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A Predictive Risk Scoring System for Clinically Relevant Pancreatic Fistula After Pancreaticoduodenectomy

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

BC 1,2 **Wuzheng Xia***
BC 2 **Yu Zhou***
BC 2 **Ye Lin***
BF 2 **Min Yu**
BDF 2 **Zi Yin**
F 2 **Xin Lu**
F 2 **Baohua Hou**
AE 1,2 **Zhixiang Jian**

1 Southern Medical University, Guangzhou, Guangdong, P.R. China
2 Department of General Surgery, Guangdong General Hospital, Guangdong Academy of Medical Sciences, Guangzhou, Guangdong, P.R. China

* These authors contributed equally to this paper

Corresponding Author: Zhixiang Jian, e-mail: jianzx_118@163.com

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Background: Postoperative pancreatic fistula remains a challenge after pancreaticoduodenectomy (PD). This study aimed to establish a scoring system to predict clinically relevant postoperative pancreatic fistula (CR-POPF) after PD.

Material/Methods: The clinical records of 361 consecutive patients who underwent PD between 2009 and 2017 were reviewed retrospectively. Patients were divided into a study group (225 patients) and a validation group (136 patients). CR-POPF was defined and classified based on the 2016 ISGPS definition and classification system. Univariate and multivariate logistic regression analyses were performed and we thus developed a scoring system based on the regression coefficient of the multivariate logistic regression model. The predictive value was determined using the receiver operating characteristic (ROC) curve.

Results: A predictive scoring system with a maximum of 6 points for CR-POPF was established using the following 4 factors: 1 point for soft pancreatic texture (OR 2.09, 95%CI 1.10–3.98, P=0.025), 1.5 points for main pancreatic duct diameter ≤2.5 mm (OR 2.72, 95%CI 1.23–5.99, P=0.013), 0.5 points for extended lymphadenectomy (OR 1.57, 95%CI 1.13–2.18, P=0.007), 0.5 points for a 25–30 g/L postoperative day 1 serum albumin (OR 1.43, 95%CI 1.02–2.00, P=0.037), and 3 points for postoperative day 1 serum albumin ≤25 g/L (OR 5.12, 95%CI 1.82–14.41, P=0.002). The ROC curve showed that this scoring system was highly predictive for CR-POPF in the validation group (AUC=0.806, 95%CI: 0.735–0.878).

Conclusions: This 6-point risk scoring system will be useful for perioperative risk management of CR-POPF.

MeSH Keywords: **Pancreatic Fistula • Pancreaticoduodenectomy • Risk Assessment**

Abbreviations: **POPF** – postoperative pancreatic fistula; **CR-POPF** – clinically relevant postoperative pancreatic fistula; **POD** – postoperative day; **Alb** – albumin; **OR** – odds ratio; **CI** – confidence interval; **ROC** – receiver operating characteristic; **AUC** – area under the curve

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Background

Pancreaticoduodenectomy (PD) is associated with high postoperative morbidity. Despite improvement in surgical techniques, instruments, and perioperative management, postoperative pancreatic fistula (POPF) still remains the major complication and a challenging event in patients undergoing PD [1]. POPF often leads to increased postoperative morbidity, prolonged hospital stays, increased medical costs, and sometimes to life-threatening complications such as massive abdominal hemorrhages. Despite significant efforts in preventing this problem, the rate of POPF remains essentially unchanged [2,3].

A uniform standard and definition for perioperative complications is crucial for surgical research. The International Study Group for Pancreatic Fistula (ISGPF) first proposed a standardized definition for POPF in 2005 [4]. In the past decade, some risk factors for POPF has been identified according to the 2005 grading system, such as sex, body mass index, status of the pancreatic parenchyma, diameter of the main pancreatic duct, kind of diseases, and bile juice infection [5,6]. However, despite the widespread use of the 2005 classification in the majority of published studies, several limitations still exist. For example, the definition of grade A POPF was considered too broad and lacks clinical consequences. The reported rates of grade A POPFs in the published literatures range from almost 0% to 50%, suggesting its rate was either over- or under-estimated in past researches [7,8]. Additionally, there is a lack of clear classification of POPF as grade B or C when requiring an "invasive procedure" due to the presence of a "grey area" in the 2005 classification regarding whether the presence of some clinical procedures should move the grade of POPF from grade B to grade C [9,10].

In order to clarify and further refine the classification, the ISGPF revised the 2005 POPF definition and published the 2016 classification and grading of POPF [11]. A new concept of "biochemical leak (BF)" replaced the former grade A POPF. The grade A POPF is no longer considered a true pancreatic fistula because it has no clinical importance. In addition to a more accurate distinction between the grades B and C, the new 2016 classification stresses that a true POPF should have an impact on the clinical invention and outcome of the patient. To be defined strictly as a POPF, this condition needs to be clinically relevant. A clinically relevant postoperative pancreatic fistula (CR-POPF) is now redefined as a drain output of any measurable volume of fluid with an amylase level >3 times the upper limit of institutional normal serum amylase activity, associated with a clinically relevant development/condition related directly to the postoperative pancreatic fistula [11].

Recent large-scale studies clarified the reliability of the new definition and revealed it could better stratify distinct conditions that differ in clinical and economic outcomes [12,13]. However, there have been no reports on the risk factors related to CR-POPF based on the new definition. The aim of the present study was to identify perioperative risk factors of CR-POPF in a retrospective cohort of 225 patients undergoing pancreaticoduodenectomy in a single center.

Material and Methods

Patients and data

We retrospectively examined our prospectively maintained database of 361 consecutive patients who underwent PD at Guangdong General Hospital between January 01, 2009 and December 31, 2017. The 225 consecutive patients who underwent PD between January 01, 2009 and November 31, 2015 were assigned to the study group and the other 136 consecutive patients who underwent PD between December 01, 2015 and December 31, 2017 were assigned to the validation group.

The primary outcome, CR-POPF, was defined in accordance with the updated 2016 ISGPF consensus guidelines. Postoperative outcomes were analyzed with regards to POPF occurrence and its management, organ failure, mortality through 90 days after the operation, the occurrence of major surgical complications [Clavien-Dindo (CD) >3], postoperative mortality, length of hospital stay, and overall hospitalization costs. Demographic and preoperative clinical data were collected and were used to construct a predictive scoring model to predict the risk of CR-POPF after PD. The data obtained from the validation group were used for the internal validation of the predictive scoring model. The study was approved by the Medical Ethics Review Committee of Guangdong General Hospital.

Surgical procedures for PD

There were 7 surgeons who performed PD during this period, and surgical technique was largely performed by standard procedures. Generally, the operation was performed by using either classic PD or pylorus-preserving PD (PPPD) techniques. End-to-side, mucosa-mucosa anastomosis was the first choice for pancreaticojejunostomy. The pancreatic duct stent was not routinely used. In cases of very narrow pancreatic duct, or if it was impossible to expose the pancreas, an end-to-end pancreaticojejunostomy was performed. Usually, 3 abdominal drainage tubes were applied. One drainage tube was placed near the site of bile duct anastomosis, and the other 2 tubes were placed near the site of the pancreatic anastomosis. The techniques used primarily included both the classic PD and PPPD. During 2009–2015, the pancreatic resection volume remained stable. During the study period, there was a transition from classic Whipple operations to PPPD.

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Table 1. Patient characteristics for 361 patients underwent pancreaticoduodenectomy.

	N	%
Age (years, mean ± sd.)	58.2±12.2	
Gender		
Male	216	59.8
Female	145	40.2
Disease		
Pancreatic ductal adenocarcinoma	92	25.5
Bile duct cancer	22	6.1
Ampullary cancer	102	28.3
Duodenal neoplasm	62	17.2
IPMN	5	1.4
PNET	23	6.4
Pancreatic serous cystadenoma	6	1.7
Papillary mucinous cystadenoma	3	0.8
Chronic pancreatitis	16	4.4
Others	30	8.3
Pathology		
Malignant	308	85.3
Benign	53	14.7

sd – standard deviation; IPMN – intraductal papillary mucinous neoplasm; PNET – pancreatic neuroendocrine tumors.

Statistical analysis

Statistical analyses were performed using SPSS Statistics for Windows version 17.0 (IBM Corp., Armonk, NY) and R for Windows version 3.4.1. Categorical variables were analyzed using the Chi-squared test and continuous variables were analyzed using the *t* test. Multivariate analysis was done for all variables with P values of less than 0.1 by univariate analysis with a logistic regression analysis. Receiver operating characteristic (ROC) curves and the corresponding area under the curve (AUC) were used to evaluate how the prediction model performed on the test data. A P value of less than 0.05 was considered statistically significant.

Results

Patients' characteristics

Table 1 summarizes the demographic character of all 361 patients. The mean age of included patients was 58.2±12.2 years, 59.8% were male, and 40.2% were female. One hundred ninety-one (85.3%) patients underwent pancreaticoduodenectomy for malignant diseases and 34 (14.7%) patients underwent pancreaticoduodenectomy for benign diseases. Serious (grades III–V) complications occurred in 101 patients (28.0%). Clinically relevant pancreatic fistulas (CR-POPF) were documented in 40 (POPF grade B occurred in 30 and POPF grade C occurred in 10) patients in the study group and in 21 (POPF grade B occurred in 16 and POPF grade C occurred in 5) patients in the validation group.

Univariate and multivariate analyses of clinical variables in relation to CR-POPF after pancreaticoduodenectomy

Table 2 lists the relationship between perioperative clinical variables and CR-POPF after pancreaticoduodenectomy based on the data of the study group. In univariate analysis, the main pancreatic duct diameter (MPD) (P=0.008), soft pancreas (P=0.019), intraoperative blood loss (P=0.011), extended lymphadenectomy (P=0.022), and serum albumin of the first postoperative day (postoperative day 1 albumin) (P=0.001) were significantly higher in patients with CR-POPF. The following factors were entered into the multivariate analysis since the P values were found to be less than 0.1 in univariate analysis: the MPD, pancreas thickness, pancreas texture, intraoperative blood loss, extended lymphadenectomy, and postoperative day 1 albumin. As shown in Table 3, multivariate logistic regression analysis identified pancreas texture (soft versus hard: OR 2.09, 95%CI 1.10-3.98, P=0.025), MPD (≤2.5 mm versus >2.5 mm, OR 2.72, 95%CI 1.23–5.99, P=0.013), extended lymphadenectomy (Yes versus No, OR 1.57, 95%CI 1.13–2.18, P=0.007), and postoperative day 1 serum albumin (≤25 g/L versus >30g/L, OR 5.12, 95%CI 1.82-14.41, P=0.002; 25–30 g/L versus >30 g/L, OR 1.43, 95%CI 1.02–2.00, P=0.037) were independent risk factors for CR-COPF.

The logistic regression model provided the estimated probability of CR-POPF after pancreaticoduodenectomy. This probability was equal to $y=1/(1+e^{-Z})$, where e is the base value of natural logarithms (a mathematical constant, ≈2.718281828459), and Z=–5.367+0.992×pancreas texture (0, hard pancreas; 1, soft pancreas) +1.421×MPD (0, >2.5 mm; 1, ≤2.5 mm) +0.587×extended lymphadenectomy (0,No; 1, Yes) +(3.87×albumin (0, >30 g/L; 1, ≤25 g/L) or 0.419×albumin (0, >30 g/L; 1, 25–30 g/L)).

We developed a score using variables based on the regression coefficient of the logistic regression model (Table 4). The equation for the scoring system was calculated on the assumption that a patient receives 1 point for a soft pancreas, 1.5 points for MPD ≤2.5 mm, 0.5 points for extended lymphadenectomy, 3 points for postoperative day 1 albumin ≤25 g/L, and 0.5 points for albumin 25–30 g/L. The predictive value of this scoring system was also assessed in a validation group. The comparison

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Table 2. Univariate analyses of factors associated with CR-POPF after pancreaticoduodenectomy in the study group.

Factor	Patients without CR-POPF (n=185)	Patients with CR-POPF (n=40)	P value
Age (years, mean ±sd.)	57.7±12.5	60.2±9.8	0.245
Gender			0.801
Male	107	24	
Female	78	16	
History of diabetes			0.376
Yes	15	5	
No	170	35	
Jaundice			0.158
Yes	100	30	
No	85	10	
ASA-PS			
1	57	9	
2 or 3	128	31	
Disease			0.341
Malignant	159	32	
Benign	26	8	
Relation to portal vein on CT			0.271
Involved portal vein	17	6	
Away from portal vein	168	34	
MPD diameter (mm, mean ±sd.)	3.65±2.36	2.70±1.60	0.008
Pancreas thickness (mm, mean ±sd.)	13.10±1.36	13.92±1.71	0.081
Pancreas texture			0.019
Soft	65	22	
Hard	120	18	
Blood loss (ml, mean ±sd.)	355.83±390.73	589.66±520.54	0.011
Operation time (min, mean ±sd.)	426.21±106.82	439.74±99.57	0.261
Procedure			0.837
PD	21	5	
PPPD	164	35	
Extended lymphadenectomy			0.022
Yes	38	15	
No	147	25	
Pncreaticojejunostomy			0.360
Duct-to-mucosa	121	22	

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Table 2 continued. Univariate analyses of factors associated with CR-POPF after pancreaticoduodenectomy in the study group.

Factor	Patients without CR-POPF (n=185)	Patients with CR-POPF (n=40)	P value
Dunking method	57	15	
Others	7	3	
Pancreatic duct stent			0.345
Internal stent	64	17	
None	121	23	
Preoperative CA19-9	180.56±289.46	192.91±269.35	0.805
Preoperative CA125	20.52±19.86	17.06±10.24	0.310
Preoperative CEA	4.92±11.36	5.69±10.20	0.691
Albumin			
Preoperative	32.9±6.1	32.7±4.8	0.898
Postoperative Day 1	25.9±4.96	23.8±4.04	0.001
Total bilirubin			
Preoperative	147.69±141.36	169.06±143.43	0.389
Postoperative Day 1	124.24±126.96	155.92±105.26	0.143
Direct bilirubin			
Preoperative	83.01±79.77	96.24±78.33	0.347
Postoperative Day 1	68.36±73.56	82.82±62.15	0.250
Hemoglobin			
Preoperative	119.34±19.04	120.18±18.66	0.799
Postoperative Day 1	114.66±75.98	105.69±14.02	0.460
White blood cell			
Preoperative	7.16±2.59	6.99±2.08	0.696
Postoperative Day 1	13.26±4.40	13.80±4.91	0.498
Platelet			
Preoperative	278.62±93.00	297.58±99.73	0.251
Postoperative Day 1	251.36±93.69	262.91±101.69	0.488
Blood glucose			
Preoperative	6.16±2.42	5.92±1.54	0.545
Postoperative Day 1	10.97±10.05	11.09±4.65	0.941
PT			
Preoperative	14.22±1.51	12.81±1.81	0.447
Postoperative Day 1	14.68±1.32	13.27±1.92	

sd – standard deviation; BMI – body mass index; PT – prothrombin time; Na – natrium; K – kalium; Mg – magnesium; Ca – calcium; MPD – main pancreatic duct diameter; ASA-PS – American Society of Anesthesiologists-physical status.

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Table 3. Results of multivariate analysis of factors predicting CR-POPF.

Variable	Category	OR	95%CI	P value
Pancreas texture	Soft versus Hard	2.09	1.10–3.98	0.025
MPD	≤2.5 mm versus >2.5 mm	2.72	1.23–5.99	0.013
Extended lymphadenectomy	Yes versus No	1.57	1.13–2.18	0.007
Postoperative day 1 serum ALB	≤25 g/L versus >30 g/L	5.12	1.82–14.41	0.002
Postoperative day 1 serum ALB	25–30 g/L versus >30 g/L	1.43	1.02–2.00	0.037

MPD – main pancreatic duct diameter; ALB – albumin; Mg – magnesium.

Table 4. Score of each variable in the predictive scoring system for pancreatic fistula.

Variables	Points
Pancreas texture	
Soft pancreas	1
Hard pancreas	0
MPD	
≤2.5 mm	1.5
>2.5 mm	0
Extended lymphadenectomy	
Yes	0.5
No	0
Postoperative day 1 albumin	
≤25 g/L	3
25–30 g/L	0.5
>30 g/L	0

between characteristics of patients are shown in Table 5. As shown in Figure 1, the ROC curves based on the above scoring system show that the area under the curve (AUC) was 0.813 (95%CI: 0.737–0.889) in the study group (AUC1) and 0.806 (95%CI: 0.735–0.878) in the validation group (AUC2), respectively. The high AUC value in the validation group suggested that this scoring system was highly predictive of CR-POPF. Based on the sensitivities and specificities of every score, we concluded that a score ≥4.5 could be used as a threshold to identify patients with high risk of developing CR-POPF.

Discussion

Postoperative PF (POPF) after pancreatic surgery remains a challenging event in high-volume pancreatic centers. Currently, a variety of risk factors related to POPF have been identified, such as sex, pancreatic texture, body mass index, and MPD. The 2016 new definition and grading of POPF by ISGPF highlighted the concept that the fistula must be a clinically relevant condition. Prediction of CR-POPF remains controversial, and many studies focused on preoperative factors but only few studies take into account postoperative factors. In the present study, we searched both preoperative and postoperative risk factors for the development of CR-POPF, and found that soft pancreatic texture, MPD, extended lymphadenectomy, and postoperative serum albumin were independent risk factors related to CR-POPF. These findings characterized a high-risk patient group for CR-POPF after pancreaticoduodenectomy.

Soft pancreatic texture and low serum albumin have been accepted as significant risk factors for POPF. In this study, both soft pancreas and postoperative serum albumin were identified as independent factors related to CR-POPF. Patients with a soft pancreas usually have a smaller pancreatic duct diameter and a larger parenchymal thickness than those with a hard pancreas. Histologic evaluation of soft pancreas showed a larger area of the cut surface, a smaller fibrosis ratio, and a larger lobular ratio.14 Decreased fibrosis in pancreatic tissue is associated with increased exocrine activity [15,16] Additionally, a fatty pancreas might be more friable and is more easily disrupted during anastomosis than is a hard pancreas [17]. Relles et al. reported that hypoalbuminemia on postoperative day 1 was an independent predictive marker for complications after pancreaticoduodenectomy, which was consistent with our findings. Serum albumin is associated with nutritional status, and hypoalbuminemia is often associated with protein turnover and poor tissue healing, which attributes to anastomotic leakage [18–20].

Extended lymphadenectomy has not been investigated previously as a risk factor for PF after PD. In an earlier study, Yeo et al. [21] reported that periampullary adenocarcinoma patients undergoing radical pancreaticoduodenectomy (with the addition of a distal gastrectomy and extended retroperitoneal lymphadenectomy to a standard pancreaticoduodenectomy) had a significantly higher incidence of pancreatic fistula when comparing the standard

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Table 5. Comparison of the characters between the study group and the validation group.

Factor	Patients without (n=225)	Patients with (n=136)	P value
Age (years, mean ±sd.)	58.1±12.1	58.3±12.5	0.986
Gender			0.422
Male	131	85	
Female	94	51	
History of diabetes			0.273
Yes	20	17	
No	205	119	
Jaundice			0.447
Yes	130	73	
No	95	63	
ASA-PS			0.987
1	66	40	
2 or 3	159	96	
CR-POPF			0.918
Grade B	30	16	
Grade C	10	5	
Disease			0.767
Malignant	191	117	
Benign	34	19	
Relation to portal vein on CT			0.282
Involved portal vein	23	19	
Away from portal vein	202	117	
MPD diameter (mm, mean ±sd.)	3.48±2.27	3.50±2.63	0.906
Pancreas thickness (mm, mean ±sd.)	13.25±1.46	13.21±1.81	0.879
Pancreas texture			0.153
Soft	87	63	
Hard	138	73	
Blood loss (ml, mean ±sd.)	397.40±424.98	367.25±390.77	0.671
Operation time (min, mean ±sd.)	428.62±105.48	409.46±112.58	0.779
Procedure			0.004
PD	26	5	
PPPD	199	131	
Extended lymphadenectomy			0.868
Yes	53	31	
No	172	105	

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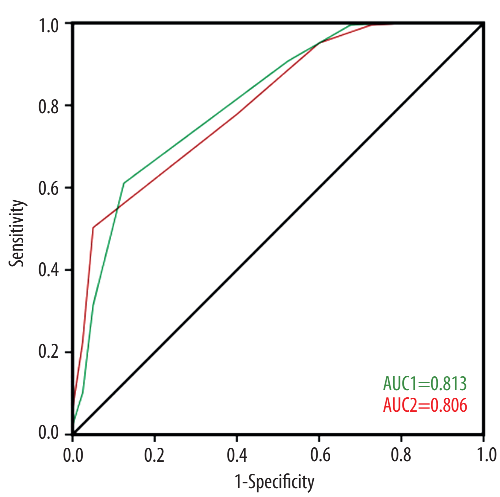
Table 5 continued. Comparison of the characters between the study group and the validation group.

Factor	Patients without (n=225)	Patients with (n=136)	P value
Pncreaticojejunostomy			0.001
Duct-to-mucosa	143	131	
Dunking method	72	0	
Others	10	5	
Pancreatic duct stent			0.163
Internal stent	81	59	
None	144	77	
Albumin			
Preoperative	32.9±5.9	35.2±5.1	0.023
Postoperative Day 1	25.5±4.9	29.8±4.8	0.001
Hemoglobin			
Preoperative	119.49±18.93	121.36±19.52	0.516
Postoperative Day 1	105.69±69.20	111.66±21.37	0.298
White blood cell			
Preoperative	7.13±2.50	7.06±2.73	0.812
Postoperative Day 1	13.36±4.49	13.47±5.62	0.701
Platelet			
Preoperative	281.99±94.28	287.71±96.43	0.834
Postoperative Day 1	253.41±95.03	249.61±97.29	0.912



Scores	AUC1: The study group		AUC2: The validation group	
	Sensitivity	Specificity	Sensitivity	Specificity
0.5000	0.000	1.000	1.000	0.000
1.0000	1.000	0.000	1.000	0.025
1.5000	1.000	0.050	1.000	0.075
2.0000	1.000	0.075	1.000	0.125
2.5000	1.000	0.150	1.000	0.200
3.0000	1.000	0.250	0.995	0.275
3.5000	0.995	0.325	0.951	0.400
4.0000	0.908	0.475	0.778	0.600
4.5000	0.611	0.875	0.503	0.950
5.0000	0.314	0.950	0.227	0.975
5.5000	0.103	0.975	0.059	1.000
6.0000	0.022	1.000	0.011	1.000

Figure 1. Two receiver operating characteristic (ROC) curves for the estimated probability of CR-POPF calculated based on the scoring system. The area under the curve for the study group (AUC1) was 0.813 (95%CI: 0.737–0.889) and the area under the curve for the validating group (AUC2) was 0.806 (95%CI: 0.735–0.878).

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Table 6. Comparison between the present scoring system and existing scoring systems.

Score system	Scoring factors	Population	AUC*
The present study	9, 10, 12, 13	Pancreatoduodenectomy	0.806
Gaujoux et al. [24]	4, 14, 15	Pancreatoduodenectomy	0.801
Wellner et al. [25]	1, 3, 5, 6, 7	Pancreatoduodenectomy	0.656
Callery et al. [26]	7, 8, 9, 10	Pancreatoduodenectomy	0.789
Roberts et al. [27]	4, 10	Pancreatoduodenectomy	0.702
Yamamoto et al. [28]	2, 7, 10, 11, 16	Pancreatoduodenectomy	0.734
Belyaev et al. [29]	10, 19	Pancreatoduodenectomy, distal pancreatectomy	NA
Nahm et al. [30]	17	Pancreatoduodenectomy, distal pancreatectomy, central pancreatectomy	NA
Nahm et al. [31]	18	Distal pancreatectomy	NA

1 – age; 2 – gender; 3 – smoking history; 4 – BMI; 5 – weight loss; 6 –, pancreatitis history; 7 – preoperative diagnosis other than pancreatic cancer or chronic pancreatitis; 8 – blood loss; 9 – pancreatic texture; 10 – pancreatic duct diameter; 11 – relation of portal vein to tumor; 12 – extended lymphadenectomy; 13 – serum albumin of postoperative day 1; 14 – pancreatic fibrosis; 15 – presence of fatty pancreas, 16 – intra-abdominal fat thickness; 17 – acinar cell density at the pancreatic resection margin; 18 – intra-operative amylase concentration; 19 – histomorphological features including periductal fibrosis, interlobular fibrosis, intralobular fibrosis, interlobular fat, intralobular fat, signs of chronic pancreatitis, signs of acute pancreatitis, tissue edema. AUC – area under the curve; NA – result was not available due to lack of data. * AUC was obtained by the receiver operating characteristic (ROC) curve analysis in the validation group.

pancreaticoduodenectomy (13% *vs.* 6%; P=0.05). A recent study reported that extended lymphadenectomy was an independent risk factor for clinical pancreatic fistula after distal pancreatectomy [22]. On the other hand, the high morbidity rate also was reported in patients with pancreatic body cancer who underwent extended lymphadenectomy.23 The higher rate of pancreatic fistula in the radical group also is not clearly explainable.

Several scoring systems have been reported before [24–28]. A comparison between the present scoring system and these existing scoring systems in term of CR-POPF based on the validation group is summarized in Table 6. The systems by Yamamoto [28], Wellner [25], and Roberts [27] use easily measurable radiological and demographic variables and may be constructed preoperatively. Preoperative risk stratification has certain advantages, including the opportunity to individualize patient consent, to facilitate training opportunities in low-risk patients, and to select optimal patients for clinical trials. However, due to the exclusion of intraoperative and postoperative factors, the predictive value of preoperative scoring systems might be compromised. Some studies included postoperative pathological factors in their scoring system. For example, Gaujoux et al. [24] proposed a predictive scoring system using BMI, pancreatic fibrosis, and the presence of fatty pancreas. Although their scoring system is quite useful for estimating POPF, it requires pathological examination; therefore, the final score can be delayed until several days after the operation. To address the risk of POPF accurately and quickly, we included preoperative and intraoperative factors, as well as factors on the first postoperative day. Additionally, unlike most other scoring systems, the present study just selected patients with "clinically relevant" pancreatic fistula (ISGPF types B and C), making our scoring system more clinically significant.

Additional scores have been proposed to predict POPF in patients undergoing a general pancreatic resection. Belyaev et al. [29] proposed a scoring system based on histomorphological features of the pancreatic remnant, and Nahm et al30 suggested that acinar cell density in the pancreatic resection margin was significantly associated with POFP for all pancreatic resections. Because the results of histomorphological features and acinar cell density depend on the pathological examination, the final score could be delayed until several days postoperatively, but these pathological parameters showed good predictive value in past studies; they warrant rapid pathological examinations if their predictive value can be firmly established by further studies. Another study, by Nahm et al. [31], reported that intraoperative amylase concentration was significantly correlated with POPF in patients who underwent distal pancreatectomy. Both intraoperative amylase concentration and acinar cell density are unconventional risk factors that were not evaluated in our center before. Further studies are needed to confirm their value in predicting CR-POPF alone or as part of a scoring system.

In the present study, the validation group had a significantly increased rate of PPPD procedure and proportion of

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duct-to-mucosa anastomosis. PPPD is now the first choice in our center, and we use duct-to-mucosa anastomosis as often as we can. The albumin level in the validation group was significantly higher than in the study group. This difference can be explained by the preoperative nutritional assessment and support. Since more than 2 years ago, we started to routinely assess nutritional status by using NRS2002 in patients who were planned to undergo pancreaticoduodenectomy, and the nutritional support treatment was performed in patients with NRS2002 score ≥3. Despite the differences in baseline characteristics of patients in these 2 groups, the AUC in the validation group was 0.806, suggesting the extrapolation of our scoring system is high.

Conclusions

Despite these limitations, this study has developed a novel predictive scoring system for CR-POPF after PD, with good extrapolation ability. This scoring system may help surgeons to identify and control CR-POPF earlier, in order to improve the management of POPF and prevent more severe complications.

Conflicts of interest

None.

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