticoduodenectomy*

KEY WORDS: Pancreaticoduodenectomy, Pancreatic Fistula, Pancreatic Resection, Postoperative Complications

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Introduction

Pancreatic cancer has a dismal prognosis after resection [1]. Pancreaticoduodenectomy (PD) is a common surgical procedure used to treat a variety of pancreatic head and

periampullary region tumours and distal pancreatectomy (DP) for pancreatic tail lesions. The operational mortality rate following open or laparoscopic PD reaches up to 15% [2-3], and the incidence of postoperative complications ranges between 30% and 65% [4]. The commonest complication is postoperative pancreatic fistula (POPF). The incidence of POPF after pancreaticoduodenectomy ranged from 6% to 14% [5-6], 20% to 63% after central pancreatectomy [7], and 5% after distal pancreatectomy [8]. Many factors have been suggested to influence POPF after PD, including older age, age, long duration of Jaundice, surgical time, intraoperative hemorrhage, pancreaticojejunal (PJ) anastomotic technique, the soft texture of the pancreatic remnant, small size pancreatic duct, body mass index (BMI) > 25 kg/m^2 and non-ligated pancreatic duct [9-11]. This study aimed to evaluate the incidence and risk factors of patients with PF from patients undergoing various pancreatic surgeries for different pancreatic diseases.

Material and Method

Design of the Study and Eligibility Criteria

A retrospective observational study was conducted in the surgical unit of our university hospitals from July 2014 to July 2019. Three hundred forty-seven patients were admitted with a clinical diagnosis of pancreatic fistula following both open and laparoscopic approaches for pancreatic benign and malignant tumors. Inclusion criteria included > 18 years, both sexes, resectable pancreaticoduodenal tumors, or chronic pancreatitis. Exclusion criteria were patients < 18 years, Patients who underwent total pancreatectomies, Patients discovered intraoperatively to be fixed to portal vein or superior mesenteric artery, traumatic pancreatic surgeries, postoperative associated gastric or biliary leak, pancreaticoduodenal cancers infiltrating the colon, stomach or liver.

Definitions of Outcomes and Measurements

According to the International Study Group on Pancreatic Fistula (ISGPF) recommendations, a pancreatic fistula was defined, diagnosed, and treated as an amylase level in the fluid collected from the drain on the third postoperative day (POD) that was > three times the serum amylase level. POPF was divided into biochemical leak (formerly known as grade A), grade B, and grade C. On POD 3, the amylase level in the drain fluid was tested in all patients [12]. The Clavien-Dindo classification [13] graded all postoperative problems. Postoperative mortality is mortality occurring within the first month after surgery. Delayed stomach emptying is intolerance to oral feeding that occurs one week after surgery and necessitates nasogastric decompression.

Method

Pathologic investigations were used to diagnose all of the patients. In the preoperative clinic, serum disease-specific tumor markers (CA 19-9) were obtained. Abdominal ultrasonography (USS), abdominal computed tomography (CT), abdominal magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP) with brushing for cytology, and endoscopic transduodenal ultrasonography with pancreatic fine needle biopsy were all used in imaging investigations. When necessary, an endoscopic stent or nasobiliary drainage was placed.

For five years, pancreatic surgeons performed all procedures in our general surgery department or under their supervision, following pancreatic surgery principles. Within one hour before the skin incision, all patients received preoperative antibiotics, often second-generation cephalosporin.

As previously described, open PD [14-15], open distal pancreatectomy [16], and laparoscopic distal pancreatectomy [14] were performed. The pancreaticojejunal anastomoses were accomplished by the invagination of the pancreatic remnant into the side of the jejunum with an absorbable (Vicryl 2/0) inner layer and a nonabsorbable (Prolene 2/0) outside layer of a suture. Side-to-side hepaticojejunostomy was used to execute the procedure after the closure of the jejunal stump by stapler.

End-to-side gastrojejunostomy was done. Suture and stapler procedures were used to accomplish gastrojejunal anastomosis with or without pylorus preservation. A typical peripancreatic lymphadenectomy was performed in cancer cases. In all cases, a 5-or 6-French (Fr) polyvinyl chloride tube was inserted inside the pancreatic duct and across the hepaticojejunostomy as an internal stent. Tube Suction drains (10-mm Jackson-Pratt) were put in all patients, one near the biliary-enteric anastomosis and the other near the pancreaticoenteric anastomosis. Distal pancreatectomy was performed with or without splenectomy. The pancreatic incision was made using a scalpel. The drain fluid was collected and tested for amylase concentration on POD 1. The volume of drain discharge was measured daily. On postoperative day (POD) 7, a CT scan was performed systematically, and the drain was removed if no abnormal findings were found.

The presence of gas bubbles and/or liquid collection near the anastomosis was deemed radiographic evidence of PF, even in the absence of amylase-rich fluid in the drain. In this case, drain removal was postponed. There was no usage of a tube gastrostomy or a feeding jejunostomy. All patients received prophylactic antibiotics for four days afterward. Octreotide was not commonly used. When the patients passed flatus, they resumed their meals with a fluid diet, followed by a regular diet. All patients were given antibiotics and H2 blockers continually. Cases lost within the 3.5-year follow-up period were eliminated from the research.

Statistical Analysis

Data was input and analyzed in Microsoft Excel before being imported into the Statistical Package for the Social Sciences (SPSS) version 20.0 for analysis. Qualitative data were represented as numbers and percentages, but quantitative data were expressed as mean SD. The distribution of quantitative data is normal. The Chi-square test was employed to evaluate differences for significance, difference, and qualitative variable relationship (X2). Differences between quantitative independent groups using the t-test or Mann Whitney, paired using the paired t or sign, multiple using ANOVA or Kruskal-Wallis, independent predictors using logistic regression, and the ROC curve for cutoff. For highly significant results, a significant P-value was chosen at 0.05 and 0.001.

Results

(Table I) shows the preoperative and demographic data of the studied group. The commonest age was >60 years (67%), with male predominance (83%). The commonest preoperative diagnosis was pancreatic head adenocarcinoma (32%), duodenal neoplasm (19%), true epithelial exocrine PCN (18%), ampullary neoplasms (15%), bile duct neoplasms (12%), neuroendocrine neoplasms (2%), and chronic pancreatitis (2%). The commonest site of the tumor in the pancreas was the head (87%), with Jaundice (47%) and epigastric discomfort (37%) being the commonest presentation. Pancreatic duct diameter > 3 mm was present in 208 patients (60%), tumor size > 3 cm in 63% of patients, hard pancreatic texture in 67% of patients, and preoperative ERCP with a stent in 37% of cases.

(Table II) displays intraoperative data from the study group. A tumor in the pancreatic head was observed in 87% of patients (302), with open pylorus-preserving% pancreaticoduodenectomy being the most commonly performed operation (227/302). Tumors in the body of the pancreas were observed in 8% of cases (28 patients), with open distal pancreatectomy with splenic preservation being the most commonly performed operation (16/28). Tumors in the tail of the pancreas were found in 5% (17 patients), with open distal pancreatectomy with splenic preservation being the most commonly performed operation (9/17). The pancreatic texture was hard in 232 (67%) of patients and soft in 23% (80 patients) of cases.

(Table III) displays the study cohort's postoperative data. Postoperative pancreatic fistula occurred in 8% of cases (27), with ISPGF grade A (biochemical leak) occurring in 17 patients (17/27) and clinically significant POPF occurring in 10 patients (10/27). POPF occurred in 13 patients after distal pancreatectomy and 11 patients after pancreaticoduodenectomy, two cases followed central pancreatectomy, and one followed enucleation. Four patients had clinically significant pancreatic fistula grade B after pancreaticoduodenectomy and two after distal pancreatectomy. Grade C POPF occurred in four patients after pancreaticoduodenectomy but not after distal pancreatectomy.

(Table IV) shows the univariate analysis of predictive factors of POPF: Age > 55 (p=0.00), male (p=0.03) (RR 2.4, 95% CI 1.3-5.5), presence of symptom (p=0.0008) (RR 2.0, 95% CI 1.5-2.7), location at Head of the pan-

Table I - *Preoperative data of studied group (n= 347)*

Data	N(%)
Age (years)	
20-40	45(13%)
40-60	69(20%)
>60	233(67%)
Sex	
Male	218(63%)
Female	129(37%)
Preoperative diagnosis	
Pancreatic head adenocarcinoma	111(32%)
Ampullary neoplasm	52(15%)
Bile duct neoplasm	41(12%)
Chronic pancreatitis	7(2%)
Duodenal neoplasm	66(19%)
Neuroendocrine neoplasm	7(2%)
True epithelial pancreatic cystic neoplasm	63(18%)
Site of tumour in pancreas (CT)	
Head	302(87%)
Body	28(8%)
Tail	17(5%)
c/p	
asymptomatic	41(12%)
jaundice	163(47%)
epigastric discomfort	128(37%)
palpable epigastric mass	87(25%)
vomiting	41(12%)
anemia	31(9%)
Diabetes mellitus	76(22%)
BMI, kg/m²(mean ±SD)	21.5
Serum albumin(mean ±SD)	3.1 ± 0.3
bilirubin, mg/dl (mean ±SD)	3.9± 0.3
Serum creatinine, mg/dl(mean ±SD)	0.73 ± 0.17
CA19-9, U/ml(range)	45.1 (11.9-75.8)
Main pancreatic duct diameter (mm)	
>3mm	208(60%)
≤3mm	139(40%)
Tumor size	
<3cm	128(37%)
>3cm	219(63%)
Preoperative ERCP and stenting	128(37%)
Preoperative radiotherapy	12(3.5%)
ASA	
I	59(17%)
II	42(12%)
III	170(49%)
IV	76(22%)

Table II - *Intraoperative data of studied group (n= 347)*

Data	N (%)
Types of surgery	
a-tumor in head of pancreas	302(87%)
open Pylorus preserving pancreatico-duodenectomy	227
open Pancreaticoduodenectomy without pylorus preserving	75
b- tumor in body of pancreas	28(8%)
open distal pancreatectomy with splenic preservation	16
open Distal pancreatectomy with splenectomy	5
lap Distal pancreatectomy with splenic preservation	2
lap Distal pancreatectomy with splenectomy	1
Central pancreatectomy	1
Enucleation	1
Wedge resection.	2
c-tumour in tail of pancreas	17(5%)
open distal pancreatectomy with splenic preservation	9
open Distal pancreatectomy with splenectomy	3
lap Distal pancreatectomy with splenic preservation	3
lap Distal pancreatectomy with splenectomy	2
Operative time (mean ± SD)	
Pylorus preserving pancreatico-duodenectomy	195.3±7.3
Pancreatico-duodenectomy without pylorus preserving	186.1±0.1
Distal pancreatectomy with splenic preservation	142.2±0.1
Distal pancreatectomy with splenectomy	220.2±0.4
Blood loss, ml	
>1000ml (30%)	250(72%)
≤1000ml (70%)	97(28%)
Pancreatic texture	
Soft	232(67%)
Hard	80(23%)
Not defined	35(10%)

Table III - *Data of studied group (n= 347)*

Data	N (%)
Mean Duration of hospital stay (d)	12±5.61 days
Pancreatic fistula grade	27(8%)
a-ISPGF grade A(biochemical leak)	17(5%)
Following open or lap distal pancreatectomy	11
Following open pancreaticoduodenectomy	3
Central pancreatectomy	2
Enucleation	1
b-clinically-relevant pancreatic fistula	10(3%)
1-ISPGF grade B	6(1.8%)
Following open or lap distal pancreatectomy	2
Following open pancreaticoduodenectomy	4
2-ISPGF grade C	4(1.2%)
Following open or lap distal pancreatectomy	0
Following open pancreaticoduodenectomy	4

creas (p=0.0004) (RR 4.1, 95% CI 1.9-8.3), elevated CA19-9 (p=0.004) (RR 2.2, 95% CI 1.35-3.96), jaundice (p=0.0001) (RR 47, 95% CI 3.6-156), and pancreatic texture (p=0.00**)(RR 9, 95% CI 3.3-23.9) were significantly associated with postoperative pancreatic fistula. Logistic regression for independent factors is shown in (Table V). Age (p=0.002) and high CA19-9 (p=0.041) (OR 3.88, 95% CI 1.86-16.96) were both independent predictors of postoperative pancreatic fistula.

Table IV - *Univariate analysis of risk factors of fistula*

	Fistula (n=27)	No fistula (n=320)	P	RR (CI 95%)
Age, years, median (range)	58.52±10.63	41.21±12.01	0.00**	
Gender (n)				
Male	15(56.2%)	88(27.6%)	0.03*	2.4 (1.3-5.5)*
Female	12(43.8%)	232(72.4%)		
Symptoms				
Yes	27 (100.0%)	157(48.9%)	0.0008**	2.0 (1.5-2.7)*
No	0(0.00%)	163(51.1%)		
Tumor location (n)				Head
Head	19(68.7%)	54(17.0%)		
Body	7(25.0%)	163(51.0%)	0.0004**	4.1 (1.9-8.3)*
Tail	1(6.3%)	103(32.0%)		
CA19-9				
Elevated	20(75.0%)	109(34.1%)	0.004*	2.2 (1.35-3.96)*
Low	7(25.0%)	211(65.9%)		
Tumor size (cm)				
<3cm	5(18.7%)	68(21.2%)	0.82	
≥3cm	22(81.3%)	252(78.8%)		
Jaundice				
Yes	10(37.5%)	7(2.1%)	0.0001*	47 (3.6-156)*
No	17(62.5%)	313(97.9%)		
Tumor size (cm)				
<3cm	5(18.7%)	68(21.2%)	0.82	
≥3cm	22(81.3%)	252(78.8%)		
Pancreatic texture				
Soft	20(75.0%)	11(3.3%)	0.00**	9 (3.3-23.9)*
Hard	7(25.0%)	309(83.4%)		
Pancreatic Duct diameter				
<3mm	3(12.5%)	75(23.4%)	0.35	
≥3 mm	24(87.5%)	245(76.6%)		

Table V - *Logestic regression for independent predictors*

Factor	Wald	P	OR (CI 95%)
Age >55	4.523	0.002*	6.25 (1.2-8.63)
Sex (male)	2.145	0.185	3.85 (0.85-7.69)
Symptom	1.745	0.185	2.87 (0.62-8.96)
Head	1.236	0.398	1.85 (0.58-22.65)
Elevated CA19-9	2.999	0.041*	3.88 (1.86-16.96)
Jaundice	2.677	0.0741	1.77 (0.85-7.63)

Discussion

Postoperative pancreatic fistula is a dangerous complication following pancreatic surgeries. The prevalence of all POPF might range from 4% [17] to more than 30% [18]. The incidence of POPF in our study was within the typical range in the literature (8%), with distal pancreatectomy being the most prevalent procedure, followed by POPF. Various researches addressed the risk factors for POPF so that precautions may be made to avoid this deadly complication. Age > 70 years old [19], Jaundice [19], Preoperative ERCP and stents, intraoperative blood loss [20], and coronary artery disease [21]. In our Univariate analysis, POPF predicted factors coinciding with earlier studies regarding age > 55 and Jaundice. Other risk factors we discovered included symptomatic cases, tumour at the head of the pancreas, high CA 19-9, and soft pancreatic texture.

Although our study was retrospective, we have data on the texture of the pancreatic remnant (67% of cases were soft pancreatic remnants, 23% were hard pancreatic remnants, and 10% were undetermined). Univariate analysis in our study confirmed that soft pancreatic remnants were associated with developing POPF due to the difficulty of holding the soft pancreas's suture. Furthermore, while suturing the distal pancreas following distal pancreatectomy, the sutures cut through the soft pancreatic more easily than the hard pancreas. This viewpoint was supported by earlier research [22-23]. A study confirmed that soft pancreatic texture was associated with a 22.6% fistula rate and a greater risk of POPF in large cohorts that underwent pancreaticoduodenectomies [19]. The soft pancreas was related to a 75% fistula rate in our study, slightly higher than the prior study because of sample size variation. Although our best efforts were to avoid pancreatic fistulas with stents, a soft pancreas was most likely a role. Another indication of the importance of pancreatic texture in the development of fistulas is that no fistulas developed in our study after chronic pancreatitis surgery because a hard pancreatic remnant in patients with chronic pancreatitis facilitates holding the sutures during pancreaticojejunostomy, which was confirmed by previous research[24-25].

POPF was reported in nearly one-third of 232 patients who underwent DP (grade A = 18%, grade B = 6%, and grade C = 8%). A DP with splenectomy was linked to an increased risk of grade B or C PF. Notably, 92% of PF cases were successfully handled nonoperatively [26]. In our study, pancreatic fistulas formed more frequently after distal pancreatectomy (13/27) than after PD (11/27). However, the severity was greater after PD. Following distal pancreatectomy, 11 cases were grade A, two were B, and no C was graded. While three cases were grade A, four were grade B, and four were grade C after pancreaticoduodenectomy.

The small size of the pancreatic duct was associated with a higher risk of POPF. The pancreatic duct size is determined by preoperative imaging and intraoperative by the surgeon [27]. The most common cutoff value for the presence of POPF was 3 mm [28]. A study found that pancreatic ducts with diameters ≤ 3 mm predispose to pancreatic fistulae [24]. Furthermore, the technique of dealing with pancreatic remnants varies between studies aiming to decrease POPF. A study by Di Carlo et al performed intraductal injection of Neoprene which is a fluid, synthetic glue which polymerized and hardened when in contact with the pancreatic juice, inducing a fibrosis tissue that spares the endocrine component; however, the incidence of POPF was 17%, and in all cases, an intuitive solution of the fistula was observed and confirmed that this technique is a valuable alternative to pancreatico-jejunal anastomosis [29]. The anastomosis between the pancreatic duct and jejunal mucosa in PJ prevents the direct effect of the pancreatic enzymes with the pancreatic remnant and thus aiding mucosal healing and protecting the anastomosis by embedding the pancreatic remnant under jejunal serosa and thus decreasing POPF incidence [30]. However, another study found no significant difference in morbidity and PF rate between duct-to-mucosa anastomosis and single-layer end-to-side pancreaticojejunostomy [31]. Our study did not find that pancreatic duct size less than 3mm was connected with POPF, but we found that POPF was higher in dilated ducts. This is most likely due to differences in sample size, pancreaticojejunal anastomosis technique (we used a stent while other studies used mucosal to mucosal anastomosis), and finally, the soft texture of the pancreas in most of our cases, which poorly holds the pancreaticojejunal anastomosis and suture cut-through during the control of pancreatic distal cut after distal pancreatectomy). In our study, A pancreatic stent provided benefits such as diverting pancreatic enzymes away from the anastomosis and decreasing POPF. However, stent obstruction and migration are disadvantages. There have been few investigations on pancreatic stenting, and the outcomes have been mixed. In a cohort study, internal trans anastomotic stenting minimizes the pancreatic fistula of pancreaticojejunal anastomosis [32]. However, other studies found no significant difference in POPF between end-to-side pancreaticojejunostomy utilizing stented and non-stented methods [33-34].

Conclusions

POPF was connected with several risk factors such as age, Jaundice, gender, pancreatic head malignancy, symptomatic, high CA 19-9, and soft pancreas. POPF incidence was higher after distal pancreatectomy, whereas POPF severity was higher after pancreaticoduodenectomy. Soft pancreas texture is an important risk factor for POPF.

Riassunto

INTRODUZIONE: La fistola pancreatica postoperatoria è complicanza molto grave caratterizzata da rilevante morbidità e da mortalità. Lo scopo di questo studio è valutare l'incidenza e i fattori di rischio di fistola pancreatica in pazienti sottoposti a chirurgia pancreatica per varie patologie.

METODI: Lo studio osservazionale retrospettivo è stato condotto nelle unità chirurgiche degli Ospedali della nostra Università dal luglio 2014 al luglio 2019. Sono stati studiati 347 pazienti con la diagnosi di fistola pancreatica in seguito ad interventi chirurgici, con approccio open e laparoscopico, per patologie pancreatiche.

RISULTATI: Le diagnosi preoperatorie più frequenti in questa serie sono state adenocarcinoma pancreatico (32%), neoplasie duodenali (19%), neoplasie *pancreatiche* cistiche (18%); vi era inoltre prevalenza dell'età superiore ai

60 anni (67%) e del sesso maschile (83%). La sezione pancreatica maggiormente interessata dalla patologia è stata la testa (87%), condizione clinica accompagnata da ittero (47%) e da epigastralgia (37%). Il dotto pancreatico con diametro maggiore di 3 mm era presente in 208 pazienti (60%), tumori più grandi di 3 cm nel 63% e tessuto pancreatico duro nel 67% dei casi; è stato posizionato lo stent biliare preoperatorio con ERCP nel 37% dei casi. La localizzazione di lesione nella coda del pancreas è stata registrata nel 5% dei casi (17 pazienti). Le procedure operatorie, con approccio open, comunemente poste in atto sono state la pancreatico-duodenectomia con conservazione e senza conservazione del piloro, la pancreasectomia distale con conservazione della milza. La fistola pancreatica postoperatoria si è verificata nell'8% dei casi (27 pazienti) con grado A (biochemical leak - ISPGF) in 17 pazienti e con manifestazione clinicamente significativa in 10 pazienti. La fistola pancreatica postoperatoria è comparsa in 13 pazienti dopo pancreasectomia distale con manifestazione clinica di grado B in 2 casi, mentre è stata registrata in 11 casi dopo pancreatico-duodenectomia, ma con grado B in 4 pazienti e con grado C in altri 4. La valutazione dei fattori di rischio nel nostro studio ha prodotto questi risultati: età > 55 (p=0.00), sesso maschile (p=0.03), presenza di sintomi (p=0.0008), localizzazione testa pancreas (p=0.0004), CA 19-9 elevato (p=0.0004), ittero (p=0.0001) e tessuto pancreatico (p=0.00**).

CONCLUSIONI: Frequenza della fistola pancreatica meno elevata (8%) nel confronto con dati della letteratura. La fistola pancreatica postoperatoria risulta connessa con età, genere, presenza di sintomi, localizzazione testa pancreas, CA 19-9 elevato, ittero e tessuto pancreatico soffice. L'incidenza della complicanza è stata più alta dopo pancreasectomia distale, ma con gravità clinica maggiore dopo pancreatico-duodenectomia.

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