ORIGINAL PAPER

Anatomy at Pancreatic Transection Point in Predicts Occurrence of Postoperative Pancreatic Fistula

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ABSTRACT

Introduction Postoperative pancreatic fistula is a dreaded complication following pancreatic head resections. There are many variables which predict occurrence of pancreatic fistula we analysed the anatomical factors at the pancreatic transection to predict occurrence of pancreatic fistula. **Materials and methods** It is a prospective observational study done from 2014 July to 2015 December. Eighty patients were included, intraoperatively we measured the anteroposterior thickness, cranio caudal thickness and thickness anterior, posterior, cranial and caudal to duct. We correlated these anatomical factors with postoperative complications. **Results** POPF was seen in 19 patients (23.75%) of which clinically significant fistula was seen in 5 patients (6.25%) and biochemical fistula is seen in 14 patients (17.5%). As the parenchymal thickness cranial to duct increased the chance of POPF increased (mean ± SD-15.26 ± 3.03mm, p=0.014). As the thickness anterior to duct increases (7.18 ± 1.50mm, p=0.023) and mean thickness posterior to duct decreases (5.34 ± 3.32mm, p=0.036) chance of POPF increased. Clinically relevant fistula was significantly seen to be related with thickness anterior to duct, at a thickness >6.5mm sensitivity of occurrence of fistula 68.4% and specificity was 74%. **Conclusions** At the transection point when the thickness anterior to duct increases chances of clinically relevant fistula increases. As the thickness anterior to duct increases duct would be positioned more posteriorly creating difficulty while placing sutures.

INTRODUCTION

Anastomotic leak complicates in 0-30% of pancreatico-intestinal anastomosis following PD(pancreático-duodenectomy)[1–3]. Anastomotic leak initiates subsequent complications like intraabdominal abscess, sepsis, erosion into surrounding vessels requiring further intervention [4]. Mortality was increased when a reoperation was required, a biliary-enteric leak occurred, or an intra-abdominal abscess developed [4]. In a Japanese survey of 3109 patients mortality was 13% in patients with anastomotic leak [2]. With the advancement in surgical techniques and critical care management, mortality was decreased but morbidity is high even in high volume centers [5]. Risk factors include preoperative patient related factors, gland related (texture, size of the main pancreatic duct diameter), intra operative factors. Hard texture, pancreatic fibrosis, diameter of the pancreatic duct >3mm, good anastomotic technique were associated with decreased incidence of pancreatic fistula [5–8].

Anatomical features vary greatly at the transection point among the, in the present study we analyzed the anatomy at the transection point in relation to clinically significant pancreatic fistula.

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Materials and Methods

From July 2014 to December 2015 eighty consecutive patients undergoing PD (Pancreatico duodenectomy) were prospectively enrolled in department of surgery at Post graduate institute of medical education and research Chandigarh. Patients who refused consent and underwent duodenum preserving pancreatic head resections, central pancreatectomy, distal pancreatectomy were excluded from the study. Patients were evaluated for demographic, biochemical and radiological parameters. Biliary drainage (endoscopic / percutaneous) was done either in the presence of cholangitis, nutritionally depleted state and if serum bilirubin >15 mg/dl. All patients underwent PD with standard lymphadenectomy, single loop reconstruction using child's method.

Intra operative assessment

During the procedure after transection of the pancreas, pancreatic stump was evaluated by measuring the duct diameter using a catheter which snuggly fits in to the pancreatic duct. Thickness cranially, caudally,

posteriorly and anteriorly by using vernier calipers in millimeters, the relative location of the duct antero-posteriorly and craniocaudally were also noted. In our study we defined eccentrically placed and posteriorly placed duct. Eccentrically placed duct was defined as parenchymal thickness cranial to duct >2/3rd of the cranio-caudal thickness **(Figure 1).** Posteriorly placed duct was defined when the duct was placed more than two third of the thickness from the anterior margin of the total anteroposterior thickness Figure 1. Dilated duct was defined as main pancreatic duct diameter >3mm and nondilated duct as main pancreatic duct diameter <3mm. The pancreaticojejunal anastomosis was completed using duct to mucosa technique. Post operatively all the patients were monitored for POPF (postoperative pancreatic fistula) as per ISGPF classification [7], along with POPF other complications were also noted.

Statistical analysis

Continuous parametric data was expressed as mean ± standard deviation; categorical data was expressed in numbers and percentages. To compare two independent groups for a continuous parametric variable an independent t-test was done and Mann-Whitney U test for non-parametric variable. Analysis of variance (ANOVA) was applied to compare more than two independent groups of a continuous parametric variable. To compare two independent groups of categorical variable, the chi-square test was applied. Receiver Operator Curve analysis was performed and sensitivity and specificity were assessed based on Youden's method. P value < 0.05 was taken as statistical significance for all the analyses.

RESULTS

Preoperative characteristics

A total of 80 patients were included in the study, of which 28 were females and 52 were males, mean age was 52.9 ± 11.1 years. Preoperative tissue diagnosis was present in 33(41.25%) patients with most common etiology being adenocarcinoma seen in 22(66%). Other demographic and operative details were given in the **(Table 1).**

Intra operatively parenchymal thickness at the transection point in relation to the duct was noted, 33(41.25%) patients had dilated ducts and 47(58.75%) patients had non dilated duct, eccentrically placed ducts were seen in 21(26.3%) and posteriorly placed ducts were seen in 39(48.8%) patients. In patients with dilated ducts, ducts were posteriorly placed in 23(28.75%) and ducts were eccentrically placed in 13(16.25%). In patients with non-dilated, ducts were posteriorly placed in 16(20%) and eccentrically placed in 8(10%) patients. It was observed that duct was seen more posteriorly when it was dilated (p=0.008). Mean pancreatic diameter was 3.53 ± 1.55mm, texture of the pancreas was soft in 24(30%) patients, firm to hard in consistency in 56(70%) patients. Mean thickness anterior to duct, posterior to duct, cranial to duct, caudal to duct were 6.03 ± 2 .54 mm, 4.46 ± 2.61mm, 13.58 ± 3.46mm, 12.5 ± 4.24mm respectively. Mean anteroposterior and craniocaudal thickness were 14.08 ± 3.41mm, 29.63 ± 5.36mm respectively.

Parenchymal thickness in relation to dilated ducts

In patients with dilated ducts mean anteroposterior, craniocaudal parenchymal thickness were 14.24 ± 3.37mm, 29.78 ± 5.55mm respectively. Mean thickness cranial to duct, caudal to duct, anterior to duct, posterior to duct were 13.47 ± 3.49mm, 11.41 ± 3.76mm, 5.14 ± 2.44mm, 3.74 ± 2.18mm respectively. Mean pancreatic duct diameter in dilated duct group was 4.97 ± 1.31mm.

Parenchymal thickness in relation to non-dilated ducts

In patients with non-dilated ducts mean anteroposterior and craniocaudal thickness were 14.02 ± 2.37, 29.5 ± 5.29mm respectively. Mean thickness anterior, posterior, cranial and caudal to duct were 6.66 ± 2.44mm, 4.97 ± 2.72mm, 13.66 ± 3.46mm and 13.36 ± 4.41mm respectively.

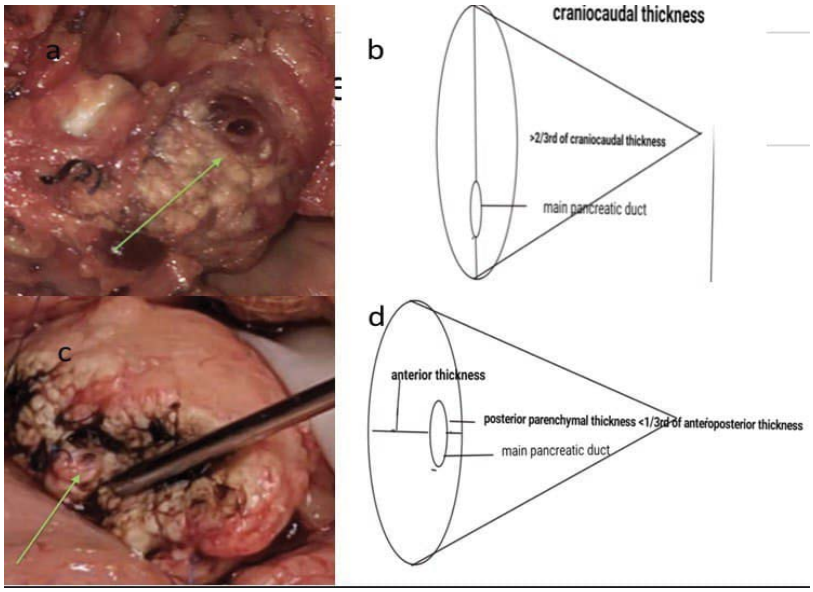

Figure 1: a, b showing eccentrically placed ducts. c, d showing posteriorly placed ducts.

Table 1: Baseline characteristics between two groups.

Variables	Entire cohort(n=80)	No Fistula(n= 61)	Fistula(n=19)	p value
Age in years	52.9 ± 11.1 years(20-75 years)	54.38 ± 10.43	48.37 ± 12.11	0.067
Sex Male Female	 52 28	 40 21	 12 7	 0.89
Symptoms Jaundice Abdominal pain Jaundice and abdominal pain New onset diabetes mellitus	 49(62%) 59(73.75%) 33(41.25%) 16(20%)	 39(48%) 53(65%) 27(33%) 12(14%)	 10(12%) 6(7%) 6(7%) 4(5%)	 0.79
Preoperative biliary drainage Endoscopic stenting Percutaneous drainage	26(27.75%) 22(22.75%) 4(5%)	18(22.5%)	8(42.1%)	0.561
Histological diagnosis Adenocarcinoma Malignancy could not be ruled out Neuro endocrine tumour Adenoma with high grade dysplasia Chronic pancreatitis with high grade dysplasia Tubulovillous adenoma Duodenal adenocarcinoma	80 55(68%) 3(3.8%) 10(12.5%) 2(2.5%) 5(6.25%) 1(1.25%) 4(3%)	61(76.2%) 45(65%) 2(2%) 7(10%) 1(1%) 4(5%) 0 2(2%)	19(14%) 10(52%) 1(5%) 3(15%) 1(5%) 1(5%) 1(5%) 2(10%)	 0.98
Operative parameters Blood loss in ml Operative time in hours Vascular resections Portal vein resection and end to end anastomosis Sleeve resection Replaced right hepatic artery reconstruction	303 ± 143ml 4.82 ± 0.77hrs 7(8.7%) 4(57%) 2(28%) 1(14%)	307 ± 145ml 4.77 ± 0.68 4(57%) 2(50%) 1(25%) 1(25%)	289 ± 141ml 300 ± 60 3(43%) 2(50%) 1(25%) 0	 0.635 0.360 0.781
Post-operative complications Delayed gastric emptying Grade A Grade B Grade C Post pancreatectomy hemorrhage Surgical site infections Organ space infections Re exploration Radiological intervention Acute pancreatitis Mortality	 48(60%) 23(28.75%) 20(25%) 5(6.25%) 5(6.25%) 25(31.25%) 7(8.75%) 3(3.75%) 6(7.5%) 1(1.25%) 2(4%)	 38(47.5%) 21(26.25%) 13(16.25%) 4(5%) 3(3.75%) 17(21.25%) 2(2.5%) 0 1 0 0	 19(100%) 11(13.75%) 7(8.75%) 1(1.25%) 2(2.5%) 8(42%) 5(26%) 3(100%) 5(26%) 1(1.25%) 2(4%)	 0.761 0.403 0.05 0.001 0.003 0.453 0.004

Mean pancreatic duct diameter was 2.52 ± 0.42mm **(Table 2).**

Postoperative complications

Postoperative pancreatic fistula was seen in 19(23.75%) patients, biochemical fistula in 14(17.5%) and clinically significant fistula in 5(6.25%) patients, delayed gastric emptying was seen in 60% of the patients (Grade A -28.75%, B-25%, C-6.25%. Postoperative hemorrhage was seen in 5(6.25%), organ space infections in 7 (8.75%), superficial surgical site infections in 25(31.25%) of the patients.

Comparison of anatomical factors in relation to postoperative pancreatic fistula

Parenchymal thickness in patients with postoperative pancreatic fistula

Mean pancreatic duct diameter in this group was 2.71 ± 1.03mm (p=0.001), texture of the pancreas was soft in 11(13.75%) and firm in 8(10%) patients. It was observed that, as the thickness increases cranially and anteriorly chances of occurrence of postoperative pancreatic fistula increases and also as the thickness posterior to duct decreases chances of occurrence of postoperative pancreatic fistula increases. Mean thickness cranial, anterior and posterior to duct at which fistula occurred were 15.26 ± 3.03mm, 7.18 ± 1.50mm and 5.34 ± 3.32mm respectively. It was found that at a thickness of 5.7 mm posterior to duct sensitivity was 39% and specificity was 79% **Figure 2,** at a thickness of 6.5mm anterior to duct sensitivity was 68.4% and specificity was 74% **Figure 3** and at a thickness of 15.5 mm cranial to the duct sensitivity at which fistula occurred was 52.6% and specificity of 79% **Figure 4**. Eccentrically placed ducts were seen in 3(3.75%) and posteriorly placed ducts were seen in 8(10%) patients with pancreatic fistula but the difference was not significant.

Parenchymal thickness in patients without postoperative pancreatic fistula

Mean pancreatic duct diameter in this group was 3.79 ± 1.60mm, texture was soft in 13(16.25%) and firm to hard in 48(60%) patients. Mean anteroposterior and

Table 2: Anatomical factors at transection point between dilated and nondilated ducts.

Thickness	Entire study population	Dilated duct	Non dilated duct	P value
Anteroposterior	14.08 ± 3.41mm	14.24 ± 3.37mm	14.02 ± 2.37mm	0.261
Craniocaudal	29.63 ± 5.36mm	29.78 ± 5.55mm	29.5 ± 5.29mm	0.738
Anterior to duct	6.03 ± 2.54mm	5.14 ± 2.44mm	6.66 ± 2.44mm	0.002
Posterior to duct	4.46 ± 2.61mm	3.74 ± 2.18mm	4.97 ± 2.72mm	0.099
Cranial to duct	13.58 ± 3.46mm	13.47 ± 3.49mm	13.66 ± 3.46mm	0.479
Caudal to duct	12.5 ± 4.24mm	11.41 ± 3.76mm	13.36 ± 4.41mm	0.28
Main pancreatic duct diameter	3.53 ± 1.55mm	4.97 ± 1.31mm	2.52 ± 0.42mm	

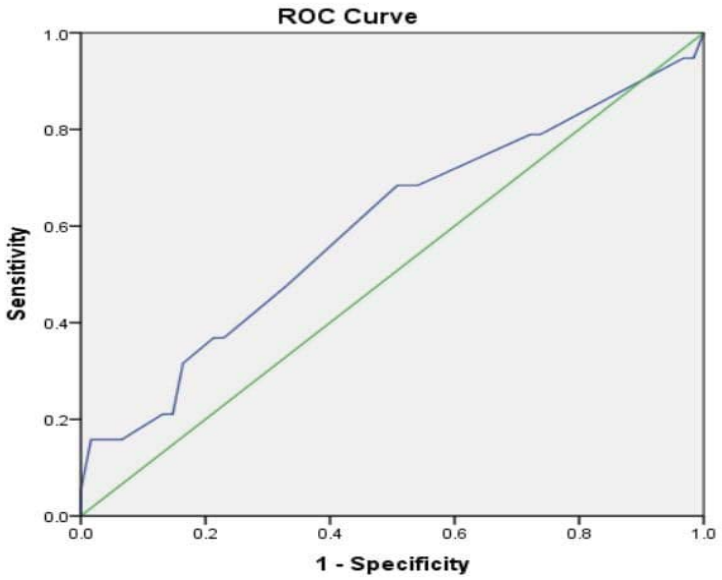

Figure 2: ROC curve plotted between parenchymal thickness posterior to duct and pancreatic fistula.

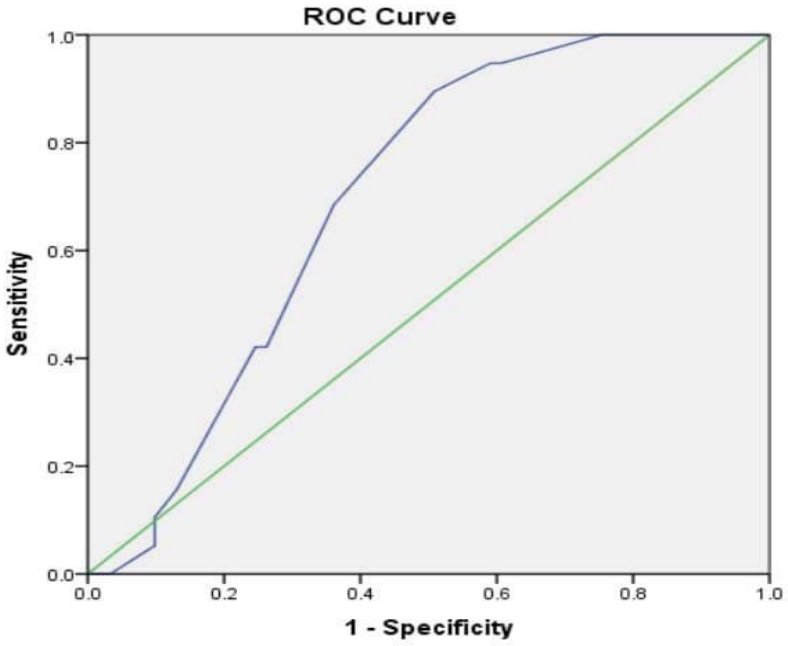

Figure 3: ROC curve plotted between parenchymal thickness anterior to duct and pancreatic fistula.

craniocaudal diameter were 13.73 ± 3.49mm and 29.13 ± 5.56 mm respectively. Mean thickness anterior to duct, posterior to duct, cranial and caudal to duct were 5.67 ± 2.70, 4.19 ± 2.32mm, 13.06 ± 3.43mm and 12.29 ± 4.19mm respectively. Eccentrically placed ducts were seen in 18 and posteriorly placed ducts were seen in 13 patients and the difference was not significant (p=0.193).

Comparison of parenchymal thickness in relation to biochemical and clinically significant fistula on comparing the anatomic factors in relation to biochemical and clinically significant fistula it was observed that as the thickness anterior to duct increases the rate of clinically significant fistula increased. Mean thickness anterior to duct at which fistula occurred was 8 ± 1.22mm. thickness

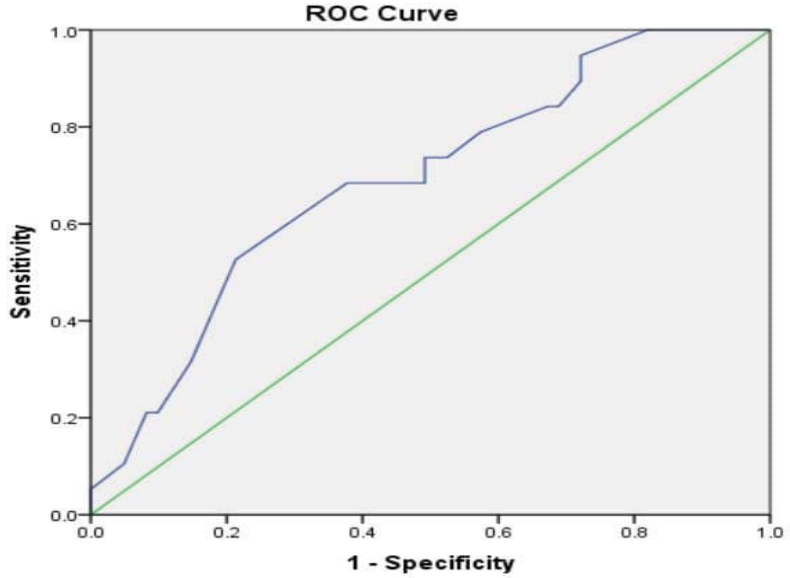

Figure 4: ROC curve plotted between parenchymal thickness cranial to duct and pancreatic fistula.

Table 3: Anatomical and parenchymal characteristics.

	No fistula (n=69)	POPF (n=19)	p value	Clinically significant fistula (n=5)	Biochemical fistula (p value) (n=14)	p value
MPD in mm	3.79+/-1.60	2.71+/-1.03	(p=0.001)	2.60+/-0.98	3+/-1.22	0.366
Dilated duct	29(36.25%)	4(5%)	(p=0.08)	3(3.75%)	1(1.25%)	0.12
Non dilated duct	32(40%)	15(18.75%)	(p=0.76)	11(13.75%)	4(5%)	0.23
Soft pancreas	13(16.25%)	11(57.89%)	(p=0.049)	8(10%)	3(3.75%)	0.657
Hard pancreas	48(60%)	8(42.11 %)	(p=0.07)	7(75%)	3(3.75%)	0.867
Antero posterior thickness in mm	13.73+/-3.49	15.18+/-2.96	(p=0.10)	15.6+/-3.29)	14+/-1.41	0.09
Cranio caudal thickness in mm	29.13+/-5.56	31.26+/-4.42	(p=0.13)	30.7+/-4.54	32.8+/-4.08	0.175
Thickness Cranial to duct in mm	13.06+/-3.43	15.26+/-3.03	(p=0.014)	15.07+/-2.90	15.8+/-3.70	0.140
Thickness Caudal to duct in mm	12.29+/-4.19	13.39+/-4.40	(p=0.34)	13.29+/-3.19	14.19+/-4.30	0.23
Thickness anterior to duct in mm	5.67+/-2.70	7.18+/-1.50	(p=0.023)	6.89+/-1.52	8+/-1.22	0.013
Thickness posterior to duct in mm	4.19+/-2.32	5.34+/-3.32	(p=0.036)	6.17+/-3.27	3+/-2.34	0.366
Eccentrically placed	18(22.5%)	3(3.75%)	(p=0.19)	2(2.5%)	1(1.25%)	0.761
Posteriorly placed duct	13(16.25%)	8(10%)	(p=0.07)	4(5%)	4(5%)	0.174

posterior to duct and thickness cranial to duct were not significantly associated with occurrence of clinically significant fistula but the thickness posterior to duct at which clinically significant fistula occurred was 3 ± 2.34mm **(Table 3).**

DISCUSSION

Postoperative pancreatic fistula remains the pacemaker for most of the complications following PD. High BMI, intraoperative blood loss, soft pancreas, non-dilated pancreatic duct have been identified as the risk factors for postoperative pancreatic fistula [5, 6, 9-11]. In present study anatomical characteristics in relation to POPF were assessed. In the present study it was observed that in patients with soft pancreas and in patients with MPD diameter <3.15 mm rate of POPF increased which was similar to previous studies [12-15]. In patients with soft pancreas and un dilated MPD despite of good surgical technique chances of leak increases, this might be due to presence of multiple secondary ducts which secrete the pancreatic juice leading to POPF [16, 17]. In soft pancreas even though it offered less resistance, tissue easily crushed while placing the knots [12]. Dilated duct helps the surgeon in precisely localizing suture placement, parenchyma around the duct helps in placing the suture and to hold the knot, in case where there is little parenchyma around the duct placing the suture, knotting and doing a multilayered anastomosis becomes technically challenging [18]. However, anatomy of the pancreatic stump at the transection point also plays an important role in the integrity of pancreaticojejunal anastomosis, it is not only the texture and main pancreatic duct diameter but also the parenchymal thickness which is essential in placing the sutures. Besides placement of sutures parenchymal thickness describes functionality of the gland, as the thickness increases there will be more secondary ducts secreting the pancreatic juice [12, 16, 17, 19].

Ridolfi et al. [19] analyzed area of the stump, mobilization of the pancreas and pancreatic duct position in 145 patients. Wide mobilization of the stump is required to place the jejunal loop deeply in front of the pancreatic stump, in their study it was observed that wide mobilization of the stump was associated with increased rates of fistula (p=0.001) due to relative ischemia and they recommended avoiding mobilization of the stump not more than 2.5

cm [19]. They also tried to analyze the position of duct in relation to POPF, it was observed that anteroposterior decentralization of the duct was associated with increased incidence of fistula but not when there was craniocauadal decentralization. In another study by Tajima et al. [18] anteroposterior decentralization of the duct that is when the thickness posterior to duct is <3mm, they observed higher incidence of POPF (p=0.037). In the present study it was observed that posterior decentralization of the duct did not have significant effect on POPF but we have found that 42% of anteroposterior decentralization, 15% cranio caudal decentralization had POPF, this might be because of fewer no of patients with POPF in our study. We also tried to compare the anatomy of the pancreatic stump in dilated and nondilated duct ,it was found that in dilated ducts both anterior and posterior thickness were less in comparison to nondilated ducts. This shows that as the duct becomes dilated secondary to obstruction parenchyma reduces in size circumferentially, even though duct can be localized easily in case of dilated ducts if there is little parenchyma around the duct it may jeo paradise the anastomosis. Reduced parenchymal thickness makes placement of sutures difficult especially when double layered anastomosis is done [12, 18]. In a study by Tajima et al [18], El Nakeeb et al. [15] and in a recent study [20] it was observed that as the parenchymal thickness posterior to duct decreased placing the sutures become difficult and incidence of POPF increased ,mean thickness in their studies where POPF was seen were 3.3 ± 1.92, 3.2 ± 1.20 and 3.17 ± 0.72mm respectively. In our study we observed mean thickness posterior to duct at which clinically significant fistula occurred was 3 ± 2.34mm which is similar to study by Tajima et al. [18], mean thickness at which POPF occurred was 5.34 ± 3.32mm slightly higher in comparison to other studies. This can be explained due to functional aspect of gland where there might be leak from the secondary duct at the cut edge of the pancreatic stump [18, 20]. The functioning gland has larger area and secretes large volume of pancreatic secretions as has been in observed in study by Ridolfi et al. [19] where they show that large stump area (219 vs. 138 mm^2) results in increased incidence of fistula (p<0.00). In the present study it was observed that as the thickness anterior to duct increases chance of clinically significant fistula increases, as the parenchyma around the duct decreases, placement of suture becomes challenging especially in the non-dilated ducts. To conclude besides the ductal dilation and texture it is the anatomy at the transection point and functionality of the gland determines the POPF.

Highlights

- Posteriorly placed non dilated ducts pose difficulty in placing sutures.
- Little parenchyma is left to hold the sutures when duct is positioned posteriorly.
- Anatomical factors at transection point also pose significant technical challenges.

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare no conflict of interest.

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