

# End-to-side duct-to-mucosa pancreaticojejunostomy after pancreaticoduodenectomy

## A comparison trial of small *versus* larger jejunal incision. A single center experience



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### End-to-side duct-to-mucosa pancreaticojejunostomy after pancreaticoduodenectomy. A comparison trial of small *versus* larger jejunal incision. A single center experience

**AIM:** The rates of post-operative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD) are between 5% and 30%. Nowadays, pancreaticojejunostomy (PJ) represents the most common type of reconstruction after PD, but the ideal technique is still debated.

Our randomized trial was conceived with the intent to evaluate if two variants of PJ could influence the post-operative outcome in term of early complications.

**MATERIAL AND METHODS:** Forty-eight consecutive patients treated with PD were randomized into 2 groups (Group 1 or Large Jejunal Incision or LJI group and Group 2 or Small Jejunal Incision or SJI group). Outcome measures were the operative time, postoperative complications, length of postoperative hospital stay, amylase content in drains.

**RESULTS:** twenty-two patients were enrolled in the LJI and 26 in the SJI group. Median operative times did not differ between the 2 groups. The groups were homogeneous in respect to the median age of patients, the clinical presentation of jaundice and the presence of percutaneous biliary drainage (PBD). POPF developed in 3/22 (13.6%) and 1/26 (4%) patients among the LJI and SJI group respectively (3 grade B and 1 grade C respectively) ( $p=0.341$ ). PPH occurred in 8/22 (36%) and 2/26 (8%) patients among the LJI and SJI group, respectively ( $p=0.018$ ). The Amylase content in the drainage fluid measured at the 5th postoperative day showed a higher value in patients who underwent LJI anastomosis compared to those with SJI anastomosis [LJI group: 26.5 (6-254) U/l vs SJI group: 7 (0-38) U/l;  $p=0.051$ ]. Delayed Gastric Emptying (DGE) was not different. The multivariate logistic regression analysis demonstrated both LJI anastomosis and DGE as independent predictors for pancreatic fistula (DGE: OR=20.04, CI 95%=1.92-208.83,  $P=0.012$ ; LJI anastomosis: OR=24.58, CI 95%=1.71-354.32,  $P=0.019$ ) and PPH (DGE: 30.5, CI 95%=3.02-308.16,  $P=0.004$ ; LJI anastomosis: OR=12.71, CI 95%=1.23-131.55,  $P=0.033$ ).

**CONCLUSIONS:**Based on the present results, we suggest to adopt what a "pancreas duct-oriented" approach: if pancreas duct is large a SJI-PJ is recommended; if the duct is < than 3 mm, a LJI must be preferred. Our conclusion is that the association of some surgeons to perform always the techniques with them are more confident is a concept of the past: recent data suggest that the pancreatic surgeon must have the different techniques in his "armamentarium" and varying the technique depending on local characteristic of the pancreas to allow a tailored approach to the patient.

**KEY WORDS:** Pancreaticojejunostomy, Pancreatic fistula, Surgical Outcome

### Introduction

Pancreatoduodenectomy (PD) represents the most demanding operation for every gastrointestinal surgeon. It is usually performed for tumors of pancreatic head, periampullary region and for chronic pancreatitis. Although the mortality rate is decreased to less than 2%

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## ABBREVIATIONS

PJ: Pancreaticojejunostomy  
 PHH: Post-pancreatectomy haemorrhage  
 DGE: Delayed gastric emptying  
 POPF: Post-operative pancreatic fistula

at high volume experienced centers, the percentage of patients with perioperative complications remains still high (around 20-40%)<sup>1</sup>. Leakage from pancreatic anastomosis with subsequent fistula is the most impactful problem<sup>2</sup>. Every pancreatic surgeon must take in account to deal with pancreatic anastomosis leakage and subsequent long lasting post-operative pancreatic fistula (POPF) and sometimes with catastrophic consequence for patients and increase of local recurrence rate<sup>3</sup>.

Indeed, depending on the severity, POPF can determine the prolongation of the hospital stay only or the appearance of other severe secondary complications<sup>4</sup>.

Recent series reported POPF rates after PD ranging between 5-30%. Different potential risk factors for pancreatic anastomotic leakage emerged: - Patient-related risk factors (age, gender and malnutrition); - disease-related risk factors (pancreatic texture and pancreatic duct diameter); - procedure-related factors (operative time, anastomotic technique and surgeon's experience)<sup>5</sup>. Pancreatic texture is the most cited: soft/normal pancreatic parenchyma (the so called "butter like" pancreas) increases the risk of POPF up to 10-fold<sup>6</sup>. In contrast, it is well known that in patients with painful chronic pancreatitis, although pancreatic resection might be more demanding, the pancreatic anastomosis is less difficult to perform due to the intense fibrotic texture of the pancreatic gland resulting in an excellent substrate for a safe suture<sup>7,8</sup>.

The diameter of the pancreatic duct plays also a role as predictor of POPF. If compared with the most commonly encountered 5-mm pancreatic duct, a 3-mm ducts show a 3-fold higher risk, and nearly 10-fold for 1-mm ducts<sup>6</sup>.

Many different techniques have been described for pancreatic anastomosis. The most common are pancreatojejunostomy (PJ) and pancreatogastrostomy (PG), and for each one several subtypes have been also invented<sup>9</sup>.

Studies comparing PG and PJ, mainly based on retrospective cohorts of patients, reported a reduction of POPF rate in PG<sup>10-11</sup>. In contrast, different randomized controlled trials (RCTs) did not validate this finding on meta-analysis<sup>11-14</sup>. All RCTs reported so far show certain limitations, accordingly to which results cannot be generalized. First, the definitions of POPF vary across the studies and are different from the currently accepted International Study Group of Pancreatic Surgery (ISGPS) definition<sup>15</sup>.

In addition, two trials used intraoperative randomization, which probably may lead to a selection bias<sup>16-17</sup>. Till now, the PJ represents the most used type of anastomosis, and in high volume centers report a major reduction in POPF rates due to ongoing efforts to standardize surgical techniques, improving perioperative management strategies and leading to the concept that pancreatic anastomosis might be adaptable to the individual pancreas texture and anatomical finding<sup>18</sup>.

The aim of the present study is to evaluate if between two different subtypes of the duct to mucosa PJ (large jejunal incision *vs* small jejunal incision) may influence the POPF rate. The two above-mentioned subtypes of PJ anastomosis are well known and standardized technique which are chosen based on the surgeon's experience and preference and often calibrated on the type of pancreas texture or Wirsung's diameter.

## Material and Methods

## PATIENTS

Forty-eight patients were enrolled in the study and divided as follow: 22 patients in the Group 1 named "Large Jejunal Incision (LJI)" and 26 in the Group 2 or "Small Jejunal Incision (SJI)".

TABLE I - Demographical characteristics of the 48 enrolled patients

Gender, Male/female (% Male)	29/19 (60)
Age, median (IQR)	67 (57-73)
Jaundice, y/n (%y)	22/26 (46)
PBD, y/n (%y)	15/33 (31)
Histology, n (%)	
PDAC	18 (37.5)
PVAC/Adenocarcinoma CBD	20 (41.7)
Benign lesions	10 (20.8)
Wirsung's duct diameter, n (%)	
< 3 mm	22 (45.8)
> 3 mm	26 (54.2)
Pancreas consistency, n (%)	
Hard	21 (44.8)
Soft	27 (56.2)
Pancreatic fistula, y/n (%y)	9/39 (19)
PPH, y/n (%y)	10/38 (21)
DGE, y/n (%y)	9/39 (19)
Therapy with Octreotide (days), median (IQR)	7 (5-7)
Removal of left drainage (days), median (IQR)	6 (5-7)
Amylase content in drain fluid (U/l), median (IQR)	
1 <sup>st</sup> post-operative day	881 (71-3400)
3 <sup>rd</sup> post-operative day	101 (18-719)
5 <sup>th</sup> post-operative day	10 (0-75)
Operative time Group LJI (min), median (IQR)	372.5 (350-405)
Operative time Group SJI (min), median (IQR)	380 (330-400)
Postoperative hospital stay (days), median (IQR)	9 (7-35)

PBD: Preoperative biliary drainage; PDAC: Pancreatic ductal adenocarcinoma; PVAC: Papilla of Vater adenocarcinoma; Benign lesions include: Chronic pancreatitis, Pancreatic Neuroendocrine Tumours and adenomas; PPH: Post-pancreatectomy haemorrhage; DGE: delayed gastric emptying.

TABLE II - Demographical and pathological characteristics in the two study Groups

	Group LJI n=22	Group SJI n=26	P-value
Gender, Male/female (% Male)	17/5 (77)	12/14 (45)	0.028
Age, median (IQR)	66.5 (56-73)	69 (61-76)	0.264
Jaundice, y/n (%y)	12/10 (55)	10/16 (38)	0.265
PBD, y/n (%y)	9/13 (41)	6/20 (23)	0.185
Histology, n (%)			
PDAC	6 (27)	12 (46)	
PVAC/Adenocarcinoma CBD	5 (23)	5 (19)	
Benign lesions	11 (50)	9 (35)	0.367
Wirsung's duct diameter, n (%)			
< 3 mm	12 (55)	10 (38)	
> 3 mm	10 (45)	16 (62)	0.265
Pancreas consistency, n (%)			
Hard	8 (36)	13 (50)	
Soft	14 (64)	13 (50)	0.343
Operative time (min), median (IQR)	372.5 (350-405)	380 (330-400)	0.270

PBD: Preoperative biliary drainage; PDAC: Pancreatic ductal adenocarcinoma; PVAC: Papilla of Vater adenocarcinoma; Benign lesions include: Chronic pancreatitis, Pancreatic Neuroendocrine Tumors and adenomas; PPH: Post-pancreatectomy haemorrhage; DGE: delayed gastric emptying.

TABLE III - Postoperative course and complications of 48 patients who underwent pancreaticoduodenectomy

	Group LJI n=22	Group SJI n=26	P-value
Pancreatic fistula, y/n (%y)	3/19 (13,6)	1/25 (4)	0.341
PPH, y/n (%y)	8/14 (36)	2/24 (8)	*0.018
DGE, y/n (%y)	5/17 (23)	4/22 (15)	0.389
Therapy with Octreotide (days), median (IQR)	7 (5-10)	6 (5-7)	*0.040
Removal of left drainage (days), median (IQR)	7 (5-10)	5 (4-6)	*0.028
Postoperative hospital stay (days), median (IQR)	11.5 (9-15)	9 (7-10)	*0.042
Amylase content in drain fluid (U/l), 5th post-operative day, median (IQR),	26.5 (6-254)	7 (0-38)	0.051

PPH: Post-pancreatectomy haemorrhage; DGE: delayed gastric emptying\*Statistically significant (p<0.05)

The two above-mentioned subtypes of PJ anastomosis are well known and standardized technique which are chosen based on the surgeon's experience and preference and often calibrated on the type of pancreas texture or Wirsung's diameter.

Clinical features and demographic's characteristics are summarized in Table I. Pre- and peri-operative laboratory parameters for haematology, biochemistry, and liver function tests were prospectively collected. All patients received antibiotic prophylaxis with a single shot of cephalosporin 2g and metronidazole at a dosage of 500 mg 30 min before surgery; the drugs were re-administered if surgery lasted longer than 4h. Patients who underwent preoperative biliary drainage (PBD) continued antibiotic therapy until day 5 postoperatively. In addition, patients received weight-adapted thrombosis prophylaxis with low molecular weight heparin and pancreatic secretion inhibitor octreotide at a dosage of 0.2 mg three times daily from day 0 to the discharge. Postoperative

complications and length of postoperative hospital stay were recorded.

Post-operative complications such as POPF, delayed gastric emptying (DGE), anastomosis leak, post-pancreatectomy haemorrhage (PPH) were also evaluated and summarized in Table II. ISGPS define POPF as "an abnormal communication between the pancreatic ductal epithelium and another epithelial surface containing pancreas-derived, enzyme-rich fluid". In addition, the ISGPF defined the diagnostic criteria of POPF as an "output via an operatively placed drain (or a subsequently placed, percutaneous drain) of any measurable volume of drain fluid on or after postoperative day 3, with an amylase content greater than 3 times the upper normal serum value"<sup>16,19</sup>.

Based on the 2016 Update of ISGPS definition and grading of post-operative pancreatic fistula the former "grade A postoperative pancreatic fistula" is now redefined and called a "biochemical leak" because it has no

clinical impact and is no longer referred to a true pancreatic fistula. Grade B requires a change in the post-operative management; drains are either left in place >3 weeks or repositioned through endoscopic or percutaneous procedures. The grade C fistula required major deviations from the normal clinical pathway as invasive procedures including surgical reoperation. Moreover, sepsis and organ dysfunction might be present as death may occur<sup>16,19-21</sup>.

DGE was defined as continuous drainage via the gastric tube of more than 500 ml/day over more than five days after surgery, or recurrent vomiting in combination with swelling of the gastro-jejunosomy/duodeno-jejunosomy and dilatation of the stomach at radiological contrast examination, following the recommendation of the ISGPS<sup>22</sup>. Biliary fistula was defined as fluid with a high level of bilirubin (>3 times the bilirubin serum level) secreted for more than five days<sup>23-24</sup>. PPH was defined along the guidelines set up by the ISGPS<sup>25-26</sup>.

#### RANDOMIZATION CRITERIA

Patients with inoperable disease or underwent neoadjuvant therapy were excluded from the study.

Forty-eight consecutive patients with radiologically resectable pancreatic disease were enrolled in the study. They were randomized as follow: 22 patients in the Group 1 named "Large Jejunal Incision (LJI)" and 26 in the Group 2 or "Small Jejunal Incision (SJI)". Patients were assigned to the LJI or SJI group through a simple random sampling procedure. After confirming that all inclusion criteria were fulfilled a nurse randomly drew a piece of paper from a box and disclosed the allocation group.

A written informed consent for study participation was submitted to all patients, and it were kept blind to the

treatment allocation. The study protocol was approved by the ethics committee of the IRCCS - Casa SollievodellaSofferenza Hospital in San Giovanni Rotondo (No. 8450/08).

#### SURGICAL TECHNIQUE

Surgical procedures consisted of pylorus-preserving pancreaticoduodenectomy (PPPD) with standard lymphadenectomy in all patients. One patient required a superior mesenteric vein resection to achieve R0 status. The same team of 3 surgeons conducted all pancreatic resections (ADB, FFD and PDS). We performed the duct to mucosa pancreatico-jejunosomy with the technique described by Büchler et al. and here briefly summarized<sup>27</sup>. After the placement of pancreatic stay stitches to close the marginal arches, the pancreas was transected with a sharp knife at the neck anterior to the superior mesenteric/portal vein. The bleeding from the pancreatic cut surface was controlled with 5/0 PDS II stitches (polydioxanone) (Ethicon, US LLC) with an atraumatic fine needle. The pancreatic remnant was then mobilized, carried out in a completely avascular plane, for at least 2 cm from the retroperitoneum. For ease of this dissection, the stitches on the superior and inferior border of the pancreatic remnant are gently lifted up by the first assistant. Furthermore, placement of a fine probe (or an infant feeding tube) into the pancreatic duct also helps in lifting the remnant to aid posterior dissection. An adequate mobilization of the pancreatic remnant is necessary for a correct placement of the posterior outer layer of the PJ. Now at least three single stitches 5/0 PDS II JRB - 1 (5/8 needle) were placed (variable depending on main pancreatic duct size) on the anterior wall of the pancreatic duct and on the posterior wall of the duct respectively. At

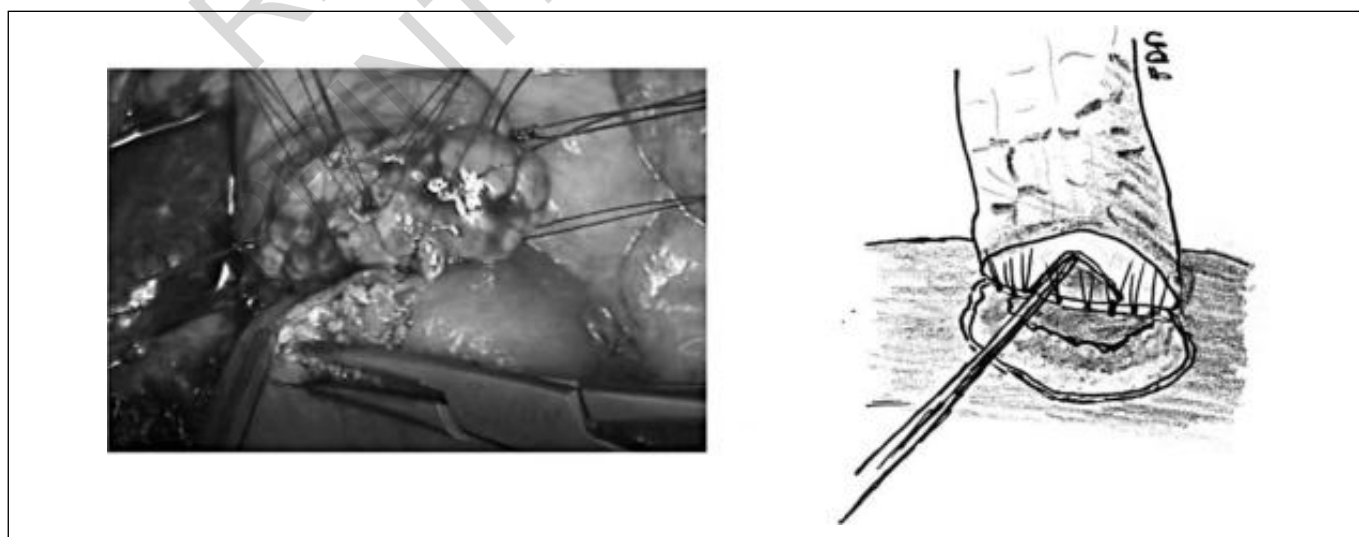


Fig. 1: Large Jejunal Incision (LJI)

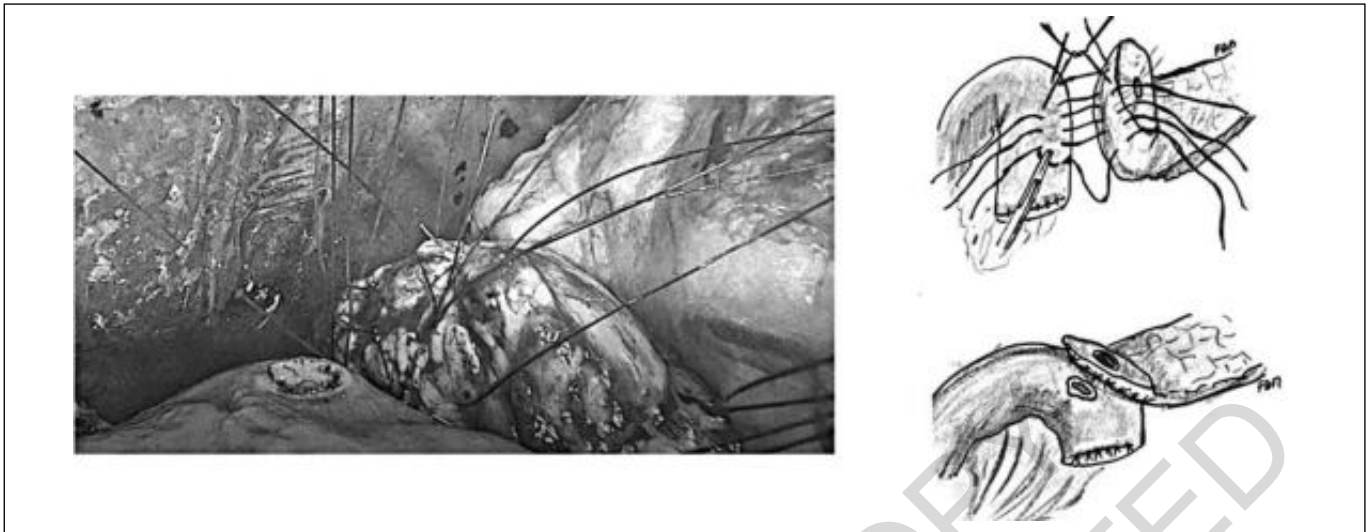


Fig. 2: Small Jejunal Incision (SJI)

this point we started the placement of interrupted sutures 5/0 PDS II JRB – 1 (5/8 needle) beginning on the posterior aspect of the mobilized pancreatic parenchyma and coming onto the seromuscular sidewall of the jejunal loop to complete the “posterior outer layer”. After that, we started the “posterior inner layer” with the placement of interrupted sutures to anastomose the posterior cut margin of the pancreas with the posterior wall (full thickness) of the now opened jejunum. According to the wideness of the jejunal incision, patients were divided in two group named: Group 1 or Large Jejunal Incision (LJI) and Group 2 or Small Jejunal Incision (SJI) as illustrated in Fig. 1 and Fig. 2 respectively. In the SJI group, the incision was large as the diameter of the pancreatic duct meanwhile in the LJI group the jejunum was opened a little smaller in length than the upper-lower extent of the pancreatic remnant. Progressing upwards, the preplaced posterior ductal sutures were also used to ensure that the posterior wall of the pancreatic duct was correctly anastomosed to the jejunal mucosa posteriorly.

Afterwards, as done for the posterior inner layer, the “anterior inner layer” was sutured incorporating also here the preplaced anterior ductal sutures. The final step involves the placement of interrupted sutures beginning on the anterior aspect of the mobilized pancreatic parenchyma and coming onto the seromuscular sidewall of the jejunal loop completing the “anterior outer layer”. Thus, the completed anastomosis is an end to side duct-to-mucosa anastomosis with an outer seromuscular and inner full thickness layer. Pancreatic stents are usually not used. Concluding the procedure, a side-to-end single layer hepaticojejunostomy and an antecolic side-to-end two-layer fashion duodenojejunostomy were performed on the same jejunal loop.

#### STATISTICAL ANALYSIS

Patients’ baseline characteristics were reported as medians with interquartile ranges (continuous variables), absolute and relative frequencies respectively (categorical variables) and compared between the two groups of patients by using non-parametric 2 (k)-independent sample test according to Mann-Whitney or Kruskal-Wallis, the Pearson Chi-square test or Fisher’s exact test, where appropriate. Interactions between variables (pancreatic fistula, Wirsung’s duct diameter and pancreas consistency) were assessed in logistic regression models. The independent effect of pancreatic anastomosis on categorical clinical variables were analysed by means of univariate analysis and subsequently expressed as Odds Ratios (OR) with 95% confidence intervals (95% CI) by means of logistic regression analysis based on forward stepwise selection procedures. Furthermore, multiple linear regression analysis was performed to examine the effects of independent variables on continuous dependent variable. All the clinical variables, which could have a relationship with the clinical outcome of interest, were included in each model. Cohen’s  $f^2$  was used as the effect size measure. Cohen suggests  $f^2$  values of 0.02, 0.15, and 0.35 represent small, medium, and large effect sizes<sup>28</sup>. All analyses were performed using the SPSS software package v.13 (Chicago, IL, USA), and p values < 0.05 were considered statistically significant<sup>29</sup>.

#### Results

In the LJI anastomosis group, 5/22 patients (23%) were female and 17/22 (77%) were male compared to 14/26 females (54%) and 12/26 males (46%) of the SJI anastomosis group (p=0.028). The two groups were homo-

geneous in respect to the median age of patients (LJI group: 66.5 [56-73] yrs.; SJI group 69 [61-76] yrs.), the clinical presentation of jaundice (LJI group: 12/22 patients; SJI group: 10/26 patients), and the presence of percutaneous biliary drainage (PBD) (LJI group: 9/22 patients; SJI group: 6/26 patients). The indication for surgery was pancreatic ductal adenocarcinoma in 18 patients (LJI group: 6 patients; group SJI: 12 patients), adenocarcinoma of Vater's papilla or common bile duct cancer in 20 patients (LJI group: 11 patients; group SJI: 9 patients), benign lesions (3 chronic pancreatitis, 5 neuroendocrine tumor, 1 mucinous cystadenoma and 1 ampullarian adenoma) in 10 patients (LJI group: 5 patients; group SJI: 5 patients). There was no significant difference between the two groups. Similarly, the median operative times did not differ between patients underwent LJI or SJI anastomosis: 380 min (330-400) in the latter group compared to 372.5 min (350-405) among LJI treated patients.

Intra-operatively, no significant difference emerged between the two groups in relation to the Wirsung's diameter < 3 mm [LJI group: 12/22 (55%) vs SJI group: 10/26 (38%) patients] and soft pancreatic consistency [LJI group: 14/22 (64%) vs SJI group: 13/26 (50%) patients]. Postoperatively 4/48 (8.3%) patients developed pancreatic fistula (3 grade B, 1 grade C): 3/22 (13.6%) belong to the LJI group and 1/26 (3.8%) to the SJI group ( $p=0.48$ ). In details, 1 Grade C fistula occurred in a patient who underwent SJI anastomosis, whereas 3 Grade B fistula were experienced from patients belonging to the LJI subgroup.

As expected, we observed that pancreatic fistula developed in 3/22 (14%) patients with Wirsung's diameter < 3 mm (LJI group: 2 patients; SJI group: 1 patient), in 4/27 (15%) patients with soft pancreas consistency (LJI group: 3 patients; SJI group: 1 patient), and in 3/18 (17%) patients characterized by both Wirsung's diameter < 3 mm and soft pancreas consistency (LJI group: 2 patients; SJI group: 1 patient). In addition, the amylase content in the drain fluid at the 5th postoperative day showed a higher amount in patients who underwent LJI anastomosis compared to those with SJI anastomosis [LJI group: 26.5 (6-254) U/l vs SJI group: 7 (0-38) U/l] although this value did not reach a statistical significance ( $p=0.051$ ).

PPH was diagnosed in 10 out of 48 (21%) patients (5 Grade A, 4 Grade B, 1 Grade C): 8/22 (36%) and 2/26 (8%) patients among the LJI and SJI group, respectively ( $p=0.018$ ). In details: Grade C PPH occurred in one patient of SJI anastomosis group (the same patients that experienced fistula grade C), whereas Grade A PPH was experienced from 5 and 1 patients among LJI and SJI group, respectively, and Grade B PPH in 3 of the LJI group. Conversely, no significant difference was found regarding the distribution of the nine patients who experienced DGE (Grade A in all cases) between the two groups (LJI group: 5/22; SJI group: 4/26). Regarding

postoperative medical management of patients, both duration of octreotide therapy and removal of left drainage were longer among patients with LJI anastomosis [7 (5-10) and 7 (5-10) days,  $p=0.040$ ] compared to those with SJI anastomosis [6 (5-7) and 5 (4-6) days,  $p=0.028$ ].

The cumulative median post-operative hospital stay was nine days (7-35). The postoperative median hospital stay was significantly longer among patients underwent LJI anastomosis [11.5 (9-15) days] compared to those treated with SJI anastomosis [9 (7-10) days,  $p=0.042$ ].

To evaluate the possible independent effect of pancreatic anastomosis technique on the clinical variables whose distribution differed significantly between patients underwent LJI or SJI anastomosis, different regression models were used. In addition, among patients who suffered from POPF, a subgroup had a post-operative course complicated also by PPH or DGE: 2/4 patients (50%) of the LJI group and 1/4 patients (25%) of the SJI group.

The multivariate logistic regression analysis demonstrated DGE as independent predictor for both pancreatic fistula (DGE: OR=20.04, CI 95%=1.92-208.83,  $P=0.012$ ) and PPH (DGE: 30.5, CI 95%=3.02-308.16,  $P=0.004$ ).

Multiple linear regression models demonstrated that patients underwent LJI anastomosis who experienced POPF had later removal of left drainage and longer octreotide treatment ( $p<0.05$ ). In these patients the removal of left drainage positively correlated with amylase content in the drainage fluid at the I, III, V post-operative days ( $p<0.05$ ). As expected, the post-operative hospital stay was longer in patients with LJI anastomosis who suffered from pancreatic fistula, DGE and PPH ( $p<0.05$ ). By multiple regression analysis only pancreatic fistula was significantly and independently associated with the removal of left drainage (Cohen's  $f^2$  0.496,  $p<0.01$ ), the duration of octreotide therapy (Cohen's  $f^2$  0.231,  $p=0.002$ ) and the post-operative hospital stay (Cohen's  $f^2$  0.166,  $p=0.03$ ).

Demographical characteristics, post-operative course and complications of all patients are detailed in Table I, Table II and Table III.

## Discussion

Nowadays two different anastomotic techniques, PG and PJ, whose outcomes are comparable in terms of survival, complications and recovery are used depending on surgeons' preference. In addition, for each technique exists almost two variant form. In PJs, the dunking procedure (i.e. invagination of the transected pancreas into the end of the jejunum) and the duct-to-mucosa technique are most commonly used. The PG is technically easier to perform than pancreatojejunostomy because of the proximity of the stomach and the pancreatic remnant, which usually assures that the anastomosis is well perfused.

Moreover, pancreatic enzymes are not directly activated in the acidic milieu of the stomach. Nevertheless, duct-to-mucosa PJ seems to be the most used technique for reconstruction and this motivated our study concept. In the daily surgical practice often happen, especially when it comes to high volume center, that surgeons, by packing a PJ, open the jejunal loop with different sizes of incision, either large as the remnant pancreas or small as the Wirsung diameter, and this only based on its own experience without any scientific criterion.

Our randomized trial was conceived with the intent to evaluate if these two variants of PJ, could influence the POPF rate.

In the present study no significant difference in POPF rate between the two subgroups of patients in terms of gender, Wirsung's diameter, pancreatic texture consistency and operative times were observed. This might be due to the small sample size of the present study. Indeed, a deep analysis of the data clearly shows that especially for POPF one case only was observed in the SJI group: it was a grade C fistula requiring a relaparotomy with completion pancreatectomy and complex post-operative course. On the other hand, 3 patients of the LJI group suffered from grade B POPF that did not necessitate a reoperation. Obviously, the hospital stays and the amylase content in the drain fluids were higher in the group with LJI where we reported 3 Grade B fistulas *vs* only 1 in the SJI.

In details, the SJI subgroup of patients, when compared with the LJI subgroup, exhibited a post-operative lower level of amylase content in the drain fluids. This may be of interest if we consider that the probability to develop a POPF is made mainly based on the amount of amylase content in the drainage fluids<sup>30-33</sup>. Noteworthy, on post-operative day I, the patient of the SJI subgroup who developed a grade C fistula, the amylase content in the drain was < of 5000 (predictive fistula cut-off). This might suggest that at least a part of patients who underwent PJ with the LJI are overvalued in terms of the probability of developing a POPF just because in the post-operative period the amount of amylase content in the drains are extremely elevated. In addition, a major incidence of PPH was noted in the LJI group; however, most of the PPH were grade A (5 out of 8 cases). As reported for other surgical technique, it is worth to note that, the different procedures show excellent results in the hands of small groups or individual surgeons who promote that technique<sup>34</sup>. Conversely, when tested in randomized trials with large numbers the results could be of less impact.

Indeed, a major problem in the present study is the low number of patients in the two groups.

## Conclusions

Based on the present results, we suggest to adopt what we have called a "*pancreas duct-oriented*" approach: if

pancreas duct is large a SJI-PJ is recommended; if the duct is < than 3 mm, a LJI must be preferred. This consideration is made also combining the duct diameter with pancreas texture. In fact, when Wirsung diameter is small, the SJI technique is difficult to perform even with surgical loops, considered that in these cases the pancreatic texture is usually soft or "butter-like". This is in line with the present results: the only Grade C fistula in SJI appeared in a soft pancreas with small Wirsung. Our conclusion is that the association of some surgeons to perform always the techniques with them are more confident is a concept of the past: recent data suggest that the pancreatic surgeon must have the different techniques in his "armamentarium" and varying the technique depending on local characteristic of the pancreas to allow a tailored approach to the patient.

## Author's contributions

FFDM, TG and PP contributed equally to this work and should be considered co-first authors. Study conception and design: FFDM, TG, PDS, PP; Acquisition of data: FFDM, TG, ADB, MRV; Analysis and interpretation of data: FT, FFDM, PP; Drafting of manuscript: FFDM, PDS, TG, PP, ADB; Critical revision: PDS and FFDM

## Riassunto

**INTRODUZIONE:** Il tasso di fistola pancreatica post-operatoria (POPF) post- duodenopancreatectomia (PD) oscilla tra il 5% e il 30%. Ad oggi, nonostante la tecnica ideale è ancora oggi oggetto di dibattito scientifico, la pancreaticodigiunostomia (PJ) risulta essere la tipologia più frequente di ricostruzione dopo PD. Questo studio è un trial randomizzato finalizzato a valutare come due varianti tecniche di PJ possano influenzare l'outcome post-operatorio in termini di complicanze precoci.

**MATERIALI E METODI:** Quarantotto (48) pazienti sottoposti a PD sono stati randomizzati in due (2) gruppi (Gruppo 1 o Large Jejunal Incision o Gruppo LJI, e il Gruppo 2 o Small Jejunal Incision o Gruppo SJI). Le variabili post operatorie valutate sono state il tempo operatorio medio, le complicanze post-operatorie, la degenza ospedaliera ed il contenuto di amilasi nel liquido di drenaggio.

**RISULTATI:** Venti-due pazienti sono stati arruolati nel gruppo LJI e venti-sei nel gruppo SJI. I due gruppi sono risultati omogenei per quanto riguarda età media, presentazione clinica con ittero e la presenza di drenaggio biliare percutaneo (PBD). Nei 2 gruppi non si sono osservate differenze in termini di tempo operatorio medio. In 3/22 (13.6%) pazienti del gruppo LJI e in 1/26 (4%) pazienti del gruppo SJI (3 grado B e 1 grado C, rispettivamente) (p=0.341) hanno sviluppato una

fistola pancreatica post operatoria. L'emorragia post-pancreatectomia (PPH) si è sviluppata rispettivamente in 8/22 (36%) pazienti del gruppo LJI e 2/26 (8%) pazienti del gruppo SJI, rispettivamente ( $p=0.018$ ). Il dosaggio dell'amilasemia eseguito in quinta giornata post operatoria nel liquido di drenaggio ha evidenziato un valore più alto nei pazienti del gruppo LJI rispetto ai pazienti del gruppo SJI [gruppo LJI: 26.5 (6-254) U/l vs gruppo SJI: 7 (0-38) U/l;  $p=0.051$ ]. Non sono state osservate differenze statisticamente significative in termini di ritardato svuotamento gastrico [Delayed Gastric Emptying (DGE)]. L'analisi di regressione logistica ha dimostrato come sia l'anastomosi LJI che DGE risultano essere fattori indipendenti predittivi di POPF (DGE: OR=20.04, CI 95%=1.92-208.83,  $P=0.012$ ; anastomosi LJI: OR=24.58, CI 95%=1.71-354.32,  $P=0.019$ ) e PPH (DGE: 30.5, CI 95%=3.02-308.16,  $P=0.004$ ; anastomosi LJI: OR=12.71, CI 95%=1.23-131.55,  $P=0.033$ ).

CONCLUSIONI: I risultati del presente studio ci consentono di suggerire un approccio basato sul dotto pancreatico o "pancreas duct-oriented": in casi con dotto pancreatico > 3 mm è raccomandata una anastomosi di tipo SJI, viceversa, se il dotto è inferiore ai 3 mm è preferibile confezionare una anastomosi LJI. Concludendo, riteniamo che non sia più valido il vecchio paradigma secondo cui il chirurgo pancreatico debba eseguire ed affinare la tecnica ricostruttiva con cui egli è più confidente. I dati più recenti suggeriscono che ogni chirurgo, bensì, debba possedere nel proprio armamentario le diverse tecniche ricostruttive e, pertanto, adattare alle caratteristiche locali del pancreas affinché si possa raggiungere un approccio "su misura" per ogni paziente.

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