Digestive Diseases and Sciences (2023) 68:1574–1584
https://doi.org/10.1007/s10620-022-07649-8

ORIGINAL ARTICLE

A Risk Prediction Model for Post-endoscopic Retrograde Cholangiopancreatography Pancreatitis After Stent Insertion for Malignant Biliary Obstruction: Development and Validation

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Received: 27 January 2022 / Accepted: 25 July 2022 / Published online: 22 August 2022

Abstract

Objectives Pancreatitis is the most common complication of post-endoscopic retrograde cholangiopancreatography (ERCP). There are currently no prediction models, particularly for post-ERCP pancreatitis (PEP) after biliary stent placement due to malignant biliary obstruction (MBO). To that end, we aim to develop and validate a predictive model for PEP.

Methods We retrospectively analyzed the data of patients who underwent ERCP for biliary stent placement due to MBO at the Second Affiliated Hospital of Harbin Medical University from January 1, 2014 to August 31, 2021. The eligible patients were randomly allocated to the development and validation cohorts. A prediction model was built using the development cohort, and the model's effect was validated using a validation cohort.

Results A total of 1524 patients were enrolled, including 1016 in the development cohort and 508 in the validation cohort, with an overall PEP rate of 7.1%. The model's predictors included acute pancreatitis history, the absence of pancreatic duct dilation, nonpancreatic cancer, difficult cannulation, and pancreatic injection. The area under the curve (AUC) in the development cohort was 0.810, and the incidence of PEP in the low-risk, medium-risk, and high-risk groups was 1.53%, 9.12%, and 36.36%, respectively. Meanwhile, the AUC of the validation cohort was 0.781, and the incidence of PEP in the low-risk, medium-risk, and high-risk groups was 4.17%, 8.75%, and 41.67%, respectively.

Conclusions This study was the first to build and validate a risk prediction model, especially for PEP after biliary stent placement due to MBO. Moreover, this model might assist clinicians in identifying high-risk patients and help implement preventive measures in a more timely manner.

Keywords Malignant biliary obstruction (MBO) · Endoscopic retrograde cholangiopancreatography (ERCP) · Post-ERCP pancreatitis (PEP) · Risk factors · Prediction model

Introduction

Malignant biliary obstruction (MBO) is commonly caused by pancreatic cancer, cholangiocarcinoma, ampullary cancer, gallbladder cancer, and hepatocellular cancer, to name a few. MBO causes pruritus, weight loss, abdominal discomfort or pain, and obstructive jaundice, and it can be complicated by severe cholangitis, sepsis, or liver failure, all of which have a negative impact on the patient's survival and quality of life [1, 2]. Unfortunately, many patients are deemed unfit for surgery when they are diagnosed. Biliary stent placement for MBO via endoscopic retrograde cholangiopancreatography (ERCP) is widely accepted as the first-line palliative strategy, helping improve affected patients' quality of life [3]. However, the procedure can occasionally result in serious, even fatal, adverse events, the most common and feared of which is post-ERCP pancreatitis (PEP). According to previous reports, the rate of PEP after stent insertion for MBO ranges from 1.3 to 26.8%, with the incidence of bleeding (including early bleeding and delayed bleeding) ranging between 0.5 and 5.1%, while the incidence of perforation is less common with a rate of 0.3% to 2% [4–12]. Notably, the management of MBO is different in malignant versus benign disorders. In MBO treatment, radical surgery will be performed if the tumor is resectable.

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If the tumor has metastasized or the patient's condition does not allow for radical operation, palliative care is given instead. Palliative surgery includes cholecystogastrostomy, hepaticojejunostomy, cholecystojejunostomy, and choledochoduodenostomy. However, as preoperative imaging and interventional surgery have improved, the rate of palliative surgery has decreased. The most widely used palliative treatment is the placement of a self-expandable metal stent (SEMS) via ERCP. Other treatment options, such as EUS-guided biliary drainage and percutaneous biliary drainage, are also widely used for palliative treatment [1, 13, 14]. For benign biliary obstruction, inserting SEMS via ERCP is highly recommended. Surgery or percutaneous transhepatic biliary drainage (PTBD) may be considered for patients who are not candidates for stent placement [15, 16].

To prevent or decrease the occurrence of PEP, it is essential to recognize the risk factors of PEP. PEP risk factors include patient and procedure-related risk factors, such as female gender, history of pancreatitis, younger age, difficult cannulation, repetitive pancreatic guidewire cannulation, and pancreatic injection [17–19]. Since the etiology, clinical features, and therapeutic strategy of MBO differ from those of other biliopancreatic diseases, the risk factors for PEP in MBO patients may differ from those previously reported. Recently, several risk prediction models for predicting the occurrence of PEP have been developed [20–23]. Nevertheless, no prediction models exist for PEP after biliary stent placement due to MBO. As a result, we aim to build and validate a predictive model for it.

Methods

Patients

Radical surgery was conducted at our center if the tumor was resectable in MBO patients; otherwise, palliative treatment was given. We first considered biliary stent placement via ERCP for palliative treatment, while SEMS was the first choice for patients with an expected survival of more than 3 months. If these procedures were unsuccessful, PTBD would be performed instead. Chemotherapy, radiotherapy, transarterial chemoembolization (TACE), and transarterial radioembolization (TARE) could be used in conjunction with the above treatments. Patients who underwent biliary stent insertion for MBO via ERCP from January 1, 2014, to August 1, 2021 were identified retrospectively at the Second Affiliated Hospital of Harbin Medical University. MBO was diagnosed based on clinical, laboratory, radiological, and pathological examinations. All included patients underwent palliative treatment. The exclusion criteria were as follows: (1) non-native papilla, (2) ongoing acute pancreatitis, (3) failed operation, (4) age < 18, (5) replacement of stent, and (6) incomplete medical record. Before the procedure, all patients undergoing ERCP at our hospital were given rectal nonsteroidal anti-inflammatory drugs (NSAIDs). All procedures were carried out by experienced endoscopists who have completed over 200 cases in our hospital. The endoscopist was in charge of deciding which type of stent to use during the procedure. The study adhered to the Helsinki Declaration's ethical principles. The Medical Ethics Committee of the Second Affiliated Hospital of Harbin Medical University approved this data-only retrospective study. Informed consent was not required because of the retrospective nature of the study.

Data Collection

We collected two types of data: (1) Patient-related data which included gender, age, hypertension, cholecystectomy, gastrectomy, diabetes, history of chronic pancreatitis, history of acute pancreatitis, total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), aspartate aminotransferase (AST), γ-glutamyl transferase (GGT), alanine aminotransferase (ALT), white blood cell (WBC), pancreatic duct (PD) diameter, common bile duct (CBD) diameter, cancer type, location of stricture, and periampullary diverticulum. (2) Procedure-related data included difficult cannulation, pancreatic injection, stent type, endoscopic sphincterotomy (EST), precut sphincterotomy, PD stenting, and double guidewire technique. Although SOD has been proposed as an independent risk factor for PEP, the disease entity is uncommon in Asian populations, so we did not include it in our study [22].

Definitions

The diagnosis of PEP conformed to Cotton's criterion: new or worsening abdominal pain continuing for at least 24 h after ERCP, with elevated serum amylase levels three times the normal upper limit or higher [24]. Computed tomography (CT) was performed for all patients suspected of PEP to confirm the diagnosis radiologically. The revised Atlantic classification defined the severity of PEP: (1) mild: no organ dysfunction and other complications, (2) moderate: transient organ failure < 48 h or local or systemic complications, and (3) severe: persistent single or multi-organ failure > 48 h [25]. Difficult cannulation was defined as more than five cannulation attempts or a long cannulation time (> 10 min). PD dilation was defined as PD maximum diameter ≥ 4 mm in the preoperative imaging examinations (ultrasound, CT, MRCP), and CBD dilation was defined as CBD maximum diameter of ≥ 8 mm. In our study, the definition of the distal bile duct was the common bile duct located downstream of the cystic duct confluence, and the definition of the hilar bile duct was the bile duct located upstream of the cystic duct. The diagnosis of cholangitis is based on

the Tokyo Guidelines 2018 [26]. ECOG criteria were used to assess the performance status of patients, patients with 0 points were assigned to group 1, patients with 1–2 points were assigned to group 2, and patients with 3–4 points were classified into group 3 [27].

Statistical Analysis

We allocated eligible patients to the development and validation cohorts at a ratio of 2:1 randomly. According to the optimal sensitivity and specificity, continuous variables were dichotomized based on the cutoff value of each indicator [28]. Categorical variables were presented as frequency and were compared between groups using the Chi-square test.

To develop the prediction model, logistic regression analysis was used to evaluate the risk factors of PEP in the development cohort. Variables with P values < 0.05 in the univariable logistic regression model were selected as covariates in the multivariable analysis. Variables with P values < 0.05 in the multivariable analysis were selected as predictors in the risk prediction model. Each predictor was assigned a score. Scores were calculated by dividing each predictor's regression coefficient by the smallest one in the model and rounding it to the nearest integer. A patient's total risk score was calculated by adding each predictor's score. Then, the total risk score of each patient was calculated in both the development and validation cohorts. According to the total risk score, patients were allocated to the low-risk group (0–1 points), medium-risk group (2–3 points), and high-risk group (≥ 4 points).

The area under the receiver operating characteristics (ROC) curve (AUC) was used to evaluate the discrimination of the prediction model. Calibration is another measure of prediction model performance used to test how well the predicted results match the actual results. The actual rate of PEP was calculated in the three different risk groups, respectively. The predicted rate of PEP for each group was calculated by the model regression formula and was presented as the mean predicted rate and the standard deviation (SD). Then, the predicted rate was compared with each group's actual rate to verify the model's calibration. Hosmer–Lemeshow (H–L) test was also used to evaluate the model's goodness of fit. SPSS 24.0 (IBM Corp, USA) was utilized to analyze all the data. P value < 0.05 (two-sided) was considered statistically significant.

Results

Patient Characteristics

A total of 1937 patients who underwent biliary stent insertion for MBO via ERCP were considered. After excluding patients for non-native papilla (104 patients), ongoing acute pancreatitis (3 patients), failed ERCP (45 patients), replacement of stent (204 patients), and incomplete medical records (57 patients), 1524 patients were finally included. 1016 and 508 patients were randomly assigned to the development and validation cohorts, respectively. The baseline information of the included patients is shown in Tables 1, 2, and 3. The proportion of males was 55.5% in the development cohort and 53.3% in the validation cohort ($P = 0.423$). The proportion of patients aged > 65 was 51.7% in the development cohort and 52.0% in the validation cohort ($P = 0.913$). The most common cause of biliary stent placement was pancreatic cancer (72.3% and 76.2%), followed by cholangiocarcinoma (17.8% and 14.0%) and ampullary cancer (8.9% and 8.3%) in the development and validation cohorts. None of the baseline characteristics significantly differed between the development and validation cohorts.

Incidence of PEP and Its Severity

A total of 108 patients developed PEP among the 1524 patients who underwent ERCP, with a rate of 7.1%. Of which, 66 (6.5%) patients had PEP in the development cohort, and 42 (8.3%) had PEP in the validation cohort. According to the revised Atlantic classification, 60 (5.9%) patients had mild, 4 (0.4%) had moderate, and 2 (0.2%) had severe PEP in the development cohort, and 37 (7.3%) patients had mild, 3 (0.6%) had moderate, and 2 (0.4%) had serve PEP in the validation cohort.

Developing the Risk Prediction Model

Univariate analysis was performed to ascertain the potential risk factors related to PEP in the development cohort. In the univariable analysis, age ≤ 65, acute pancreatitis history, the absence of PD dilation, nonpancreatic cancer, difficult cannulation, pancreatic injection, and double guidewire technique were associated with the development of PEP (Table 4). These seven risk factors were included in our multivariate analysis, revealing that acute pancreatitis history (OR = 4.517, 95% CI 1.667–12.245), absence of PD dilation (OR = 2.813, 95% CI 1.519–5.208), nonpancreatic cancer (OR = 2.218, 95% CI 1.210–4.066), difficult cannulation (OR = 5.807, 95% CI 3.237–10.417), and pancreatic injection (OR = 4.365, 95% CI 1.653–11.524) were independent risk factors for the occurrence of PEP (Table 5). As a result, these five independent risk factors were chosen as predictors in the model.

Scores were allocated to each predictor based on their β coefficient. The β coefficient and scores are shown in Table 3. The total risk score of each patient in the development and validation cohorts was calculated by adding up the scores of each predictor. Based on their total risk scores,

Table 1 Demographic parameters of patients in the development and validation cohorts

Factors (%)	Development cohort ($N=1016$)	Validation cohort ($N=508$)	P
Gender			0.423
Male	564 (55.5%)	271 (53.3%)	
Female	452 (44.5%)	237 (46.7%)	
Age			0.913
> 65 years	525 (51.7%)	264 (52.0%)	
≤ 65 years	491 (48.3%)	244 (48.0%)	
PD diameter			0.592
Dilated	676 (66.5%)	331 (65.2%)	
Not dilated	340 (33.5%)	177 (34.8%)	
CBD diameter			0.638
Dilated	816 (80.3%)	402 (79.1%)	
Not dilated	200 (19.7%)	106 (20.9%)	
Cancer type			0.185
Pancreatic cancer	735 (72.3%)	387 (76.2%)	
Cholangiocarcinoma	181 (17.8%)	71 (14.0%)	
Ampullary cancer	90 (8.9%)	42 (8.3%)	
Others	10 (1%)	8 (1.5%)	
Obstruction location			0.569
Distal	875 (86.1%)	432 (85%)	
Hilar	141 (13.9%)	76 (15%)	
Periampullary diverticulum			1
No	940 (92.5%)	470 (92.5%)	
Yes	76 (7.5%)	38 (7.5%)	
Difficult cannulation			0.613
No	764 (75.2%)	388 (76.4%)	
Yes	252 (24.8%)	120 (23.6%)	
Pancreatic injection			0.675
No	986 (97.0%)	491 (96.7%)	
Yes	30 (3.0%)	17 (3.3%)	
Stent type			0.176
PS	215 (21.2%)	121 (23.8%)	
uSEMS	510 (50.2%)	263 (51.8%)	
cSEMS	291 (28.6%)	124 (24.4%)	
EST			0.560
No	456 (44.9%)	220 (43.3%)	
Yes	560 (55.1%)	288 (56.7%)	
Precut sphincterotomy			0.242
No	821 (80.8%)	423 (83.3%)	
Yes	195 (19.2%)	85 (16.7%)	
PD stenting			0.871
No	962 (94.7%)	482 (94.9%)	
Yes	54 (5.3%)	26 (5.1%)	
Double guidewire technique			0.378
No	933 (91.8%)	473 (93.1%)	
Yes	83 (8.2%)	35 (6.9%)	
Papillary balloon dilatation			
No	890 (87.6%)	442 (87.0%)	0.743
Yes	126 (12.4%)	66 (13.0%)	
Emergency ERCP			0.652
No	925 (91.0%)	458 (90.3%)	
Yes	91 (9.0%)	49 (9.7%)	
Performance status			0.560
Group 1	30 (3.0%)	20 (3.9%)	
Group 2	678 (66.7%)	340 (66.9%)	
Group 3	308 (30.3%)	148 (29.1%)	

Table 2 Co-morbidities of patients in the development and validation cohorts

Factors (%)	Development cohort ($N=1016$)	Validation cohort ($N=508$)	P
Diabetes			0.914
No	884 (87.0%)	441 (86.8%)	
Yes	132 (13.0%)	67 (13.2%)	
Hypertension			0.582
No	816 (80.3%)	414 (81.5%)	
Yes	200 (19.7%)	94 (18.5%)	
Cholecystectomy			0.201
No	987 (97.1%)	499 (98.2%)	
Yes	29 (2.9%)	9 (1.8%)	
Gastrectomy			0.103
No	1000 (98.4%)	505 (99.4%)	
Yes	16 (1.6%)	3 (0.6%)	
Chronic pancreatitis history			0.615
No	1003 (98.7%)	503 (99.0%)	
Yes	13 (1.3%)	5 (1.0%)	
Acute pancreatitis history			0.847
No	978 (96.3%)	490 (96.5%)	
Yes	38 (3.7%)	18 (3.5%)	
Cholangitis			0.759
No	16 (1.6%)	8 (1.6%)	
Suspected	769 (75.7%)	393 (77.4%)	
Definite	231 (22.7%)	107 (21.1%)	

patients were classified into three different groups: low-risk (0–1 points), medium-risk (2–3 points), and high-risk (≥ 4 points). Furthermore, each patient's predicted rate was calculated using the model formula and assigned to each patient in both the development and validation cohorts.

Performance of the Model

The H–L test showed good fitness for the model in both development cohort ($\chi^2 = 8.35$, $P = 0.423$) and validation

Table 3 Laboratory parameters of patients in the development and validation cohorts

Factors (%)	Development cohort ($N=1016$)	Validation cohort ($N=508$)	P
TBIL			0.192
> 34.2umol/L	954 (93.9%)	468 (92.1%)	
≤ 34.2umol/L	62 (6.1%)	40 (7.9%)	
DBIL			0.919
> 6.2umol/L	983 (96.8%)	491 (96.7%)	
≤ 6.2umol/L	33 (3.2%)	17 (3.3%)	
ALT			0.759
≤ 40U/L	148 (14.6%)	77 (15.2%)	
> 40U/L	868 (85.4%)	431 (84.8%)	
AST			0.312
≤ 40U/L	114 (11.2%)	66 (13.0%)	
> 40U/L	902 (88.8%)	442 (87.0%)	
GGT			0.827
≤ 60U/L	28 (2.8%)	15 (3.0%)	
> 60U/L	988 (97.2%)	493 (97.0%)	
ALP			0.846
≤ 150U/L	36 (3.5%)	19 (3.7%)	
> 150U/L	980 (96.5%)	489 (96.3%)	
WBC			0.275
$\leq 10\times10^9$/L	829 (81.6%)	426 (83.9%)	
$> 10\times10^9$/L	187 (18.4%)	82 (16.1%)	

cohort ($\chi 2 = 2.17$, $P = 0.714$). The model in the development cohort had an AUC of 0.810 (95% CI 0.751–0.868), while the model in the validation cohort had an AUC of 0.781 (95% CI 0.703–0.858) (Fig. 1).

In both the development and validation cohorts, the mean predicted rate, SD, and the actual rate of PEP were calculated for the three different risk groups. In the development cohort, the actual rates of PEP were 1.53%, 9.12%, and 36.36% in the low-risk, medium-risk, and high-risk groups, respectively. The predicted rates of PEP were $1.83\% \pm 0.92\%$, $8.55\% \pm 3.67\%$, and $36.85\% \pm 15.51\%$ in the low-risk, medium-risk, and high-risk groups, respectively. In the validation cohort, the actual rates of PEP were 4.17%, 8.75%, and 41.67% in the low-risk, medium-risk, and high-risk groups, respectively. Meanwhile, the predicted rates of PEP were $3.32\% \pm 2.49\%$, $11.53\% \pm 7.77\%$, and $36.63\% \pm 15.07\%$ in the low-risk, medium-risk, and high-risk groups, respectively (Fig. 2). Therefore, in each risk group, the actual rate was consistent with the predicted rate, indicating that the model was well calibrated.

In the development cohort, the incidence of PEP was higher in the medium-risk (OR = 6.540, 95% CI 3.050–13.652, $P < 0.001$) and high-risk (OR = 36.762, 95% CI 16.068–84.108, $P < 0.001$) groups compared to the low-risk group. Similarly, in the validation cohort, the incidence of PEP was higher in the medium-risk (OR = 2.205, 95% CI 1.011–4.813, $P = 0.047$) and high-risk (OR = 16.429, 95% CI 6.921–38.999, $P < 0.001$) groups compared to the low-risk group (Table 6).

Discussion

Biliary stent insertion is an important palliative treatment for MBO. PEP is the most common complication, and its incidence is about 1.3% to 26.8% [4–6]. In this study, the overall incidence of PEP was 7.1%, which is within the above-reported range.

In recent years, several risk prediction models have been established for predicting the incidence of PEP [20–23]. Nonetheless, there are no prediction models, especially for PEP after biliary stent placement due to MBO. Therefore, it is necessary to establish a risk prediction model for PEP after biliary stent placement due to MBO to facilitate the risk stratification of patients undergoing this procedure and allow physicians to implement timely preventive measures for high-risk patients. The present study is the first to build and validate a risk prediction model for PEP after biliary stent placement due to MBO. Acute pancreatitis history, the absence of PD dilation, nonpancreatic cancer, difficult cannulation, and pancreatic injection were all identified as risk factors for this procedure. Consistent with the literature, pancreatic injection, acute pancreatitis history, and difficult cannulation are well-known risk factors for PEP [17]. We also found that the absence of PD dilation and nonpancreatic cancer were associated with PEP.

The reason why PD dilation was associated with PEP could be that PD dilation is often characterized by PD hypertension. As a result, the patients may have a high tolerance for increased PD pressure and thus be resistant to PEP [29]. Nonpancreatic cancer has been reported as an independent risk factor for PEP after biliary stent insertion [30, 31], consistent with our findings. In most pancreatic cancer patients, the tumor invaded and dilated the PD. Furthermore, the exocrine function of the pancreas may decrease due to parenchymal atrophy caused by tumor compression. Studies have shown that the volume of pancreatic parenchyma is strongly associated with the occurrence of PEP [32, 33]. This suggests that pre-ERCP graphical evaluation might be useful for predicting PEP after biliary stent insertion for MBO.

Many endoscopists prefer to perform EST before inserting a biliary stent. EST is thought to make biliary stent deployment easier and may lower the risk of PEP by reducing tension at the PD opening [34, 35]. However, whether EST prior to biliary stent placement can prevent PEP is debatable. A meta-analysis that included three randomized controlled trials (RCTs) showed that EST prior to stent placement might effectively reduce the occurrence of PEP

Table 4 Univariate logistic regression analysis in the development cohort

Variables	Number	PEP (%)	OR	95% CI	*P*
Gender					
Male	564	42 (7.4%)	1		
Female	452	24 (5.3%)	0.697	0.414–1.169	0.172
Age					
> 65	525	26 (5.0%)	1		
≤ 65	491	40 (8.1%)	1.702	1.022–2.834	0.041
PD diameter					
Dilated	676	23 (3.4%)	1		
Not dilated	340	43 (12.6%)	4.111	2.433–6.946	< 0.001
CBD diameter					
Dilated	816	47 (5.8%)	1		
Not dilated	200	19 (9.5%)	1.718	0.984–2.998	0.057
Cancer type					
Pancreatic cancer	735	31 (4.2%)	1		
Others	281	35 (12.5%)	3.231	1.950–5.352	< 0.001
Obstruction location					
Distal	875	53 (6.1%)	1		
Hilar	141	13 (9.2%)	1.575	0.835–2.971	0.160
Periampullary diverticulum					
No	940	57 (6.1%)	1		
Yes	76	9(11.8%)	2.081	0.987–4.386	0.054
Difficult cannulation					
No	764	26 (3.4%)	1		
Yes	252	40 (15.9%)	5.356	3.194–8.980	< 0.001
Pancreatic injection					
No	986	56 (5.7%)	1		
Yes	30	10 (33.3%)	8.304	3.710–18.583	< 0.001
Stent type					
PS	215	11 (5.1%)	1		
uSEMS	510	32 (6.3%)	1.242	0.614–2.511	0.547
cSEMS	291	23 (7.9%)	1.592	0.758–3.340	0.219
EST					
No	456	22 (4.8%)	1		
Yes	560	44 (7.9%)	1.682	0.993–2.851	0.053
Precut sphincterotomy					
No	821	49 (6.0%)	1		
Yes	195	17 (8.7%)	1.505	0.846–2.675	0.164
PD stenting					
No	962	64 (6.7%)	1		
Yes	54	2 (3.7%)	0.540	0.129–2.226	0.399
Double guidewire technique					
No	933	56 (6.0%)	1		
Yes	83	10 (12.0%)	2.145	1.051–4.381	0.036
Papillary balloon dilatation					
No	890	56 (6.3%)	1		
Yes	126	10 (7.9%)	1.284	0.637–2.586	0.484
Emergency ERCP					
No	925	59 (6.4%)	1		
Yes	91	7 (7.7%)	1.223	0.541–2.763	0.628
Performance status					
Group 1	30	2 (6.7%)	1		

Table 4 (continued)

Variables	Number	PEP (%)	OR	95% CI	*P*
Group 2	678	38 (5.6%)	0.831	0.191–3.620	0.806
Group 3	308	26 (8.4%)	1.291	0.291–5.726	0.737
Diabetes					
No	884	62 (7.0%)	1		
Yes	132	4 (3.0%)	0.414	0.148–1.158	0.093
Hypertension					
No	816	54(6.6%)	1		
Yes	200	12(6.0%)	0.901	0.472–1.718	0.751
Cholecystectomy					
No	987	62 (6.3%)	1		
Yes	29	4 (13.8%)	2.387	0.807–7.047	0.116
Gastrectomy					
No	1000	63 (6.3%)	1		
Yes	16	3 (18.8%)	3.432	0.953–12.357	0.059
Chronic pancreatitis history					
No	1003	65 (6.5%)	1		
Yes	13	1 (7.7%)	1.203	0.154–9.392	0.860
Acute pancreatitis history					
No	978	58 (5.9%)	1		
Yes	38	8 (21.1%)	4.230	1.856–9.640	0.001
Cholangitis					
No	16	1 (6.3%)	1		
Suspected	769	43 (5.6%)	0.888	0.115–6.884	0.910
Definite	231	22 (9.5%)	1.579	0.199–12.530	0.666
TBIL					
> 34.2umol/L	954	60 (6.3%)	1		
≤ 34.2umol/L	62	6 (9.7%)	1.596	0.661–3.855	0.298
DBIL					
> 6.2umol/L	983	62 (6.3%)	1		
≤ 6.2umol/L	33	4 (12.1%)	2.049	0.698–6.013	0.192
ALT					
≤ 40U/L	148	8 (5.4%)	1		
> 40U/L	868	58 (6.7%)	1.253	0.586–2.681	0.561
AST					
≤ 40U/L	114	10 (8.8%)	1		
> 40U/L	902	56 (6.2%)	0.688	0.341–1.390	0.298
GGT					
≤ 60U/L	28	2 (7.1%)	1		
> 60U/L	988	64 (6.5%)	0.900	0.209–3.879	0.888
ALP					
≤ 150U/L	36	4 (11.1%)	1		
> 150U/L	980	62 (6.3%)	0.540	0.185–1.576	0.260
WBC					
$\leq 10 \times 10^9$/L	829	55 (6.6%)	1		
$> 10 \times 10^9$/L	187	11 (5.9%)	0.880	0.451–1.715	0.706

[36]. In addition, a retrospective study also indicated that EST could prevent PEP in patients with biliary tumors, especially when transpapillary biopsy and intraductal ultrasound were performed [37]. In contrast, some studies reached the opposite conclusions. For instance, Kato et al. revealed that EST prior to biliary stent insertion could not decrease the occurrence of PEP for patients with distal MBO without PD involvement [6]. Moreover, a recent systematic review and

Table 5 Multivariate logistic regression analysis in the development cohort and scoring system

Variables	OR	95% CI	β	P	Scoring
Patient-related					
Age (≤65)	1.294	0.739–2.266	0.258	0.367	
Acute pancreatitis history	4.517	1.667–12.245	1.508	0.003	2
PD diameter (Not dilated)	2.813	1.519–5.208	1.034	0.001	1
Cancer type (Nonpancreatic cancer)	2.218	1.210–4.066	0.797	0.010	1
Procedure-related					
Difficult cannulation	5.807	3.237–10.417	1.759	< 0.001	2
Pancreatic injection	4.365	1.653–11.524	1.474	0.003	2
Double guidewire technique	0.993	0.433–2.279	− 0.07	0.987	

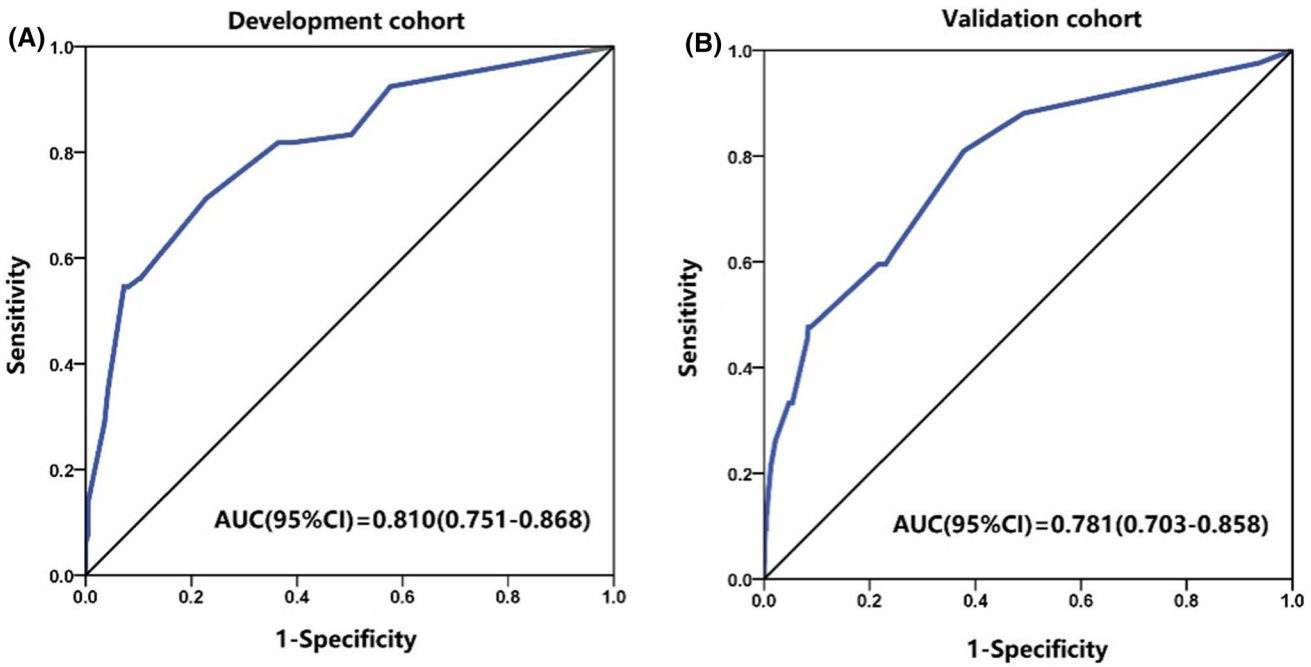

Fig. 1 ROC curves in the **A** development cohort and **B** validation cohort

Fig. 2 The actual and predicted rates PEP in the **A** development cohort and **B** validation cohort

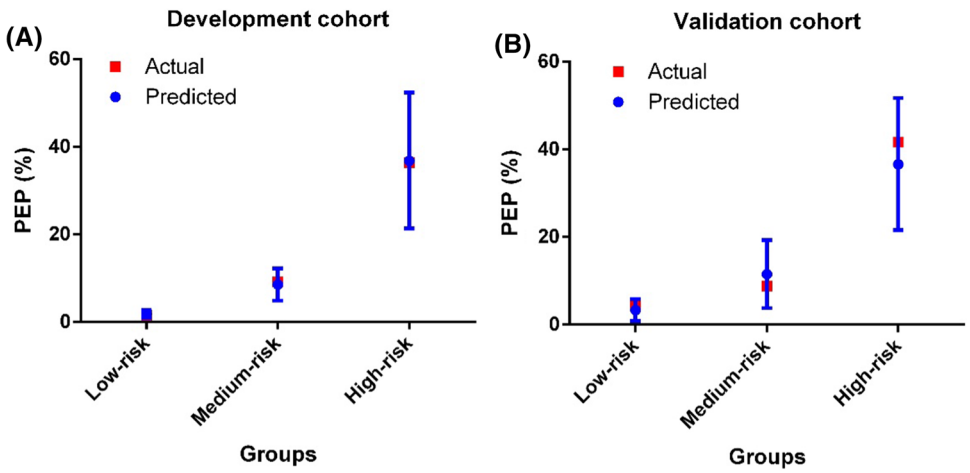

Table 6 PEP rates in different groups

Groups	Number	PEP (%)	OR (95%CI)	*P*
Development cohort				
Low-risk	588	9 (1.53)	1	
Moderate-risk	362	33 (9.12)	6.540 (3.050–13.652)	< 0.001
High-risk	66	24 (36.36)	36.762 (16.068–84.108)	< 0.001
Validation cohort				
Low-risk	312	13 (4.17)	1	
Moderated-risk	160	14 (8.75)	2.205 (1.011–4.813)	0.047
High-risk	36	15 (41.67)	16.429 (6.921–38.999)	< 0.001

meta-analysis by Sofi et al. reported that biliary stent placement without EST was not related to a higher risk of PEP in patients with distal biliary tract obstruction and PD involvement [38]. Our findings were similar to the two previous studies in that we did not find that EST prior to biliary stent placement can prevent PEP. This could be because thermal injury induced by EST can cause edema of the peripapillary tissue, compressing the PD orifice, which may counteract its effect of reducing tension in the PD opening [39]. Given the risks of EST, such as bleeding and perforation, we do not recommend EST for patients with MBO before biliary stent placement.

According to previous studies, SEMS is more likely to cause PEP than plastic stent (PS) because of its larger diameter and higher axial force compressing the opening of the PD, resulting in the obstruction of pancreatic juice outflow [4, 29, 40]. However, the relationship between stent types and PEP remains controversial. Martinez et al. found no difference in PEP rates when using SEMS versus PS for MBO in a recent large retrospective study of 1136 patients [41]. Moreover, in a retrospective study covering the national population in Korea, there was also no significant difference in the incidence of PEP between metal stents and PS [42]. In our study, we found no significant difference in the occurrence of PEP between SEMS and PS and between covered self-expandable metal stent (cSEMS) and uncovered self-expandable metal stent (uSEMS) as well; with many previous studies also confirming our conclusions [43–45]. As a result, we recommend SEMS over PS for the palliative treatment of unresectable MBO because of its longer patency time, lower stent dysfunction, and lower reintervention rates [3].

Nonetheless, our study had several limitations. First, since this was a single-center retrospective study with a relatively small sample size, the generalizability of this risk prediction model may be limited. Therefore, the validity of this model still needs to be verified by large-scale, multicenter prospective studies. Second, since this is a single-center study, the risk prediction model lacked external validation. We also hope that the findings of this study can be replicated in populations outside of China. Third, because of our hospital's current situation and the limitations of retrospective studies, we did not include operator experience or papilla type in the study. Another limitation of our study is that we did not include the outcomes of patients who had PEP.

Despite the limitations mentioned above, this is the first risk prediction model for PEP after biliary stent placement for MBO. Importantly, all risk factors for PEP included in the risk prediction model are routinely available clinical data. As a result, this predictive model can assist clinicians in identifying high-risk patients so that preventive measures can be implemented to reduce the occurrence of PEP.

Declarations

Conflict of interest All of the authors declare no conflict of interest.

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