ORIGINAL ARTICLE

Stented Pancreatico-duodenectomy: Does it lead to decreased pancreatic fistula rates? A prospective randomized study

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Abstract

Objective: To compare clinically relevant pancreatic fistula rates in patients with stented versus non-stented pancreatico-jejunostomies.

Methods: The randomised comparative clinical trial was conducted at Civil Hospital, Karachi, from September 2009 to August 2015, and comprised patients presenting to the Surgical Unit 4 with a diagnosis of resectable periampullary carcinoma, carcinoma of head of pancreas, duodenal carcinoma involving the second part, and distal cholangiocarcinomas. Pancreatic fistula or leakage was defined as amylase-rich fluid lasting over 5 days, collected from the peripancreatic drains on day 1, 3 and 7 postoperatively, and the rate of clinically relevant fistulas was taken as primary study endpoint.

Results: There were 102 patients with a male to female ratio of 2.4:1. The overall mean age was 53.16±12.11 years (range: 30-80 years). Of the total, 53(51.9%) patients had pancreatic duct stent and 49(48%) did not. Clinically relevant pancreatic leak was seen in 13(12.7%) patients of whom 8(61.5%) were stented (p=0.46), 9(69.2%) patients had soft pancreatic texture (p=0.54) and 7(53.8%) had pancreatic duct ≤3mm (p=0.11).

Conclusion: Pancreatic fistula rates between stented and non-stented anastomosis did not show any significant difference.

Keywords: Pancreatico-duodenectomy, Stented and non-stented pancreatico-duodenectomy, Postoperative pancreatic fistula rates, Pancreatic-anastomotic failure, Pancreatic fistula rate, Whipples procedure, Pancreatico-jejunostomy. (JPMA 68: 348; 2018)

Introduction

Pancreatico-duodenectomy (Whipples procedure) is a gold standard treatment for patients with resectable carcinoma head of pancreas, lower common bile duct (CBD) and duodenal carcinomas.[1-3] It is considered one of the most demanding procedures in surgery associated with increased rates of mortality and morbidity. One of the much dreaded complications of this procedure is pancreatic anastomotic leak leading to the pancreatic fistula formation in up to 20%.[4,5] Various factors have been implicated as the underlying cause of pancreatic anastomotic failure and a lot of modifications in the technique of anastomosis have been proposed. Stenting the pancreaticoenteric anastomosis has been postulated as reducing the pancreatic anastomotic leak and fistula rates.[6] The current study was planned to compare clinically relevant pancreatic fistula rates in stented versus non-stented pancreatico-jejunostomies (PJ). It was hypothesised that stenting of pancreatic duct decreases the rate of pancreatic fistula after pancreatico-duodenectomy.

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Patients and Methods

The randomised comparative clinical trial was conducted at Civil Hospital, Karachi, from September 2009 to August 2015.

After getting approval from the institutional review board of Dow University of Health Sciences (DUHS), Karachi, the sample size was calculated to detect a 23% difference in the pancreatic fistula rates between control and stented groups with a significance level of 0.05 and statistical power of 80%.[7]

Patients presenting to the Surgical Unit 4 of the hospital with a diagnosis of resectable periampullary carcinoma, carcinoma of head of pancreas, duodenal carcinoma involving the second part, and distal cholangiocarcinomas were included. Those having Whipples procedure for benign disease or trauma were excluded. Informed consent was obtained from all the subjects in the study.

Randomisation was done via balloting. An equal number of cards containing stented and non-stented procedure were put in a box and the cards were taken out at the time of surgery. Data was filled in a specially-designed proforma that included all the risk factors for pancreatic fistula formation as well as the clinical and demographic

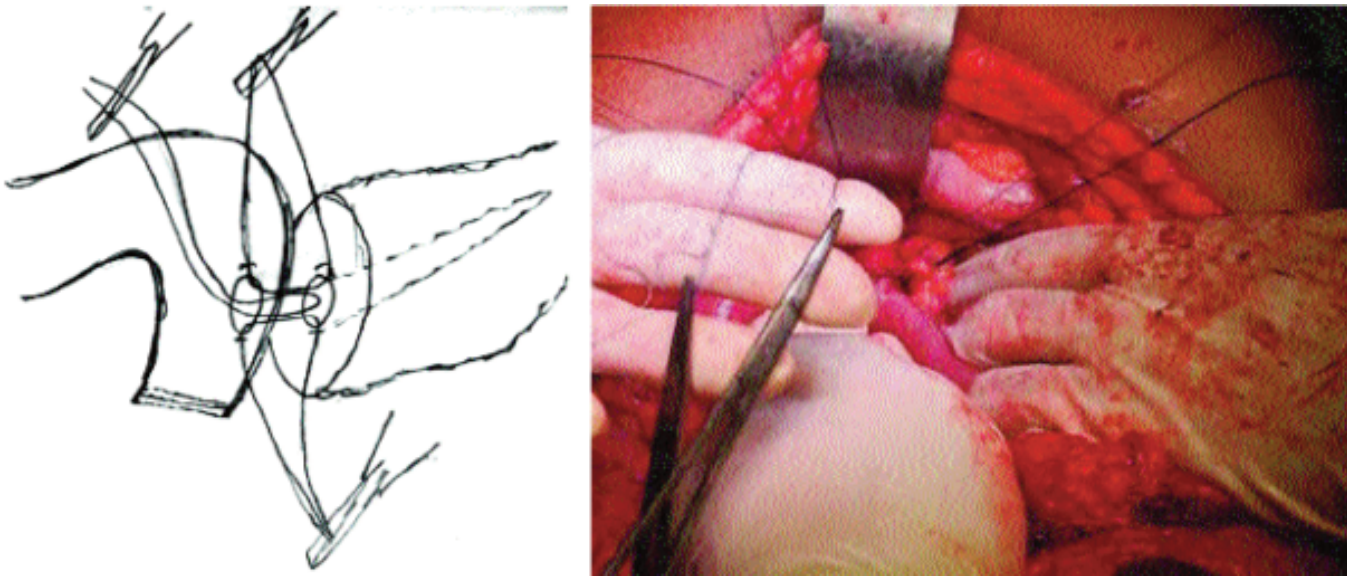

Figure-1: Technique of pancreatico-jejunostomy.

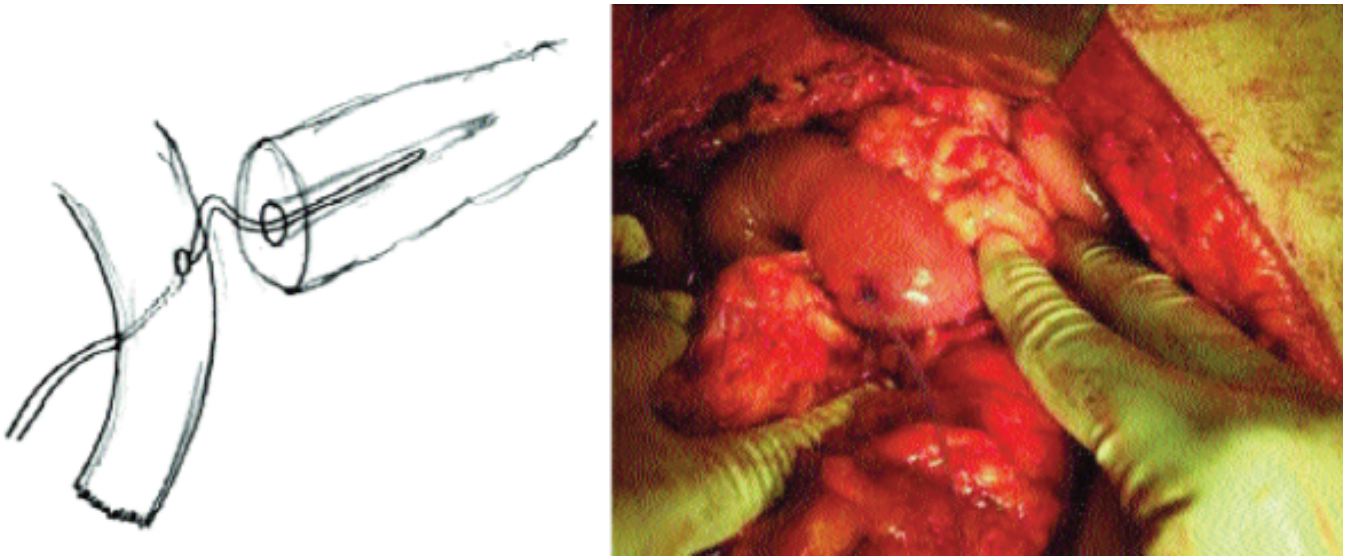

Figure-2: Technique of stented pancreatico-jejunostomy.

details of surgical procedure, histopathological diagnosis, postoperative details, including mortality and complications. A researcher not involved in the care of the patient collected data prospectively. All the procedures were performed by the same team.

The procedure performed was pancreatico-duodenectomy, the classical Whipples procedure. A single-layer pancreatico-jejunostomy (PJ) was constructed by anastomosing the jejunal limb with the pancreatic duct via mucosa to mucosa co-optation (Figure-1). In case of stented anastomosis, silastic feeding tube of appropriate size was inserted across the anastomosis with the distal limb brought out through the jejunal loop (Figure-2). Perianastomotic redivac or corrugated drain was put in all the patients. The operating surgeon was required to fill the surgical details in the proforma at the time of surgery, while the researcher collected the required data of peripancreatic drain and serum amylase levels. This fluid was collected from the peripancreatic drains on post-operative days 1, 3, 7 and 10. Pancreatic fistula or leakage was defined as

raised amylase level in drain fluid (amylase concentration >3 times the upper limit of normal serum amylase level). If this lasted beyond 5 days, it was taken as the primary endpoint. Clinically relevant pancreatic fistula was defined as International Study Group: Postoperative Pancreatic Fistula (ISGPF) Grade B and C fistulas[7] i.e. patients presenting with signs of infection, readmission, sepsis, re-operation and death related to fistula. Secondary endpoints included morbidity, in-hospital mortality rate and length of hospital stay. Morbidity was classified according to the Clavien Dindo scale.[8] Only class 2 and beyond were taken as the morbidity except for wound infection where grade 3 and beyond was considered morbidity. Statistical data was analysed using SPSS 16, and p<0.05 was considered significant.

Results

There were 102 patients with a male-to-female ratio of 2.4:1. Mean age was 52.68±11.6 years (range: 30-80 years). Overall, 97(95.1%) patients had jaundice at presentation. Of them, 93(91.2%) patients had endoscopic retrograde cholangiopancreatography (ERCP) and stenting for biliary decompression prior to surgery. Besides, 15(14.7%) patients tested positive for hepatitis, while 24(23.5%) were diabetics. Of the total, 53(51.9%) patients were included in the stented PJ arm and 49(48.1%) patients in the non-stented arm. Pancreatic duct was <3mm in 33(32.41%) patients, whereas 69(67.7%) had duct size >3mm. Soft pancreatic texture was seen perioperatively in 59(58%) patients compared to 43(42%) patients with firm to hard texture. Clinically significant pancreatic leak was seen in 13(12.7%) (Table-1).

Overall, 13(12.7%) patients developed pancreatic leak; 8(61.5%) stented patients and 5(38.5%) non-stented (p=0.46) (Table-2).

Table-1: Demographics and characteristics.

Characteristics	
Total number	102
Males (M)	72
Females (F)	30
M:F	2.4:1
Age in years range (mean ± SD)	30-80 (53.16±12.11)
Pancreatic Duct stent	53 (51.9%)
Clinically significant Pancreatic Duct leak	13 (12.7%)
Pancreatic texture soft:hard	59(57.84%):43(42.16%)
Pancreatic duct ≤3:>3	33(32.35%):69(67.65%)
Hospital stay in days	3-50 (19.79±10.18)
Morbidity	24 (23.4%)
Mortality	7 (6.9%)

Table-2: Stented versus non-stented groups.

Variables	Stented (n=53)	Non-stented (n=49)	P-value
Age (years)	54.25 ± 11.7	51.98 ± 12.5	0.74
Male:Female	41:12 (3.4:1)	31:18 (1.72:1)	0.12
Pancreatic texture - Soft : Hard	34:19	25:24	0.18
Pancreatic duct ≤ 3mm	24(45.2%)	9 (18.36%)	0.004
Pancreatic duct >3mm	29 (54.17%)	40 (81.63%)	0.004
Pancreatic leak (PL) n=36	20 (37.73%)	16 (32.65%)	0.59
Significant PL n=13 (ISGPF grade B,C)	8 (15.09%)	5 (10.02%)	0.46
Leaking Gastrojejunostomy	5 (9.4%)	2 (4%)	0.26
Bleeding Gastrojejunostomy	4 (7.5%)	2 (4%)	0.46
Morbidity	17 (32.08)	7 (14.29)	0.03
Mortality	3 (5.6%)	4 (8.16)	0.70
Hospital Stay (days)	22.16 ± 11.18	17.12 ± 8.27	0.09

Table-3: Variables in patients with significant pancreatic leak.

	Stented (n=8)	Non-stented (n=5)	p-value
Age (years)	53.50 ± 8.6	57.60 ± 12	0.49
Male:Female	8:0	1:4	0.002
Hospital stay (days)	38.50 ± 8.9	31.80 ± 2	0.0001
Pancreatic texture Soft	6	3	0.57
Duct Size ≤ 3mm	4	3	0.725
Duct Size >3mm	4	2	0.725
Secondary surgery	4	4	0.28
Leaking Gastrojejunostomy	0	2	
Leaking PJ	0	2	
Bleeding	0	0	
Mortality	0	0	

PJ: Pancreatico-jejunostomy.

There were more males in the leak stented group compared to females (p=0.002). Nine (69.2%) patients in clinically significant pancreatic fistula group had soft pancreatic texture and 7(53.8%) had duct size <3mm (Table-3).

Multivariate analysis showed that pancreatic duct size, texture or re-surgery rates did not have any impact on the fistula rates (Table 4). Mean overall Hospital stay was 19.79 ± 10.81 days (3-50). Mean hospital stay in patients with pancreatic stent was 22.16 days ±11.8 days and without stent it was 17.12 ± 8.27 days. The hospital stay in patients with pancreatic duct leak was 38.50 ± 8.9 days in stented vs. 31.80 ± 2 days in non-stented group (p=.0001).

Morbidity was seen 24(23.4%) patients. There were 7(6.9%) in-hospitalor30-day mortalitles. No mortality was seen in clinically significant pancreatic fistula group.

Table-4: Logistic regression analysis comparing significant pancreatic leak in stented and non-stented groups.

	OR	95% CI	p value
Stented vs non stented	1.56	0.47-5.15	0.462
	aOR	95% CI	p value
	0.09	0.01-1.35	0.083

OR: Odds ratio
aOR: Adjusted odds ratio
CI: Confidence interval.

Discussion

The work of Whipples et al proved to be a breakthrough in the treatment of pancreatic and duodenal cancers.[1] This surgery requires significant technical skills. It is associated with high complications rates and several modifications in the procedure have been postulated[9,10] looking at the patient, surgeon, technique-related and other factors leading to complications.

Postoperative pancreatic fistula is a major complication and it is secondary to anastomotic leakage, the rate varies from 0% to 25%.[11,12] Clinically significant pancreatic fistula classified according to the ISGPF grade B and C was 12.7% in our study, which is within the universally accepted rates amongst the high volume centres. Anastomotic leakage, pancreatic fistula or abscess is a septic complication that results in late postoperative haemorrhage which is yet another catastrophe.[13-15] Several factors have been implicated as affecting fistula formation which includes the pancreatic duct and texture, surgeons' expertise and technique of anastomosis.[16] The standard Pancreatico-jejunostomy technique which is end-to-side, duct-to-mucosa interrupted anastomosis was done in our study. All the procedures were done by the same team of experienced surgeons thereby removing the expertise bias from the study. Variations in techniques of anastomosis have also been proposed to reduce the leakage rates, such as invaginated pancreaticojejunal suture line, duct-to-mucosa anastomosis, ligation of pancreatic duct and pancreaticogastrostomy. Despite all this, controversy still persists regarding the best technique suitable for any particular case.

Other factors like gender, age, bilirubin levels, operative time, need for blood transfusion, texture of the pancreas (soft or hard), pancreatic duct size and prophylactic sandostatin have also been implicated as affecting the pancreatic leak rates. We had significantly more pancreatic leak in male patients but then we had more males in our study group compared to females. None of the patients had prophylactic sandostatin in our study. According to Yeo et al,[17] pancreatic texture and pancreatic leakage rates seems to be related. If the pancreas is fibrotic, as in patients with chronic pancreatitis, the pancreaticojejunal anastomosis is more secure. However, if pancreas has a soft parenchyma the anastomosis will be prone to leak. We did not find any significant association between the pancreatic texture and pancreatic duct size in patients with clinically significant pancreatic fistula. In addition the presence of pancreatic duct stent did not influence the fistula rates.

Our study was designed to look at pancreatic leak rates in patients with stented or non-stented PJ. Recommendations in favour of stent state that it facilitates the drainage of the pancreatic duct as well as preventing the secretion from coming in contact with the anastomosis. The accuracy of placement of sutures in enhanced, safeguarding from injury and subsequent leakage and its complications.[18,7] Opponents argue that the accidental removal of the pancreatic drain or its blockage or obstruction increases the incidence of pancreatic leakage. Several studies have shown the overall pancreatic fistula rates to be similar in patients with a stented and non-stented anastomotic groups.[19,20] However meta-analysis published by Hong et al and Motoi F et al has shown that the pancreatic stenting can decrease the rate of pancreatic fistula in comparison with non-stented anastomosis. Also the complication rates and hospital stay is markedly decreased.[6,9] In contrast the Meta analysis by Xiong JJ et al[21] which include five randomised clinical trials (RCTs) and 11 non-randomized observational clinical studies (OCS) has not shown any benefit of stented over non-stented anastomosis. They concluded that pancreatic stenting did not result in decreased postoperative pancreatic fistula rates. Our study also did not find any significant difference in terms of postoperative pancreatic fistula rates amongst the stented and non-stented anastomosis. Contrary to other studies[7,15] hospital stay was significantly increased in the stented group.

There might be an element of bias in the results as the majority of patients in stented arm had duct size $\leq$ 3mm. However logistic regression analysis between the stented versus non-stented group did not show any significance.

Limitation: Single-Centre study is a limitation of the current study.

Conclusion

There was no statistically significant difference in pancreatic fistula rates amongst the stented and non-stented arms. The rate of postoperative pancreatic fistula was 12.7% which was comparable to

international literature.

Disclaimer: This paper was presented at the International Congress of Pancreatic Disorders, Chicago, United States of America in 2016.

Conflict of Interest: None.

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