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ORIGINAL ARTICLE

Post-operative pancreatitis following ERCP and EST in elderly patients with choledocholithiasis

Pancreatitis posoperatoria tras CPRE y EE en pacientes ancianos con coledocolitiasis

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Abstract

Objective: *Herein, we identified risk factors (RFs) for post-operative pancreatitis among elderly sufferers of choledocholithiasis undergoing endoscopic retrograde cholangiopancreatography (ERCP) along with endoscopic sphincterotomy (EST), and to develop a predictive model for pancreatitis occurrence.* **Methods:** *We retrospectively collected clinical data of elderly patients (≥ 65 years old) with choledocholithiasis undergoing ERCP+EST at Affiliated Liupanshui Hospital of Zunyi Medical University from January 2017 to April 2024. Participants were stratified into pancreatitis and non-pancreatitis cohorts according to their post-operative outcomes.* **Results:** *Using multivariate analysis, we determined stand-along RFs for post-operative acute pancreatitis as follows: Age under 75 years, a history of acute pancreatitis, pancreatography, difficult intubation, and multiple guidewire insertions into the pancreatic duct (p < 0.05). The area under the curve of the predictive model was 0.783 (95% confidence interval: 0.705-0.862), indicating good predictive capability. Calibration curves showed consistency between predicted risks and observed outcomes (Hosmer-Lemeshow test, p > 0.05). Clinical decision curves demonstrated the model's clinical utility.* **Conclusions:** *In elderly patients with choledocholithiasis, factors such as younger age (under 75), history of acute pancreatitis, challenging intubation, pancreatography, and multiple guidewire insertions into the pancreatic duct are significant RFs for post-ERCP pancreatitis.*

Keywords: *Endoscopic retrograde cholangiopancreatography. Endoscopic papillary sphincterotomy. Pancreatitis. Risk factor. Nomogram.*

Resumen

Objetivo: *Identificar los factores de riesgo de pancreatitis posoperatoria en ancianos con coledocolitiasis sometidos a colangiopancreatografía retrógrada endoscópica (CPRE) y esfinterotomía endoscópica (EE), y desarrollar un modelo predictivo de pancreatitis.* **Métodos:** *Recopilamos retrospectivamente datos cllos cl de pacientes de edad avanzada (anzadaños) con coledocolitiasis sometidos a CPRE + EE en el Hospital Afiliado Liupanshui de la Universidad Médica de Zunyi, desde enero de 2017 hasta abril de 2024. Los participantes se estratificaron en cohortes con pancreatitis y sin pancreatitis según sus resultados posoperatorios.* **Resultados:** *Mediante un análisis multivariable determinamos los factores de riesgo independientes para la pancreatitis aguda posoperatoria de la siguiente manera: edad < 75 años, antecedentes de pancreatitis aguda, pancreatografía, intubación difícil e inserciones múltiples de guía en el conducto pancreático (p < 0.05). El AUC del modelo predictivo fue de 0.783 (IC 95%: 0.705-0.862), lo que indica una buena capacidad predictiva. Las curvas de calibración mostraron coherencia entre los riesgos predichos y los resultados observados (prueba de Hosmer-Lemeshow, p > 0.05). Las curvas de decisión clínica demostraron la utilidad clínica del modelo.*

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Conclusiones: *En pacientes ancianos con coledocolitiasis, factores como una edad más joven (< 75 años), antecedentes de pancreatitis aguda, intubación difícil, pancreatografía y múltiples inserciones de guías en el conducto pancreático son factores de riesgo significativos para pancreatitis tras una CPRE.*

Palabras clave: *Colangiopancreatografía retrógrada endoscópica. Esfinterotomía papilar endoscópica. Pancreatitis. Factor de riesgo. Nomograma.*

Introduction

Cholelithiasis, a common digestive system disease, represents stone formation in any part of the biliary system, such as the gallbladder and bile ducts. This condition encompasses stone generation in the gallbladder, common bile duct (CBD), and intrahepatic bile duct. The disease has a complex etiology and poses treatment challenges. The incidence rate among adults in China is currently 8-13%, and this rate is increasing with the improvement of living standards[1]. Among patients with gallbladder stones, 5-15% also have CBD stones. The elderly population exhibits the highest incidence rates, with 30% of women aged 65 and 60% of those aged 80 developing cholelithiasis[2]. Endoscopic retrograde cholangiopancreatography (ERCP) along with endoscopic sphincterotomy (EST) has emerged as a key treatment for CBD stones and related biliary diseases in recent years.

Relative to classical open surgery, this approach offers the benefits of being minimally invasive, having lower risks, providing rapid recovery, and requiring shorter hospital stays, making it particularly suitable for elderly patients[3]. However, as an invasive technique, ERCP + EST involves certain risks. Thermal injury during EST can easily lead to Oddi sphincter dysfunction, and damage to the pancreatic duct sphincter can result in impaired pancreatic juice outflow, reflux, or even leakage, significantly increasing the risk of post-operative pancreatitis[4]. Studies indicate that complications following ERCP + EST occur in 10-12% of cases, including duodenal papilla bleeding, duodenal perforation, acute pancreatitis, and cholangitis, with post-operative acute pancreatitis (post-ERCP pancreatitis, post-endoscopic pancreatitis [PEP]) being the most common, occurring in 1.6-15.0% of cases[5].

The growing elderly population and the high incidence of cholelithiasis among this group highlight the importance of timely treatment to reduce treatment difficulties and survival risks. This study investigates risk factors (RFs) for pancreatitis among elderly subjects with CBD stones undergoing ERCP + EST and establishes a prediction model to forecast PEP risk, providing valuable clinical reference.

Methods

Patients and research design

We retrospectively collected data on elderly patients aged 60 years and above with CBD stones who underwent ERCP + EST treatment at Affiliated Liupanshui Hospital of Zunyi Medical University from January 2017 to December 2023. The following patients were included for analysis in this study: elderly patients aged 60 years and above diagnosed with CBD stones who underwent ERCP + EST at Liupanshui People's Hospital and passed a preoperative risk assessment confirming their eligibility for surgery. This investigation received ethical approval from the Affiliated Liupanshui Hospital of Zunyi Medical University (No. LPSSYY-2024-25). Due to the retrospective design of this investigation, the informed consent requirement was waived. Exclusion criteria encompass patients with a preoperative diagnosis of acute pancreatitis, severe cardiopulmonary insufficiency, coagulopathy, hematologic diseases, a history of gastroduodenal surgery, or incomplete clinical data. The diagnostic criteria[6] for acute pancreatitis require a meeting of two of the three following conditions: characteristic abdominal pain, circulating amylase or lipase levels over 3 times the upper normal threshold, or imaging evidence of pancreatitis on abdominal computed tomography or ultrasound.

Date collection

The following clinical information was acquired: sex, age, body mass index (BMI), hypertension, diabetes, prior hepatitis history (if any), smoking history, drinking history, history of acute pancreatitis, previous cholecystectomy, history of bile duct surgery, presence of ampullary diverticulum, bile duct stent, pancreatic stent, endoscopic papillary balloon dilation, bile duct diameter, difficult intubation, pancreatography, and more than two guidewire insertions into the pancreatic

duct. Biochemical indicators include total bilirubin, direct bilirubin, white blood cell count, aspartate aminotransferase, alanine aminotransferase, circulating amylase, and albumin concentration. Smoking history represented smoking ≥ 1 cigarettes daily for over 6 months; or having previously met this criterion with cessation for < 6 months. Drinking history was defined as consuming alcohol at least once a week for more than 6 months; or having previously met this criterion with cessation for < 6 months. Difficult intubation was defined as more than five intubation attempts or an intubation time of more than 10 min.

Statistics

R software version 4.3.1 was employed for all data analyses. Data with normal distribution are presented as mean ± standard deviation; while remaining data are described as a median and interquartile range (Median [Q1, Q3]) and analyzed through non-parametric Mann–Whitney U tests. Continuous data were compared using t- or rank-sum tests, while categorical data were provided as counts and percentages and assessed through the X^2 or Fisher's exact test. Two-tailed $p < 0.05$ was the significance standard. We employed univariate logistic regression for potential predictor identification, with variables showing a $p < 0.10$ considered for further analysis. Significant variables were entered into multivariate logistic regression analysis for stand-alone RFs identification for post-ERCP + EST pancreatitis (PEP), with significance indicated at $p < 0.05$. Using regression coefficients, we next generated a nomogram prediction model. Model internal verification was achieved through 1,000 bootstrap resamples, and the resulting calibration curve revealed consistency between estimated and actual outcomes. The Hosmer–Lemeshow test evaluated model fitness. The model predictive ability was assessed through the receiver operating characteristic (ROC) curve and the area under the curve. Clinical applicability was examined through the clinical decision curve.

Results

Baseline characteristics

In all, 413 patients were analysis, among which, 178 were males and 235 were females, and the mean age of all participants was 69.4 years. Among these, 39 patients developed pancreatitis post-surgery, forming the PEP group. This group represents an incidence rate of 9.4% for post-surgical pancreatitis. The remaining 374 patients did not develop pancreatitis and were categorized as the non-PEP group. The baseline data for these groups are detailed in table 1. All cases of pancreatitis in the PEP group were classified as mild to moderate, and there were no in-hospital deaths attributed to PEP.

Univariate and multivariate regression analysis

Univariate analysis identified five variables with $p < 0.1$ in this cohort: age under 75 years, a history of acute pancreatitis, difficult intubation, more than two guidewire insertions into the pancreatic duct, and pancreatography. These variables were then entered into multivariate analysis, which confirmed that all five factors were statistically significant ($p < 0.05$), thereby establishing them as stand-alone RFs for post-ERCP pancreatitis (PEP) development. A detailed summary of the results is provided in table 2.

Construction of nomogram model

Based on multivariate logistic regression, a risk prediction nomogram was developed to assess the probability of PEP among elderly patients with CBD stones undergoing ERCP and EST. This nomogram included five predictive factors illustrated in figure 1.

By summing the individual scores from these factors, a total score was calculated, which then predicted the probability of PEP. The model demonstrated excellent calibration, as the calibration curve closely approximated the ideal reference line. The Hosmer–Lemeshow test confirmed the model's fit, with $p = 0.174$, suggesting no marked difference between estimated and actual risks. The area under the ROC curve was 0.783 (95% confidence interval [CI]: 0.705-0.862), suggesting the model's strong predictive accuracy. In addition, clinical DCA indicated that using this nomogram for clinical decisions provided a substantial net benefit over a wide range of decision thresholds, specifically from 2% to 76%. The detailed results are presented in figures 2-4.

Discussion

At present, ERCP + EST is one of the primary methods for treating CBD stones. Although it offers specific advantages over traditional open surgery,

Table 1. Baseline patient characteristics

Factor	Category	Non-PEP group n = 374 (%)	PEP group n = 39 (%)	Statistical value	p
Age	≥ 75 years	106 (28.3)	5 (12.8)	4.330	0.059
	< 75 years	268 (71.7)	34 (87.2)		
Sex	Male	166 (44.4)	12 (30.8)	2.670	0.143
	Female	208 (55.6)	27 (69.2)		
BMI	≥ 24	240 (64.2)	24 (61.5)	0.106	0.880
	< 24	134 (35.8)	15 (38.5)		
Hypertension history	No	253 (67.6)	26 (66.7)	0.015	1.000
	Yes	121 (32.4)	13 (33.3)		
Acute pancreatitis history	No	345 (92.2)	30 (76.9)	8.176	0.004
	Yes	29 (7.8)	9 (23.1)		
Diabetes history	No	318 (85.0)	34 (87.2)	0.130	0.902
	Yes	56 (15.0)	5 (12.8)		
Smoking history	No	300 (80.2)	34 (87.2)	1.108	0.402
	Yes	74 (19.8)	5 (12.8)		
Drinking history	No	325 (86.9)	37 (94.9)	1.403	0.236
	Yes	49 (13.1)	2 (5.1)		
Hepatitis history	No	359 (96.0)	36 (92.3)	0.435	0.510
	Yes	15 (4.0)	3 (7.7)		
Previous cholecystectomy	No	301 (80.5)	28 (71.8)	1.645	0.283
	Yes	73 (19.5)	11 (28.2)		
Bile duct surgery history	No	303 (81.0)	35 (89.7)	1.810	0.260
	Yes	71 (19.0)	4 (10.3)		
TBil	≤ 17.1	126 (33.7)	15 (38.5)	0.358	0.674
	> 17.1	248 (66.3)	24 (61.5)		
DBil	≤ 6.8	91 (24.3)	11 (28.2)	0.285	0.735
	> 6.8	283 (75.7)	28 (71.8)		
Preoperative WBC	≤ 10.0	308 (82.4)	32 (82.1)	0.002	1.000
	> 10.0	66 (17.6)	7 (17.9)		
ALT	–	86.40 (39.25, 164.00)	70.40 (24.62, 158.12)	6367.5	0.192
AST	–	62.60 (26.90, 103.40)	45.85 (22.02, 128.57)	7141.5	0.831
Albumin	≥ 40	176 (47.1)	22 (56.4)	1.238	0.345
	< 40	198 (52.9)	17 (43.6)		
Bile duct stent	No	241 (64.4)	27 (69.2)	0.357	0.674
	Yes	133 (35.6)	12 (30.8)		
Pancreatic duct stent	No	322 (86.1)	34 (87.2)	0.035	1.000

(Continues)

Table 1. Baseline patient characteristics *(continued)*

Factor	Category	Non-PEP group n = 374 (%)	PEP group n = 39 (%)	Statistical value	p
	Yes	52 (13.9)	5 (12.8)		
Pancreatography	No	331 (88.5)	23 (59.0)	25.148	< 0.001
	Yes	43 (11.5)	16 (41.0)		
Nasobiliary tube	No	147 (39.3)	12 (30.8)	1.087	0.385
	Yes	227 (60.7)	27 (69.2)		
Difficult intubation	No	311 (83.2)	21 (53.8)	19.243	< 0.001
	Yes	63 (16.8)	18 (46.2)		
Common bile duct diameter	≤ 1 cm	164 (43.9)	20 (51.3)	0.790	0.472
	> 1 cm	210 (56.1)	19 (48.7)		
Ampullary diverticulum	No	287 (76.7)	27 (69.2)	1.092	0.396
	Yes	87 (23.3)	12 (30.8)		
Guidewire insertion into pancreatic duct	< 2 times	339 (90.6)	24 (61.5)	25.444	< 0.001
	≥ 2 times	35 (9.4)	15 (38.5)		
Endoscopic papillary balloon dilation	No	267 (71.4)	24 (61.5)	1.647	0.272
	Yes	107 (28.6)	15 (38.5)		

Note: measurement data with a skewed distribution were expressed as median (Q1, Q3); count data were expressed as counts or percentages. BMI: body mass index; PEP: post-endoscopic pancreatitis.

Table 2. Multivariate regression analysis of elderly patients with common bile duct stones complicated by pancreatitis

Factor	Regression coefficient	Standard error	z	p	OR	95% CI
Age < 75 years	1.421	0.543	2.616	0.009	4.143	1.555-13.516
History of acute pancreatitis	1.212	0.475	2.551	0.011	3.361	1.275-8.364
Pancreatography	1.199	0.469	2.555	0.011	3.317	1.313-8.351
Difficult intubation	0.876	0.419	2.090	0.036	2.400	1.040-5.417
More than twice Guidewire insertions	0.966	0.449	1.782	0.031	2.629	1.071-6.277

OR: odds ratio; CI: confidence interval.

such as being less invasive and allowing faster recovery, the technique is technically demanding and carries inherent risks. The procedure requires substantial expertise, and the associated complications should not be overlooked. Common post-operative complications of ERCP + EST include pancreatitis, infection, bleeding, and perforation. PEP is the most frequent complication, with an incidence rate ranging from 1.6% to 15.0%, and approximately 1.5% of PEP cases are moderate to severe, with a mortality rate of up to 3-5%[7]. In this study, the incidence rate of PEP after ERCP + EST was 9.4%, with all cases being mild to moderate and no in-hospital deaths reported. These results align with previous research. The elderly population has a high incidence of CBD stones, and ERCP + EST is frequently performed in this group. However, studies on PEP in elderly patients are limited. Elderly patients often have reduced physiological resistance and multiple comorbidities, which may increase the incidence of

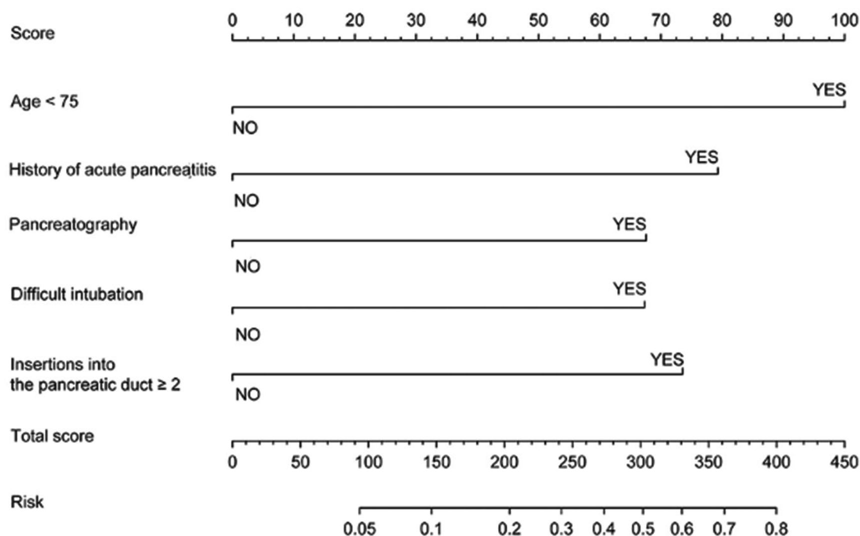

Figure 1. *Nomogram risk chart for pancreatitis in elderly patients with common bile duct stones.*

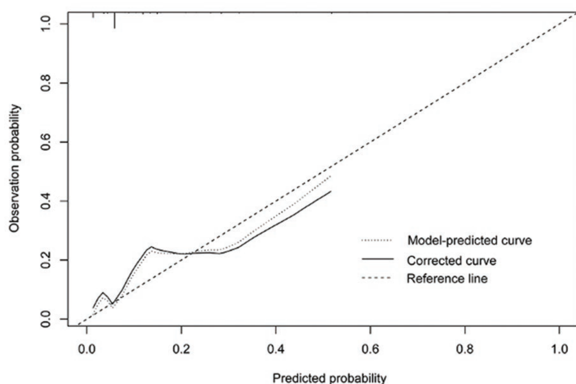

Figure 2. *Calibration curve for pancreatitis in elderly patients with common bile duct stones.*

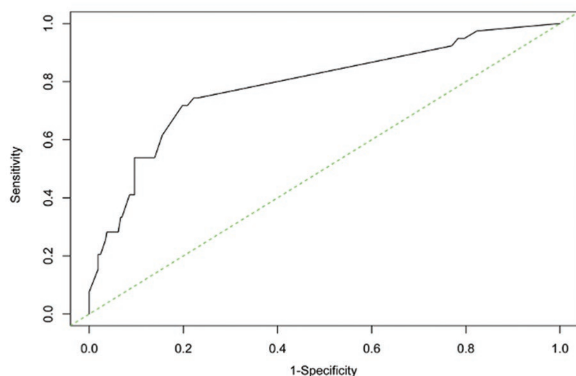

Figure 3. *Receiver operating characteristic curve for pancreatitis in elderly patients with common bile duct stones.*

post-operative complications[8]. Therefore, identifying the RFs for PEP and implementing early preventive measures are crucial. This study focused on elderly patients with CBD stones. Based on previous studies[9-11], we initially screened the variables to be collected and identified the RFs for PEP after ERCP + EST using a logistic regression model. The independent RFs identified included age under 75 years, history of acute pancreatitis, difficult intubation, pancreatography, and more than two guidewire insertions into the pancreatic duct. A clinical prediction model for PEP was constructed, and a nomogram was created to visualize the model, making it a practical tool for assessing patient risk and predicting disease occurrence.

Age is an established RF for PEP in several studies[12-15]. Younger patients are thought to be more susceptible to PEP, possibly due to the decline in pancreatic function associated with aging or pancreatic parenchymal degeneration, which leads to a reduced response to mechanical injury from ERCP. Research indicates that pancreatic exocrine function increases linearly with age up to 30 years and then begins to decline[16]. Moreover, infants under 1 year of age rarely develop PEP following ERCP[17]. Age stratification in PEP risk studies varies, with 60 years often used as the threshold, though other studies use 50, 70, or 75 years. This study focused on elderly patients aged 60 years and older and stratified them based on the World Health Organization's age classification, using

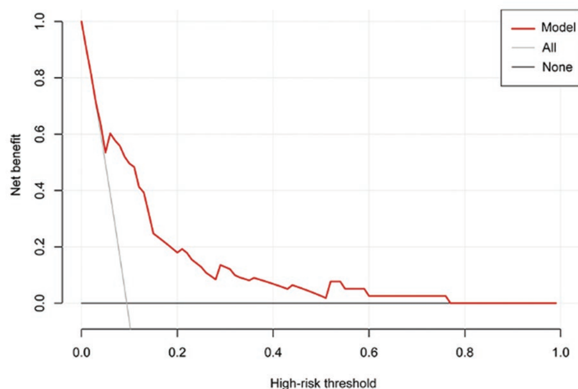

Figure 4. *Clinical decision curve for pancreatitis in elderly patients with common bile duct stones.*

75 years as the cutoff. We found that the PEP incidence was substantially elevated among the younger subgroup compared to those aged 75 years and older, with the former group having a 4.143-fold rise in risk (OR = 4.143; 95% CI, 1.555-13.516; p = 0.009). This study confirms the higher risk of PEP in relatively younger elderly patients but did not investigate those under 60 years. A study by Ergin et al.[8] found the highest PEP risk in the 21-30 years age group, though the difference was not significant. A nationwide ERCP study in Korea[14] reported a higher incidence of PEP in younger patients, with the highest rates in those under 40 years, while the incidence was lower in the elderly. In our study, the incidence of PEP was low in patients aged 75 years and older, with no cases observed in those over 80 years, likely due to age-related pancreatic changes. However, the small sample size of older patients in this study may have introduced bias. Based on these findings, it is important to inform younger patients undergoing ERCP about the risks, thoroughly evaluate their condition, and, if other RFs are present, take preventive measures to reduce the occurrence of PEP. For older patients, who often have more comorbidity and reduced physiological resistance, a thorough preoperative evaluation is necessary to determine the appropriate treatment plan[18].

The European Society of Gastrointestinal Endoscopy (ESGE) guidelines have identified prior pancreatitis history as a RF for PEP[19]. Patients with prior pancreatitis history may have underlying damage to the pancreatobiliary system, such as microinflammatory changes or metabolic damage, making them more sensitive to ERCP-related procedures. Compared with patients without a history of pancreatitis, those with such a history are at significantly higher risk for PEP due to repeated episodes of pancreatitis leading to pancreatic parenchymal damage and reduced exocrine function[20]. In this study, a history of acute pancreatitis was a significant RF, with a 3.3-fold rise in PEP risk relative to controls (odds ratio [OR] = 3.361; 95% CI, 1.275-8.364; p = 0.011). Recent studies[21] also support the association between a history of pancreatitis and the occurrence of PEP after ERCP. However, the risk of PEP may be lower among chronic pancreatitis patients. A systematic review involving 13 studies[22] revealed that chronic pancreatitis patients experienced reduced PEP incidence than controls, likely due to pancreatic atrophy and reduced enzymatic activity. This study did not include chronic pancreatitis patients, so this factor was not considered as a variable.

Procedure-related RFs identified in this study include pancreatography, more than two guidewire insertions into the pancreatic duct, and difficult intubation, consistent with previous research[23-25]. Multiple guidewire insertions or contrast medium administration into the pancreatic duct can cause chemical and mechanical damage to the ductal epithelium, leading to congestion, edema, and increased internal pressure. This can damage the acinar epithelium and ductal walls, causing membrane disruption, pancreatic tissue injury, enzyme activation, and leakage of pancreatic juice, ultimately leading to pancreatitis[26]. This study confirmed that more than two guidewire insertions into the pancreatic duct and pancreatography are RFs for PEP, with associated risks of 3.317-fold (OR = 3.317; 95% CI, 1.313-8.351; p = 0.011) and 2.400-fold (OR = 2.400; 95% CI, 1.040-5.417; p = 0.036) increases, respectively. The ESGE guidelines[19] indicate OR of 2.1-2.77 for more than one guidewire insertion and 1.58-2.72 for pancreatography. Other studies[27] have found that the risk of PEP after ERCP is positively correlated with the amount of contrast medium injected into the pancreatic duct and the number of guidewire insertions, warranting further investigation in future research.

Difficult intubation is defined as an intubation time of 10 min or more, or more than five intubation attempts. Causes of difficult intubation include anatomical abnormalities of the duodenal papilla, ampulla, and surrounding structures, as well as operator technique variability. Difficult intubation can cause sphincter spasm, papillary congestion, and edema, leading to increased biliary pressure and impaired outflow of

pancreatic juice and bile, resulting in pancreatitis. It is considered an independent RF for PEP[28]. In this study, difficult intubation was identified as a RF, with a 1.7-fold increase in PEP risk when the intubation time exceeded 10 min or more than five intubation attempts were made. The ESGE guidelines[19] reported OR of 1.76-14.9 for difficult intubation, and a recent clinical study[10] revealed that the PEP incidence among patients with difficult intubation was elevated by 5.8 folds relative to controls, with a proportional increase in PEP risk with the number of intubations attempts and duration[29]. At present, no studies have shown a correlation between difficult intubation and age. To mitigate the risks associated with these procedural factors, clinicians should enhance their technical skills, minimize technical errors, reduce the injection of contrast medium during ERCP to prevent chemical damage to the pancreatic duct, and employ guidewire and pre-cut techniques to aid intubation. This approach can increase the success rate of intubation, reduce mechanical injury to the pancreatic duct, and prevent pancreatitis.

This investigation was limited by several factors: First, because of its retrospective design, it may be subject to data bias compared to prospective studies; second, the small sample size and moderate level of evidence may result in selection and information bias; third, this study was a single-center investigation, with internal validation only and no external validation. Larger, multicenter prospective clinical investigations are warranted to assess the external applicability of the proposed model.

Conclusion

PEP is a common complication among elderly patients with CBD stones undergoing ERCP and EST. This study identified age under 75 years, history of acute pancreatitis, pancreatography, difficult intubation, and more than two guidewire insertions into the pancreatic duct as significant RFs for PEP. A nomogram was generated for PEP risk prediction following ERCP and EST, enabling early identification of patients at risk. The validation results suggest that the model is feasible and provides clinical value and guidance. Therefore, thorough pre-operative evaluation, identification of RFs, strict adherence to indications and contraindications, and enhanced procedural training are essential to minimize complications in patients undergoing ERCP and EST.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply. This study was conducted with approval from the Ethics Committee of This investigation received ethical approval from the Affiliated Liupanshui Hospital of Zunyi Medical University (No. LPSSYY-2024-25).

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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