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Duct-to-mucosa pancreaticojejunostomy can reduce the risk of pancreatic fistula after pancreaticoduodenectomy

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Research article

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Abstract

Background: Pancreaticoduodenectomy (PD) is the most effective surgical procedure to remove a pancreatic tumor. However, pancreatic fistula occurring after surgery is associated with a high incidence of life-threatening complications. Therefore, the aim of this work was to summarize the factors influencing the development of pancreatic fistula after PD and the measures to prevent it.

Methods: Clinical data of patients who were subjected to PD between January 2012 and January 2017 in the Department of General Surgery, First Hospital of Lanzhou University, China, were collected and retrospectively analyzed. The risk factors for pancreatic fistula were analyzed by univariate analysis and multivariate logistic regression analysis.

Results: Among 215 patients, 42 were suffering from a postoperative pancreatic leakage, with an incidence of 19.5% (42/215). Univariate analysis showed a significant correlation between postoperative pancreatic fistula (POPF) and the following factors: pancreaticojejunal anastomosis (end-to-side “sleeve” pancreaticojejunostomy vs duct-to-mucosa pancreaticojejunostomy: 27.8% vs 11.2%, P = 0.002), pancreatic duct diameter (≤ 3 mm vs > 3 mm: 25.2% vs 13.8%, P = 0.036), and pancreatic texture (hard vs soft: 14.2% vs 25.2%, P = 0.043). Multivariate logistic regression analysis showed that pancreaticojejunal anastomosis was the independent risk factor for POPF after PD.

Conclusions: High quality anastomosis is an important factor in the prevention of POPF. Pancreaticojejunal duct-to-mucosa anastomosis is a simple technique and results in a low incidence of pancreatic fistula.

Background

Pancreaticoduodenectomy (PD) is the most effective treatment to combat adenocarcinoma of the distal common bile duct, pancreatic head cancer, ampullary carcinoma and duodenal carcinoma. However, postoperative pancreatic fistula (POPF) occurs at a frequency of 5%–20% and is associated with a high incidence of life-threatening complications, such as intra-abdominal abscess, hemorrhage and sepsis [1–2]. For decades, POPF following PD has been a major concern for all surgeons. Therefore, the aim of this study was to analyze the risk factors influencing the development of POPF after PD to provide guidance to surgeons, to allow them the choice of the best approach with less risk of developing pancreatic fistula.

Methods

Patients and clinical data

A total number of 215 patients who were subjected to elective PD for benign or malignant pathologies of the pancreas or periampullary region at the Department of Surgery, The First Hospital of Lanzhou University were collected between January 2012 and January 2017 and retrospectively analyzed. This study included 112 male patients and 103 female patients with a mean age of 54.42 ± 9.25 years. The

following patient data were considered: gender, age, diabetes mellitus, smoking history, epigastrium surgery, preoperative total bilirubin and serum albumin levels, pancreaticojejunostomy, blood loss, operative time, *pancreatic duct diameter, and pancreatic texture. Additionally, all postoperative complications were recorded.*

Surgical technique

As regard the surgical technique, the decision to perform a duct-to-mucosa anastomosis or an invagination was made by the surgeon. The duct-to-mucosa pancreaticojejunostomy (dmPJ) was performed by a two layer end-to-side pancreaticojejunostomy. The pancreatic capsule and the jejunal serosa were anastomosed by an interrupted 4–0 silk suture to form an outer layer in both the anterior and posterior walls of the anastomosis.The posterior wall is a complete anastomosis of the pancreatic duct and jejunum with 4–5 stitches,the anterior wall is full layer of pancreas and jejunum anastomosis, non-pancreatic duct anastomosis.Then we need suture 1–2 stitches discontinuously on the upper and lower sides. A pancreatic duct stent was inserted during the anastomosis to allow an easy and accurate suture placement, ensure an adequate pancreatic duct exposure and protect the opposite wall from being unintentionally held by needles, and then it was removed at the end of the anastomosis.

The invagination pancreaticojejunostomy (iPJ) was performed as an end-to-side “sleeve” pancreaticojejunostomy. The pancreatic capsule and the jejunal serosa were anastomosed as described above. Jejunostomy was also performed as described above, the duct was taken posteriorly and anteriorly to jejunal mucosa and a pancreatic duct stent was also inserted during anastomosis and removed after stitches removal. The reconstruction was manually completed by end-to-side hepaticojejunostomy (retrocolic) and end-to-side gastrojejunostomy (antecolic).

POPF definition

Pancreatic fistula was defined according to the International Study Group on Pancreatic Fistula as any measurable volume of drainage fluid output due to operatively or postoperatively placed drains on or after postoperative day 3, with amylase content greater than three times the upper normal serum value[3].

Statistical analysis

All clinical data were inserted into an Excel spreadsheet, and SPSS 21.0 software was used for statistical analysis. Data were expressed as mean±standard deviation (SD). Student *t*-test was performed for the comparison of two groups. Categorical variables were analyzed using Fisher’s exact test and χ^2 test. Univariate analysis was performed to identify POPF risk factors. Multivariate logistic regression using stepwise model was then performed for variables with a *P* value less than 0.05 in the univariate analysis to determine the independent risk factors contributing to the development of POPF.

Results

Overall characteristics of patients and complications

Among the 215 patients, 42 (19.5%) developed POPF. The following complications were identified: 25 (11.6%) cases of abdominal bleeding, 20 (9.3%) cases of bile leakage, 11 (5.1%) cases of pancreaticojejunal anastomotic bleeding, and 28 (13%) cases of abdominal infection. However, 4 (1.8%) patients were subjected to a second operation, and 2 (0.9%) patients died after surgery due to abdominal bleeding associated with POPF.

Univariate analysis

Univariate analysis showed no significant correlation between POPF and the following factors: age, gender, smoking history, preoperative bilirubin and albumin, epigastrium surgery, blood loss, and operative time. Conversely, three factors had a significant correlation with POPF as follows: iPJ *vs* dmPJ resulted in a rate of developing fistula of 27.8% *vs* 11.2% ($P = 0.002$), pancreatic duct diameter ≤ 3 mm *vs* > 3 mm resulted in a rate of developing fistula of 25.2% *vs* 13.8% ($P = 0.036$), and hard pancreatic texture *vs* soft resulted in a rate of developing fistula of 14.2% *vs* 25.2% ($P = 0.043$) (Table 1).

Multivariate logistic regression analysis

The risk factors for POPF (pancreaticojejunal anastomosis technique, pancreatic duct diameter, and pancreatic texture) demonstrated in the univariate analysis were incorporated into the logistic regression analysis. The results showed that dmPJ had a lower incidence of POPF than that of iPJ after PD (Table 2).

Discussion

Surgery of the pancreatic head had in principle a high risk of complication. The gastrointestinal reconstruction includes pancreatojejunostomy, biliary-enteric anastomosis, and gastrointestinal anastomosis. The most common postoperative complication for PD is the pancreatic fistula. The factors leading to POPF are the following: 1. Systemic factors, such as elderly age (>65 years), epigastrium surgery, preoperative nutritional status, preoperative jaundice, preoperative hemoglobin, hypertension, diabetes and other associated underlying diseases. However, Liu Qiuyu et al. found that age, gender, body mass index, hypertension, diabetes mellitus, history of jaundice, serum albumin level, and blood loss volume have no statistical difference related to the morbidity of POPF after multivariate analysis [4]. 2. Local factors, such as pancreatic duct diameter, and pancreas texture. Residual pancreas size, texture and thickness of the pancreatic duct and pancreatic exocrine function are factors affecting the occurrence of POPF. Indeed, a soft pancreas and small duct are the risk factors for pancreatic leakage after PD [5–6]. 3. Anastomosis. Various anastomotic techniques and pharmacological measures are

preferred to prevent fistula, such as pancreaticojejunostomy (PJ) *vs* pancreaticogastrostomy (PG), and duct-to-mucosa *vs* invagination technique [7–8]. Currently, the reconstruction of the pancreatic duct can be performed using different approaches in clinical practice, such as classic invagination pancreaticojejunostomy, end-to-side invagination pancreaticojejunostomy of U type, bundling invagination pancreaticojejunostomy, duct-to-mucosa anastomosis, duct-to-seromuscular anastomosis and PG. The main pancreatic duct, pancreatic stump and pancreatic juice in the classic invagination pancreaticojejunostomy, can all enter into the bowel, which is a relatively simple and easy approach to perform, although it can lead to pancreatic stump local ischemia because the sutures are too many. Compared with the iPJ and end-to-side invagination pancreaticojejunostomy of U type, duct-to-mucosa anastomosis can effectively avoid the loss of the pancreas. The relationship between the incidence of pancreatic leakage and the type of anastomotic technique has been investigated by various authors. Duct-to-mucosa anastomosis is a two-layered anastomosis intended to prevent POPF and to maintain pancreatic exocrine function. As early as in 1946, Waugh and Clagett designed the PG to replace pancreaticojejunostomy thanks to the following advantages: first, it is a tension-free anastomosis since the pancreas lies adjacent to the stomach. Second, the stomach, which is rich in blood vessels, provides sufficient blood supply to the anastomosis. Last, the lack of gastric juice and enterokinase activity makes the activation of pancreatin incomplete, reducing the erosion of the anastomosis.

Several studies showed no significant difference in the incidence of POPF when dmPJ and iPJ were compared [9], while some scientists made a prospective analysis of the above two anastomotic methods, resulting in dmPJ less likely associated with pancreatic leakage than iPJ [10]. Indeed, dmPJ is more effective than iPJ in preventing POPF. However, in elderly people who often suffer from coronary heart disease, hypertension and diabetes, Lin et al. found that these associated diseases are the significant risk factors for POPF [11]. Multivariate analysis reveals that patients with soft pancreas and non-dilated pancreatic duct have higher incidence of POPF, further supporting the fact that the classical invagination pancreaticojejunostomy technique is safer for patients at high risk. Patients with hard pancreas and dilated pancreatic duct should be subjected to dmPJ [12]. In recent years, many scholars showed through clinical studies that the incidence of POPF by bundling pancreaticojejunostomy is significantly lower than the incidence obtained when iPJ is performed [13]. Several ways of digestive tract reconstruction after PD were developed to prevent POPF, including “Colonial Wig” pancreaticojejunostomy, modified Heidelberg technique, Hong’s single-stitch to obtain the satisfied results the authors described [14,15]. Recent studies suggest that duct-to-mucosa anastomosis has lower incidence of POPF after PD [16].

Conclusions

In our present retrospective analysis of 215 patients who were subjected to either dmPJ or iPJ, the incidence of POPF in the dmPJ patients was lower than that in the iPJ patients, thus confirming the conclusions of Sugiyama M [17]. So far, no exact evidence can fully prove which approach has more advantages in the prevention of POPF between dmPJ and iPJ. However, dmPJ not only has a lower incidence of POPF in clinical practice, but is also good for patency of the pancreatic duct, thus, it should

be the ideal method to perform PJ. To achieve the desired objective, a strong technical team of professionists in the pancreatic disease sector is also needed. Our conclusion is that a standardized technique of the pancreatic anastomosis could potentially minimize the incidence of leakage.

Abbreviations

pancreaticoduodenectomy (PD)

postoperative pancreatic fistula (POPF)

duct-to-mucosa pancreaticojejunostomy (dmPJ)

invagination pancreaticojejunostomy (iPJ)

standard deviation (SD)

Declarations

Ethics approval and consent to participate

The study involving human participants was approved by the institutional review board of the Lanzhou University First Affiliated Hospital(No. 2019–189). Written consent was obtained from all the participants. The methods were carried out in accordance with the approved guidelines. All clinical research was performed on the basis of the principles expressed in the Declaration of Helsinki.

Publication

All authors consent for publication

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Libin Ma, Xingcheng Wang, Qiang Li and Chen Chai declare that they have no conflict of interest financial or otherwise to disclose.

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Contributions

M.L.B. and C.C. conceived and designed the study. W.X.C. and L.Q collected the data. M.L.B.and W.X.C. did the analysis. M.L.B. and C.C. wrote the paper. All authors have read and approved the manuscript.

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References

[1] Hashimoto D, Chikamoto A, Harimoto N, Ikegami T, Uchiyama H, Yoshizumi T, Baba H, Maehara Y. A comparative study on the complications of conventional and end-to-side inserting pancreatojejunostomy after pancreaticoduodenectomy. Surg Today, 2017,47(2):238-44.

[2] Senda Y, Shimizu Y, Natsume S, Ito S, Komori K, Abe T, Matsuo K, Sano T. Randomized clinical trial of duct-to-mucosa versus invagination pancreaticojejunostomy after pancreatoduodenectomy. Br J Surg, 2018,105(1):48-57.

[3] Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M, International Study Group on Pancreatic Fistula D. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery, 2005,138(1):8-13.

[4] Liu QY, Zhang WZ, Xia HT, Leng JJ, Wan T, Liang B, Yang T, Dong JH. Analysis of risk factors for postoperative pancreatic fistula following pancreaticoduodenectomy. World J Gastroenterol, 2014,20(46):17491-7.

[5] Fu SJ, Shen SL, Li SQ, Hu WJ, Hua YP, Kuang M, Liang LJ, Peng BG. Risk factors and outcomes of postoperative pancreatic fistula after pancreatico-duodenectomy: an audit of 532 consecutive cases. BMC Surg, 2015,15:34.

[6] Sugimoto M, Takahashi S, Kojima M, Kobayashi T, Gotohda N, Konishi M. In Patients with a Soft Pancreas, a Thick Parenchyma, a Small Duct, and Fatty Infiltration Are Significant Risks for Pancreatic Fistula After Pancreaticoduodenectomy. Journal of Gastrointestinal Surgery, 2017,21(5):846-54.

[7] Crippa S, Cirocchi R, Randolph J, Partelli S, Belfiori G, Piccioli A, Parisi A, Falconi M. Pancreaticojejunostomy is comparable to pancreaticogastrostomy after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. Langenbecks Arch Surg, 2016,401(4):427-37.

[8] Qin H, Luo L, Zhu Z, Huang J. Pancreaticogastrostomy has advantages over pancreaticojejunostomy on pancreatic fistula after pancreaticoduodenectomy. A meta-analysis of randomized controlled trials. Int J Surg, 2016,36(Pt A):18-24.

[9] Sun X, Zhang Q, Zhang J, Lou Y, Fu Q, Zhang X, Liang T, Bai X. Meta-analysis of invagination and duct-to-mucosa pancreaticojejunostomy after pancreaticoduodenectomy: An update. Int J Surg, 2016,36(Pt A):240-7.

[10] Bai X, Zhang Q, Gao S, Lou J, Li G, Zhang Y, Ma T, Zhang Y, Xu Y, Liang T. Duct-to-Mucosa vs Invagination for Pancreaticojejunostomy after Pancreaticoduodenectomy: A Prospective, Randomized Controlled Trial from a Single Surgeon. J Am Coll Surg, 2016,222(1):10-8.

[11] Lin JW, Cameron JL, Yeo CJ, Riall TS, Lillemoe KD. Risk factors and outcomes in postpancreaticoduodenectomy pancreaticocutaneous fistula. J Gastrointest Surg, 2004,8(8):951-9.

[12] Xu J, Zhang B, Shi S, Qin Y, Ji S, Xu W, Liu J, Liu L, Liu C, Long J, Ni Q, Yu X. Papillary-like main pancreatic duct invaginated pancreaticojejunostomy versus duct-to-mucosa pancreaticojejunostomy after pancreaticoduodenectomy: A prospective randomized trial. Surgery, 2015,158(5):1211-8.

[13] Zhang X, Dong X, Liu P, Yan Y, Wei Y, Zechner D, Gong P, Vollmar B. Binding versus Conventional Pancreaticojejunostomy in Preventing Postoperative Pancreatic Fistula: A Systematic Review and Meta-Analysis. Dig Surg, 2017,34(4):265-80.

[14] Yang X, Aghajafari P, Goussous N, Patel ST, Cunningham SC. The "Colonial Wig" pancreaticojejunostomy: zero leaks with a novel technique for reconstruction after pancreaticoduodenectomy. Hepatobiliary Pancreat Dis Int, 2017,16(5):545-51.

[15] Hong DF, Liu YH, Zhang YH, Wang YC, Wang ZM, Wu WD, Shen GL, Zhang JG, Zhang W, Cheng J, Peng SY. The role of Hong's single-stitch duct to mucosa pancreaticojejunostomy in laparoscopic pancreaticoduodenectomy. Zhonghua Wai Ke Za Zhi, 2017,55(2):136-40.

[16] Sun Y-L, Zhao Y-L, Li W-Q, Zhu R-T, Wang W-J, Li J, Huang S, Ma X-X. Total closure of pancreatic section for end-to-side pancreaticojejunostomy decreases incidence of pancreatic fistula in pancreaticoduodenectomy. Hepatobiliary & Pancreatic Diseases International, 2017,16(3):310-4.

[17] Sugiyama M, Suzuki Y, Nakazato T, Yokoyama M, Kogure M, Abe N. Pancreatic Duct Holder and Mucosa Squeeze-out Technique for Duct-to-Mucosa Pancreatojejunostomy After Pancreatoduodenectomy: Propensity Score Matching Analysis. World J Surg, 2016,40(12):3021-8.

Tables

Table 1 Risk factors for pancreatic fistula according to the univariate analysis

Variable	POPF occurrence			
	YES	NO	χ^2	*P* value
Gender			0.149	0.7
Male	23 (20.5%)	89 (79.5%)		
Female	19 (18.4%)	84 (81.6%)		
Age			1.731	0.188
≥ 60	16 (25.0%)	48 (75.0%)		
< 60	26 (17.2%)	125 (82.8%)		
Diabetes mellitus			0.63	0.427
Yes	8 (15.7%)	43 (84.3%)		
No	34 (20.7%)	130 (79.3%)		
Smoking history			0.497	0.481
Yes	20 (21.7%)	72 (78.3%)		
No	22 (17.9%)	101 (82.1%)		
Epigastrium surgery			0.323	0.57
Yes	8 (16.7%)	40 (83.3%)		
No	34 (20.4%)	133 (79.6%)		
Preoperative total bilirubin (μmol/L)			0.511	0.475
> 171	28 (21.1%)	105(78.9%)		
≤ 171	14 (17.1%)	68 (82.9%)		
Serum albumin (g/L)			1.191	0.275
< 35	12 (15.6%)	65 (84.4%)		
≥ 35	30 (21.7%)	108 (78.3%)		
Pancreaticojejunostomy			9.38	0.002
End-to-side invagination pancreaticojejunostomy	30 (27.8%)	78 (72.2%)		
duct-to-mucosa pancreaticojejunostomy	12 (11.2%)	95 (88.8%)		
Pancreatic duct diameter (mm)			4.401	0.036
≤ 3	27 (25.2%)	80 (74.8%)		
> 3	15 (13.8%)	93 (86.2%)		
Operative time (min)			0.114	0.735
> 300	25 (20.3%)	98 (79.7%)		
≤ 300	17 (18.5%)	75 (81.5%)		
Blood loss (mL)			0.205	0.65
> 600	19 (18.3%)	85 (81.7%)		
≤ 600	23 (88.0%)	88 (12.0%)		
Pancreatic texture			4.098	0.043
Hard	16 (14.2%)	96 (85.8%)		
Soft	26 (25.2%)	77 (74.8%)		

Table 2 Logistic regression for the predictors of pancreatic fistula following pancreaticoduodenectomy

Variable	B	S.E	Wald	df	Sig.	Exp (B)
Pancreaticojejunostomy	-2.342	0.502	21.719	1	0.000	0.096
Pancreatic duct diameter	-1.106	0.490	5.083	1	0.024	0.331
Pancreatic texture	1.272	0.505	6.340	1	0.012	3.568

B=partial regression coefficient; S.E.= standard error; Wald= $(B/SE)^2$; df=degree of freedom; Sig.=*P* value; Exp (B)=OR

Supplementary Files

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