Journal of Hainan Medical University

http://www.hnykdxxb.com

# Analysis of related risk factors for pancreatic fistula after pancreaticoduodenectomy

Qi−Song Yu✉, He−Chao Huang, Feng Ding, Xin−Bo Wang

*Department of General Surgery, New Area People's Hospital of Luoyang, Henan, 471023, China*

ARTICLE INFO

*Article history:*
Received
Received in revised form
Accepted
Available online

*Keywords:*
Pancreaticoduodenectomy
Pancreatic fistula
Risk factor
Analysis

ABSTRACT

**Objective:** To explore the related risk factors for pancreatic fistula after pancreaticoduodenectomy to provide a theoretical evidence for effectively preventing the occurrence of pancreatic fistula. **Methods:** A total of 100 patients who were admitted in our hospital from January, 2012 to January, 2015 and had performed pancreaticoduodenectomy were included in the study. The related risk factors for developing pancreatic fistula were collected for single factor and Logistic multi-factor analysis. **Results:** Among the included patients, 16 had pancreatic fistula, and the total occurrence rate was 16% (16/100). The single-factor analysis showed that the upper abdominal operation history, preoperative bilirubin, pancreatic texture, pancreatic duct diameter, intraoperative amount of bleeding, postoperative hemoglobin, and application of somatostatin after operation were the risk factors for developing pancreatic fistula ($P$<0.05). The multi-factor analysis showed that the upper abdominal operation history, the soft pancreatic texture, small pancreatic duct diameter, and low postoperative hemoglobin were the dependent risk factors for developing pancreatic fistula ($OR$=4.162, 6.104, 5.613, 4.034, $P$<0.05). **Conclusions:** The occurrence of pancreatic fistula after pancreaticoduodenectomy is closely associated with the upper abdominal operation history, the soft pancreatic texture, small pancreatic duct diameter, and low postoperative hemoglobin; therefore, effective measures should be taken to reduce the occurrence of pancreatic fistula according to the patients' own conditions.

## 1. Introduction

Pancreaticoduodenectomy (PD) is currently the standard method for the treatment of benign and malignant tumors of pancreas head, ampulla, and the lower segment of common bile duct. With the continuous development of surgical technology and the gradual maturity of perioperative methods, the postoperative death rate of PD patients has been reduced to below 2%[1], but due to numerous surgical incisions, large trauma, and complex gastrointestinal incision reestablishment, there are still high and severe complications after operation with an occurrence rate of 65%[2]. Pancreatic fistula (PF) is the most common and most severe complication after PD, can not only extend the hospitalization time and increase the treatment cost, but also can increase the early mortality risk rate after operation[3]. Currently, various studies have been conducted to explore the risk factors for developing PF after PD, but the conclusion is not consistent. The study is aimed to explore the related risk factors for pancreatic fistula after PD to provide a theoretical evidence for effectively preventing the occurrence of pancreatic fistula.

## 2. Materials and methods

### 2.1. General materials

A total of 100 patients who were admitted in our hospital from

✉Corresponding author: Qi-Song Yu, M.B., Associate Chief Physician.
Tel: 13526993366
E-mail: zhantyj@163.com
Foundation project: The study was supported by the Natural Science Research Planning Project of Henan Province with the number of 201310471055.

January, 2012 to January, 2015 for PD were included in the study, among which 58 were male, and 42 were female; aged from 27 to 80 years old, with an average age of (53.6±10.1) years old; 26 had pancreatic head cancer, 15 had duodenal papilla cancer, 23 had distal common bile cancer, 15 had periampullary cancer, 18 had benign tumor of pancreas head, 2 had duodenal papilla adenoma, and 1 had common bile adenoma. The diagnosis of all cases was consistent with the diagnosis by the postoperative histopathology.

### 2.2. Perioperative treatment

All the patients were performed with related examinations, such as various functional examinations of vital organs, blood routine examination, biochemistry, blood coagulation, and other related examinations in order to guarantee the patients can accept or endure the complex PD. Sufficient preoperative evaluation and preoperative preparations were performed. Contraindications to the operation were strictly excluded. Symptomatic treatments before operation were positively performed for some controllable and remediable diseases, such as anemia correcting, improvement of jaundice and coagulation with vitamin K1, and anti-infection. For patients with hypertension, diabetes, and other chronic diseases, blood sugar adjustment and blood pressure reduction were positively performed in order to be suitable for the surgery according to the consultation opinions of related experts. The operation procedures were accomplished by the chief physicians with abundant experience. Pancreaticojejunostomy and pancreatogastrostomy were involved in the digestive tract reconstruction. The peritoneal drainage tube was routinely placed. The amount of drainage liquid and amylase level were intensively monitored after operation. The drainage tube could be removed about one week after operation if no related complications occurred. If PF occurred after operation, a continuous peritoneal drainage was required and the amylase level should be periodically detected again. For patients accompanied by infection, antibiotics should be applied; meanwhile, somatostatin and nutrition support should be given for the symptomatic treatments.

### 2.3. Diagnosis of PF

The diagnosis of PF was in reference to the newest standard diagnosis of PF by ISGPF[4]. The standard was that after PD, the peritoneal drainage volume was exceeding 50 mL/d, the amylase level was 3 times of the normal level, or PF was confirmed by the ultrasound, CT, or other image examinations. PF was divided into A, B, and C grades according to different prognosis by ISGPF. Grade A referred to transient PF with no clinical significance and no special treatments. Grade B referred to PF with clinical significance and symptoms, but could be cured by symptomatic treatments and sufficient drainage, with longer hospitalization than grade A. Grade C referred to PF which could severely endanger the life, requiring intensive care and percutaneous cather drainage, and probably inducing infection, septicemia, and even multiple organ failure. According to the above standards, the patients were divided into PF group ($n$=16) and no PF group ($n$=84) in order to analyze the related risk factors for developing PF.

### 2.4. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. *Chi*-square test or Fisher′s exact test was used for the single factor analysis. Then the factors with statistical significance were included in Logistic regression model for multi-factor analysis. $P$<0.05 was regarded as statistically significant difference.

## 3. Results

### 3.1. Occurrence of PF after operation

Among the included patients, 16 had PF, and the total occurrence rate was 16% (16/100), among which 2 were dead due to invalid treatment, with a mortality rate of 12.5%. The severity degree of PF contained grade A (7, 43.75%) and grade B (6, 37.5%), and grade C (3, 18.75%), among which 10 had pure PF, 3 had PF merged with biliary fistula, 1 had PF merged with biliary fistula hemorrhage which could be cured by conservative treatment and hemostasis, 1 had gastrointestinal bleeding after PF, and 1 had PF merged with abdominal infection who was dead after positive treatment.

### 3.2. Single factor analysis of the occurrence of PF

The single factor analysis showed that the gender, age, hypertension, diabetes, preoperative bilirubin, intraoperative amount of bleeding, and application of somatostatin were not associated with the occurrence of PF ($P$>0.05), while the upper abdominal operation history, pancreatic texture, pancreatic duct diameter, surgical method, and postoperative hemoglobin level were closely associated with the occurrence of PF ($P$<0.05) (Table 1).

### 3.3. Multi-factor analysis of the occurrence of PF

The multi-factor analysis showed that the upper abdominal operation history, the soft pancreatic texture, small pancreatic duct diameter, and low postoperative hemoglobin were the dependent risk factors for developing pancreatic fistula ($OR$=4.162, 6.104, 5.613, 4.034, $P$<0.05), while the surgical method was not an independent

risk factor (Table 2).

**Table 1**

Single factor analysis of the occurrence of PF [*n* (%)].

| Factors | PF group (*n*=16) | No PF group (*n*=84) | $\chi^2$ value | *P* vlaue |
|---|---|---|---|---|
| Gender | | | | |
| Male 58 | 9(15.5%) | 49(84.5%) | 0.024 | 0.877 |
| Female 42 | 7(16.7%) | 35(83.3%) | | |
| Age (years old) | | | | |
| ≤60 | 6(10.9%) | 49(89.1%) | 2.357 | 0.125 |
| >60 | 10(22.2%) | 35(77.8%) | | |
| Hypertension | | | | |
| Yes | 1(16.7%) | 5(83.3%) | 0.002 | 0.963 |
| No | 15(15.9%) | 79(84.1%) | | |
| Diabetes | | | | |
| Yes | 3(20%) | 12(80%) | 0.210 | 0.647 |
| No | 13(15.3%) | 72(84.7%) | | |
| Upper abdominal operation history | | | | |
| Yes | 4(44.4%) | 5(55.6%) | 5.954 | 0.015 |
| No | 12(13.2%) | 79(86.8%) | | |
| Pancreatic texture | | | | |
| Soft | 9(29.0%) | 22(71.0%) | 5.677 | 0.017 |
| Hard | 7(10.1%) | 62(89.9%) | | |
| Pancreatic duct diameter (mm) | | | | |
| 3 | 11(12.4%) | 78(87.6%) | 7.978 | 0.005 |
| <3 | 5(45.5%) | 6(54.5%) | | |
| preoperative bilirubin (μmol/L) | | | | |
| <117 | 6(10.2%) | 53(89.8%) | 3.640 | 0.056 |
| 117 | 10(24.4%) | 31(75.6%) | | |
| Surgical methods | | | | |
| pancreatogastrostomy | 2(5.1%) | 37(94.9%) | 5.623 | 0.018 |
| Pancreaticojejunostomy | 14(22.9%) | 47(77.1%) | | |
| Intraoperative amount of bleeding (mL) | | | | |
| 300 | 10(16.4%) | 51(83.6%) | 0.018 | 0.893 |
| <300 | 6(15.4%) | 33(84.6%) | | |
| Postoperative hemoglobin (g/L) | | | | |
| 90 | 11(12.5%) | 77(87.5%) | 6.684 | 0.010 |
| <90 | 5(41.7%) | 7(58.3%) | | |
| Application of somatostatin | | | | |
| Yes | 7(20%) | 28(80%) | 0.641 | 0.423 |
| No | 9(13.8%) | 56(86.2%) | | |

**Table 2**

Multi-factor Logistic analysis of the occurrence of PF.

| Variables | Parameter estimate value | *OR* | 95%*CI* | *P* value |
|---|---|---|---|---|
| Upper abdominal operation history | 1.439 | 4.162 | 1.407～6.154 | 0.024 |
| Soft pancreatic texture | 1.921 | 6.104 | 1.915～11.834 | 0.005 |
| Pancreatic duct diameter <3 mm | 1.715 | 5.613 | 1.857～10.371 | 0.018 |
| Postoperative hemoglobin <90 g/L | 1.335 | 4.034 | 1.066～5.921 | 0.039 |

## 4. Discussion

PD is one of the abdominal operations characterized by extreme complexity, great difficulty, and numerous postoperative complications, and the occurrence rate of fistula is much higher than the other gastrointestinal operations. PF is a common postoperative complication, and will usually cause serious clinical consequences which are not easy to be processed, with an occurrence rate of about 20%[5]. Due to the special physiological anatomic site of pancreas and the great corrosion destruction on the vital organs and vessels caused by the secreted pancreatic fluid mixed with gastric fluid, PF can induce massive hemorrhage and other fatal consequences, with a mortality rate of 40%[6]. The occurrence of PF after PD will bring great threat to the patients′ life and health, and meanwhile will pose great challenge to the abdominal surgery physicians. Therefore, looking for early accurate prediction and estimation of related risk factors for developing PF is of great significance in preventing PF and its complications, and in taking targeted treatments. Studies have been studied by many scholars from the patients, the disease, and the surgeons, but the results are different. The results in the study showed that the upper abdominal operation history, the soft pancreatic texture, pancreatic duct diameter<3 mm, and postoperative hemoglobin<90 g/L were the dependent risk factors for developing PF.

In the study, 9 cases had upper abdominal operation history, among which 4 had cholecystectomy, 3 had gastrectomy, and 2 had cholangiojejunostomy. Among the 9 cases with upper abdominal operation history, 4 cases had PF, with an occurrence rate of 44.4% (4/9), significantly higher than those with no upper abdominal operation history 13.2%（12/91）(*P*<0.05). The multi-factor analysis showed that the occurrence rate of PF with upper abdominal operation history was 4.162 times than those with no upper abdominal operation history (95%*CI*: 1.407-6.154, *P*=0.024). Some researches demonstrate that the upper abdominal operation history will alter the normal anatomic site or structure of human organs, and probably can cause the peripheral visceral adhesion, which can increase the operation difficulty and operation damage, and is not beneficial for the complete anastomosis of the pancreatic stub-end to induce the occurrence of PF[7]. It is also reported that the palliative cholangiojejunostomy can increase the operation difficulty to add the risk of PF. In the study, the occurrence rate of PF after PD in the soft pancreas was 6.104 times than that in the hard pancreas (95%*CI*: 1.915-11.834，*P*=0.005). The soft pancreas as an independent risk factor for developing PF has been widely acknowledged probably in that the soft texture will increase the difficulty of surgical stub-end anastomosis, which is not beneficial for the tight suture to induce a poor integrity of anastomotic stoma, thus the possibility of the occurrence of PF after operation is large[8]. The results in the study showed that the occurrence rate of PF with pancreatic

duct diameter ＜3 mm was 5.613 times than that with pancreatic duct diameter 3 mm (95%*CI*: 1.857-10.371, *P*=0.018). The small pancreatic duct diameter will increase the difficulty of pancreatic stub-end anastomosis, and even in some situations, the surgeons can not accomplish the complete suture. It is recommended by some researches that for patients with small pancreatic duct diameter, drainage tube placed in the pancreatic tube for unobstructed drainage can reduce the occurrence of PF and its complications to a certain extent[9]. The results in the study showed that the occurrence of PF in patients with hemoglobin <90 g/L was 4.034 times that in patients with hemoglobin 90 g/L (95%*CI*: 1.066-5.921, *P*=0.039). Some researches demonstrate that the hemoglobin content will affect the healing of anastomotic stoma of gastrointestinal surgery. Too low hemoglobin content will affect the cell infiltration and blood vessel formation of the anastomotic stoma, resulting in the reduction of fibroblasts and collagen fibers to delay the healing of anastomotic stoma[10], and can also significantly reduce the oxygen content of microcirculation which can supply blood for the anastomotic stoma to cause cell hypoxia and local edema to delay the healing, which can increase the risk of PF.

In conclusion, the upper abdominal operation history, the soft pancreatic texture, pancreatic duct diameter<3 mm, and postoperative hemoglobin<90 g/L are the independent risk factors for developing PF after PD. Therefore, an accurate operation by physicians with abundant experience, appropriate placement of pancreatic duct stent for drainage, close monitoring of hemoglobin, and timely symptomatic treatments can effectively avoid the intraoperative accidental injury, reduce the operation difficulty, and maintain the integrity of anastomotic stoma to reduce the occurrence of PF, thus the goal of early prevention and early treatment for PF can be reached, which can improve the prognosis for patients after PD.

## References


[1] Zhang B, Abula Y, Yi C. Risk factors for pancreatic fistula after pancreaticoduodenectomy. *Chin J Dig Surg* 2015; **24**(3): 327-331.

[2] Shen YF, Jin W. Reconstruction by Pancreaticogastrostomy versus pancreaticojejunostomy following pancreaticoduodenectomy: A meta-analysis of randomized controlled trials. *Gastroenterol Res Pract* 2012; 2012:627095.

[3] Wu MP, Zhang X, Liu XJ, et al. Pancreatic duct diameter and pancreatic gland thickness measured using preoperative CT imaging in predicting pancreatic fistula following pancreaticoduodenectomy. *Chin J Bases Clin General Surg* 2014; **21**(8): 1019-1023.

[4] Ridolfi C, Angiolini MR, Gavazzi F, et al. Morphohistological features of pancreatic stump are the main determinant of pancreatic fistula after pancreatoduodenectomy. *Biomed Res Int* 2014; **17**(5): 101-106.

[5] Ma BQ, Zhang S, Zhang B, et al. Clinical analysis of 34 cases with bleeding after pancreatoduodenectomy. *Chin J Hepatobil Surg* 2012; **18**(12): 908-911.

[6] Chen Y, Ke N, Tan C, et al. Continuous versus interrupted suture techniques of pancreaticojejunostomy after pancreaticoduodenectomy. *J Surg Res* 2015; **193**(2): 590-597.

[7] He Y, Zhou WC, Zhang H, et al. Research development of the prevention of pancreatic fistula after pancreaticoduodenectomy. *Chin J Bases Clin General Surg* 2015; **22**(12): 1530-1534.

[8] Liu QY, Li L, Xia HT, et al. Risk factors for pancreatic fistula after pancreaticoduodenectomy. *Acad J Pla Postgrad Med School* 2014; **35**(11): 1109-1115.

[9] Chen JY, Feng JW, Xian Q, et al. Analysis of the risk factors for pancreatic fistula after pancreaticoduodenectomy. *Chin J Curr Adv General Surg* 2015; **18**(3): 192-195.

[10]u N, Guo WD, Wu LQ, et al. Analysis of the risk factors for pancreatic fistula after pancreaticoduodenectomy. *Chin J Bases Clin General Surg* 2015; **22**(8): 967-971.