Isolated Roux loop versus conventional pancreaticojejunostomy following pancreaticoduodenectomy

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AIM: *This study aimed to examine the effects of isolated Roux loop (IP) versus conventional pancreaticojejunostomy (CP) techniques on the rate of postoperative pancreatic fistula and its severity.*
MATERIAL AND METHODS: *This study included retrospectively collected data from 132 patients who underwent pancreaticoduodenectomy in a single institute. Collected data were compared between IP and CP groups. Postoperative pancreatic fistula and its grades were defined according to International Study Group on Pancreatic Fistula (ISGPF) definition.*
RESULTS: *A total of 58 patients had IP and 74 patients had CP. Biochemical leak (IP 20.6% versus CP 14.9%, p=0.38) and grade B/C pancreatic fistula (IP 20.6% versus CP 32.4%, p=0.13) rates of both groups were similar. Durations of hospital stay and intensive care unit stay and 30-day mortality rates of the two groups were similar.*
CONCLUSION: *Isolated Roux loop reconstruction following pancreaticoduodenectomy is not associated with a lower rate of pancreatic fistula but may contribute to reducing the severity of pancreatic fistula.*

KEY WORDS: Anastomotic leak, Pancreatic fistula, Pancreaticoduodenectomy, Roux en y anastomosis

Introduction

Pancreaticoduodenectomy is a commonly applied operation for the treatment of benign and malignant diseases of the periampullary region. Although recent progress in surgical techniques and medical care reduced the mortality rate of this operation below 5% in some institutes, the morbidity rate remains as high as 40-50% [1]. Pancreatic anastomotic leaks and fistulas continue to be the main source of morbidity and mortality after pancreaticoduodenectomy. Although there are several recommended techniques to reduce the rate of pancreatic fistulas, optimal pancreatic reconstruction technique is still controversial. One of the recommended techniques for pancreatic reconstruction is isolated Roux loop pancreaticojejunostomy (IP) [2]. With this method, as pancreatic anastomosis is kept away from biliary and gastric anastomoses, activation of the pancreatic enzyme precursors is blocked and in this way, a reduction in the rate and severity of pancreatic fistula and also in the overall morbidity and mortality can be achieved [2, 3].
In this study, it is aimed to examine whether IP is superior to conventional pancreaticojejunostomy (CP) on postoperative outcomes.

Materials and Methods

Data from 200 patients who underwent pancreaticoduodenectomy in a single institute between January 2009 and December 2019 were retrospectively examined. A total of 68 patients with missing data, who underwent total pancreatectomy, had pancreaticogastrostomy as

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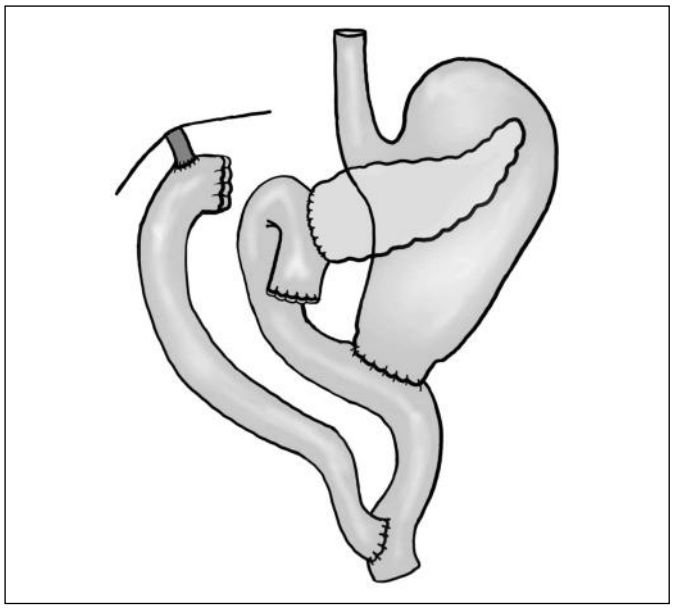

Fig. 1. Isolated Roux loop reconstruction following pancreaticojejunostomy.

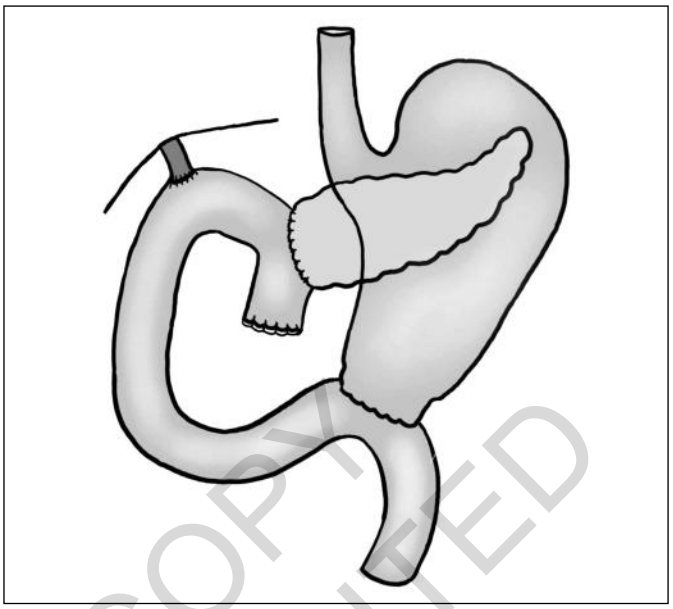

Fig. 2. Conventional single loop reconstruction following pancreaticojejunostomy.

reconstruction method, laparoscopic or emergency surgery were excluded from the study. The remaining 132 patients were included in the study. This study was approved by the Institutional Review Board and Ethics Committee of our institute (no: 2018/16-22) and registered on an international database (clinicaltrials.gov identifier: NCT03671031). The study has been reported in line with the STROCSS criteria [4].

Patients were separated into two groups according to their reconstruction type of pancreatic remnant. Patients with isolated Roux loop reconstruction were defined as the first group and patients with conventional single loop reconstruction as the second group. Reconstruction technique was the surgeon's choice. The technique of pancreaticojejunal anastomosis, choice of pylorus-preserving resection or not and use of pancreatic duct stent were not standard practises and they were performed as the surgeon's choice.

In the isolated Roux loop reconstruction, transected jejunum was anastomosed with the hepatic duct in an end-to-side fashion at first and hepaticojejunostomy was formed. A separate Roux loop was used to form the end-to-side pancreaticojejunostomy by dividing jejunum 50-60 cm distal to this anastomosis. A duodenojejunostomy was added 25-30 cm distal to this anastomosis. Lastly, the hepaticojejunostomy loop was anastomosed to the main loop in an end-to-side fashion (Fig. 1).

In the conventional single loop reconstruction, first an end-to-side pancreaticojejunostomy, and then sequentially an end-to-side hepaticojejunostomy and a gastrojejunostomy or a duodenojejunostomy were formed (Fig. 2).

Preoperative and demographic data, operative data and postoperative data of all patients were analyzed in the study. The primary outcome of the study was to examine the effects of two reconstruction types on the rate of postoperative pancreatic fistula and its severity. Postoperative pancreatic fistula and its grades were defined according to International Study Group on Pancreatic Fistula (ISGPF) definition [5]. According to this definition, the postoperative pancreatic fistula was accepted as clinically relevant drainage of any measurable volume of fluid through operatively placed drains with an amylase level greater than three times the upper limit of institute. The former "grade A pancreatic fistula" was called a "biochemical leak". Pancreatic fistulas were graded as B or C in terms of clinical courses according to ISGPF criteria. Secondary outcomes of the study were operation time, duration of hospital stay, duration of intensive care unit stay and 30-day mortality.

Statistical analyses were performed with SPSS Version 17.0 (SPSS, Inc., Chicago, IL, USA). Continuous variables were analyzed with Mann-Whitney U test and reported as "median (range)". Categorical variables were analyzed using Chi-square or Fisher's exact test by frequency distribution and reported as "frequency (percentage)". A p-value <0.05 was considered statistically significant.

Results

IP was used for 58 (43.9%) patients and CP was used for 74 (56.1%) patients of totally 132 patients in the study. Median age of the study population was 63 (26-95) years. Median age was 61 (36-87) years in the IP group and 66 (26-95) years in the CP group (p=0.01).

Table I - *Preoperative data and patient characteristics*

	All patients (n=132)	IP (n=58)	CP (n=74)	p value
Age (years)*	63 (26-95)	61 (36-87)	66 (26-95)	0.01
Sex, n (%)				0.04
Male	98 (74.2)	38 (65.5)	60 (81.1)	
Female	34 (25.8)	20 (34.5)	14 (18.9)	
Comorbidity, n (%)	81 (61.4)	37 (63.8)	44 (59.5)	0.61
Diabetes mellitus	33 (25.0)	14 (24.1)	19 (25.7)	0.84
Hypertension	36 (27.3)	17 (29.3)	19 (25.7)	0.64
Cardiovascular disease	16 (12.1)	6 (10.3)	10 (13.5)	0.58
Respiratory disease	9 (6.8)	3 (5.2)	6 (8.1)	0.38
Smoking	32 (24.2)	15 (25.9)	17 (23.0)	0.70
ASA score, n (%)				0.24
I	14 (10.6)	4 (6.9)	10 (13.5)	
II	95 (72.0)	41 (70.7)	54 (73.0)	
III	23 (17.4)	13 (22.4)	10 (13.5)	
Laboratory values*				
WBC (109/L)	7.5 (3.8-27.4)	7.2 (4.2-17.9)	7.9 (3.8-27.4)	0.16
Hemoglobin (g/dL)	13.2 (8.2-17.3)	13.4 (8.2-16.7)	12.8 (8.3-17.3)	0.25
Creatinine (mg/dL)	0.7 (0.2-2.7)	0.7 (0.2-2.7)	0.7 (0.4-1.3)	0.72
Albumin (g/dL)	3.5 (1.3-5.1)	3.6 (1.7-4.4)	3.2 (1.3-5.1)	0.03
Bilirubin (mg/dL)	1.6 (0.2-35.3)	1.1 (0.2-16.1)	1.9 (0.2-35.3)	0.28
Preoperative biliary drainage, n (%)	72 (54.5)	33 (56.9)	39 (52.7)	0.63

* values are median (range). p<0.05, statistically significant. ASA:American Society of Anesthesiologists physical status classification, CP: conventional pancreaticojejunostomy, IP: isolated Roux loop pancreaticojejunostomy, WBC: white blood cell.

Table II - *Operative data*

	All patients (n=132)	IP (n=58)	CP (n=74)	p value
Pathology (n=127), n (%)				0.52
Pancreas cancer	53 (41.7)	21 (37.5)	32 (45.1)	
Ampulla of Vater cancer	35 (27.6)	14 (25.0)	21 (29.6)	
Duodenum cancer	4 (3.1)	1 (1.8)	3 (4.2)	
Distal cholangiocellular cancer	4 (3.1)	1 (1.8)	3 (4.2)	
Neuroendocrine tumour	8 (6.3)	4 (7.1)	4 (5.6)	
Pancreas adenosqu. cancer	1 (0.8)	1 (1.8)	0 (0.0)	
Ampulla of Vater adenosqu. ca.	1 (0.8)	1 (1.8)	0 (0.0)	
IPMN	1 (0.8)	1 (1.8)	0 (0.0)	
Gastric cancer	1 (0.8)	0 (0.0)	1 (1.4)	
Recurrent colon cancer	2 (1.6)	1 (1.8)	1 (1.4)	
Lymphoma	1 (0.8)	1 (1.8)	0 (0.0)	
Benign disease	16 (12.6)	10 (17.9)	6 (8.5)	
Tumour diameter (cm)*	3 (0.1-14.0)	3 (0.1-9)	3.3 (1-14)	0.30
Intraoperative add. intervention, n (%)	23 (17.4)	10 (17.2)	13 (17.6)	0.96
Additional organ resection	13 (9.8)	4 (6.9)	9 (12.2)	0.31
Portal vein/smv reconstruction	11 (8.3)	6 (10.3)	5 (6.8)	0.33
Operation time (minutes)*	480 (210-900)	420 (240-660)	530 (210-900)	<0.001

* values are median (range). p<0.05, statistically significant. add.: additional, adenosqu. ca.: adenosquamous cancer, CP: conventional pancreaticojejunostomy, IP: isolated Roux loop pancreaticojejunostomy, IPMN: intraductal papillary mucinous neoplasia, smv: superior mesenteric vein.

The rate of male patients was 65.5% in the IP group and 81.1% in the CP group (p=0.04). Albumin level was 3.6 (1.7-4.4) g/dL in the IP group and 3.2 (1.3-5.1) g/dL in the CP group (p=0.03). There were no differences between the two groups in terms of other preoperative data (Table I).

There were no significant differences between the two groups in terms of histopathological results and tumour

Table III - *Postoperative data*

	All patients (n=132)	IP (n=58)	CP (n=74)	p value
Hospital stay (days)*	16 (3-115)	14.5 (3-94)	16 (6-115)	0.09
ICU stay (days)*	3 (1-82)	3.5 (1-54)	3 (1-82)	0.29
Complications, n (%)	81 (61.4)	34 (58.6)	47 (63.5)	0.56
Biochemical leak (grade A)	23 (17.4)	12 (20.6)	11 (14.9)	0.38
Pancreatic fistula (grade B/C)	36 (27.2)	12 (20.6)	24 (32.4)	0.13
B	18 (13.6)	6 (10.3)	12 (16.2)	1.00
C	18 (13.6)	6 (10.3)	12 (16.2)	
Hemorrhage	18 (13.6)	8 (13.8)	10 (13.5)	0.96
Intraabdominal Abscess	22 (16.7)	9 (15.5)	13 (17.6)	0.75
Pneumonia	17 (12.9)	5 (8.6)	12 (16.2)	0.19
Re-exploration, n (%)	21 (15.9)	8 (13.8)	13 (17.6)	0.55
30-day mortality, n (%)	18 (13.6)	9 (15.5)	9 (12.2)	0.57

*values are median (range). p<0.05, statistically significant. CP: conventional pancreaticojejunostomy, ICU: intensive care unit, IP: isolated Roux loop pancreaticojejunostomy.

diameter (p=0.52 and p=0.30, respectively). As benign disease, there were ten patients (chronic inflammation, n=5, pseudocyst, n=1, hyperplastic polyp of the ampulla of Vater, n=1, xanthogranulomatous inflammation, n=1, seromucinous cystic neoplasm, n=1 and villous adenoma, n=1) in the IP group and six patients (chronic inflammation, n=4, chronic pancreatitis, n=1 and adenoma of ampulla of Vater, n=1) in the CP group. There was no significant difference between the two groups in terms of intraoperative additional intervention (p=0.96). Operation time was shorter in IP group (IP 420 (240-660) minutes versus CP 530 (210-900) minutes, p<0.001) (Table II).

Complications were developed in 34 (58.6%) patients in IP group and in 47 (63.5%) patients in other group (p=0.56). Biochemical leak (IP 20.6% versus CP 14.9%, p=0.38) and grade B/C pancreatic fistula (IP 20.6% versus CP 32.4%, p=0.13) rates of both groups were similar. Grade B and C fistula rates of IP (10.3% and 10.3%) and CP (16.2% and 16.2%) groups were same. There was no significant difference between the two groups in terms of other complications. Re-exploration was needed in eight (13.8%) patients in the IP group and 13 (17.6) patients in the CP group (p=0.55). 30-day mortality was observed in nine (15.5%) patients in the IP group and nine (12.2%) patients in the other group (p=0.57). There was no significant difference between the two groups in terms of duration of hospital stay and intensive care unit stay (p=0.09 and p=0.29, respectively) (Table III).

Discussion

Pancreatic fistula is still the most important surgical problem encountered after pancreaticoduodenectomy. Various treatment modifications have been tried to minimize fistula formation [6]. Pancreatic fistula rate and its severity were tried to be reduced with various pancreaticojejunostomy techniques [7], performing pancreaticogastrostomy [8], stenting the pancreatic duct [9], using postoperative octreotide acetate [10], avoiding closed suction drains [11] and preserving vasculature of pancreatic remnant [12]. Isolated Roux loop pancreaticojejunostomy technique was first recommended by Machado et al [2] in 1976. With the isolation of pancreatic anastomosis from biliary anastomosis, inactive pancreatic enzyme precursors are prevented from being activated and hopefully minimizing the rate of pancreatic fistula and surrounding tissue damage, the severity of pancreatic fistula is thought to be reduced.

Roux-en-Y reconstruction can be performed to create pancreatic anastomosis on a separate loop [2, 3, 13-15] or pancreatic and biliary anastomoses together with on a separate loop [16]. In this study, as a different approach, the most proximal jejunal loop was used to form hepaticojejunostomy and then this loop was anastomosed to the main loop. During pancreaticoduodenectomy dissection, there can be disruptions to the blood supply of the proximal jejunal loop. That's why this different approach was preferred so as not to use that proximal jejunal loop for pancreatic anastomosis.

Machado et al [2] reported that two patients developed pancreatic fistula following isolated Roux loop reconstruction and there was no mortality in their 15-patient series of pancreaticoduodenectomy. In the study of Funovics et al [13] where they compared four methods of reconstruction following pancreaticoduodenectomy, the best results were obtained with Roux-en-Y reconstruction. Several series with isolated Roux loop pancreaticojejunostomy reported no pancreatic fistula [14–18]. Reliability of the results of these studies is weak. Because they have limited number of cases and do not have appropriate control groups. In one study, pancreatic fistula rate was higher in the Roux-en-Y reconstruction group and it was pointed out that there would be bias towards choosing

Roux-en-Y reconstruction on high-risk patients for anastomosis leak [6]. In two randomized controlled trials [19, 20] and three meta-analyses [21-23] that compare isolated Roux loop and conventional reconstruction, there was no difference in terms of pancreatic fistula rates between two groups. In our study, biochemical leak (grade A) and clinically relevant pancreatic fistula (grade B/C) rates of two separate techniques were also similar. However, biochemical leak rate in isolated Roux loop pancreaticojejunostomy group and clinically relevant pancreatic fistula rate in the other group tended to be higher. Having a more severe fistula is more influential on the need of additional percutaneous or surgical intervention, development of other complications, duration of hospital stay, treatment and medical care costs, the time between surgery and adjuvant oncologic therapy and mortality rate than the overall rate of pancreatic fistula. For that reason, the decrease on pancreatic fistula grade with isolated Roux loop pancreaticojejunostomy may be valuable.

In this study, the duration of hospital stay and intensive care unit stay were similar in the two groups. In the literature, one study [24] reported that duration of hospital stay was shorter with isolated Roux loop pancreaticojejunostomy, however, there was no difference between the two groups in the other studies [19-23, 25-27]. Relatively higher rate of clinically relevant pancreatic fistula in the CP group did not affect these durations of stay and also early mortality rate.

It was observed in this study that overall rate of clinically relevant pancreatic fistula (27.3%) and mortality (13.6%) were higher compared to other studies in the literature. In seven studies in which postoperative pancreatic fistula were determined according to ISGPF criteria, overall rates of pancreatic fistula were 10-34% and mortality rates were 0-5% [19, 20, 22, 24, 25, 28, 29]. In three of these seven studies that also examining types of pancreatic fistula, rates of clinically relevant pancreatic fistula were 7-13.9% [19, 20, 22]. Age >65 years, male sex, coronary artery disease, high body mass index, jaundice and malnutrition as patient-related factors, soft pancreatic texture, pancreatic duct diameter ≤3 mm and fatty pancreas as pancreas-related factors, longer operation time, excess blood loss and blood transfusion as intraoperative factors were identified as the main risk factors on pancreatic fistula formation [28, 30, 31]. Relatively high rate of pancreatic fistula may be a result of the high rate of male sex and longer operation time in this study. Relatively high rate of mortality may be a result of high rate of grade C pancreatic fistula in addition to these two factors.

Isolated Roux loop pancreaticojejunostomy may have a disadvantage of prolongation of the operation time due to the need for an additional anastomosis. Many studies in the literature also support this idea [6, 20-23, 25-27]. However, operation time was longer in the conventional pancreaticojejunostomy group in this study. Higher rate of additional organ resection in conventional pancreaticojejunostomy group may have an effect on the operation time.

This study has several limitations. It is retrospective and non-randomized. Feature of pancreatic tissue, pancreatic duct diameter, amount of overall blood loss and blood product replacement which are important in the development of pancreatic leak were not able to be examined in this study.

Conclusion

In conclusion, isolated Roux lovop reconstruction following pancreaticoduodenectomy is not associated with a lower rate of pancreatic fistula but may contribute to reducing the severity of pancreatic fistula. Further prospective randomized studies are needed to confirm these results.

Riassunto

INTRODUZIONE: Questo studio mirava a esaminare gli effetti delle tecniche isolata di Roux anello (IP) rispetto alle tradizionali tecniche pancreatodigiunostomia (CP) sulla frequenza della fistola pancreatica postoperatoria e sulla sua gravità.

MATERIALI E METODI: Questo studio ha incluso dati raccolti retrospettivamente da 132 pazienti sottoposti a pancreaticoduodenectomia in un singolo istituto. I dati raccolti sono stati confrontati tra i gruppi IP e CP. La fistola pancreatica postoperatoria e i suoi gradi sono stati definiti secondo la definizione dell International Study Group on Pancreatic Fistula (ISGPF).

RISULTATI: Un totale di 58 pazienti avevano IP e 74 pazienti avevano CP. Le percentuali di perdite biochimiche (IP 20.6% contro CP 14.9%, p=0.38) e fistole pancreatiche di grado B/C (IP 20.6% contro CP 32.4%, p=0.13) di entrambi i gruppi erano simili. La durata della degenza ospedaliera e della terapia intensiva e i tassi di mortalità a 30 giorni dei due gruppi erano simili.

CONCLUSIONI: La ricostruzione isolata di Roux anello in seguito a pancreaticoduodenectomia non è associata a un tasso inferiore di fistola pancreatica ma può contribuire a ridurre la gravità della fistola pancreatica.

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