Risk factors of common bile duct stones recurrence and nomogram for predicting recurrence after endoscopic retrograde cholangiopancreatography: a dual-center retrospective cohort study

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Abstract. – OBJECTIVE: Common bile duct stone (CBDS) is one of the common diseases in the digestive system, for which endoscopic retrograde cholangiopancreatography (ERCP) is a treatment procedure. However, the risk factors for CBDS recurrence after ERCP remains unclear. This study aims to compare the risk factors of CBDS recurrence after ERCP, and to set up a nomogram model to predict the long-term risk.

PATIENTS AND METHODS: A retrospective analysis of 355 patients was reviewed. Univariate and multivariate analyses were performed to identify the risk factors for recurrence. The R packages were used for the model building. The validation set contained 100 patients.

RESULTS: The patients were divided into three subgroups: treated by cholecystectomy after ERCP (11.76% recurrence rate), treated without surgery after ERCP (19.70%), and with a prior history of cholecystectomy (43.64%). Each of them has different independent risk factors, and high body mass index (BMI) is correlated with an increased risk among all the subgroups. A prior history of cholecystectomy is a candidate factor that increases the risk of CBDS recurrence in patients older than 60 years, with a greater BMI, or receiving ERCP combined with EPBD. We built a nomogram model to predict the risk of long-term CBDS recurrence based on the risk factors including age, BMI, CBD diameter, the number of CBDS, and the gallbladder- or biliary tract-related events.

CONCLUSIONS: CBDS recurrence is related to congenital and anatomical factors. Cholecystectomy would not be helpful to prevent CBDS recurrence, and a prior history of cholecystectomy may indicate a high risk of recurrence.

Key Words:
ERCP, Risk factor, Recurrence, Cholecystectomy, Nomogram model.

Introduction

Common bile duct (CBD) stone is one of the common diseases in the digestive system. Across the developed countries and worldwide, the incidence of gallstone disease (also known as cholelithiasis) is about 7%-15% with continuous improvements[1]. Common bile duct stones (CBDS) are reported to account for 20.1% of cholelithiasis[2], the etiology of which is poorly understood. Previous studies reported that it may be associated with infection, lifestyle habits, and genetic and environmental factors. The clinical presentation of CBDS varies in severity ranging from no symptoms to life-threatening complications due to biliary obstruction, such as acute obstructive suppurative cholangitis, acute pancreatitis and even shock. Guideline for the management of CBDS recommend that lithotomy is often necessary in moderate and severe cases[3].

In clinical practice, treatment options for CBDS include laparoscopic common bile duct

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exploration, choledocholithotomy, endoscopic sphincterotomy (EST), and endoscopic papillary balloon dilation (EPBD). Since the inception of endoscopic retrograde cholangiopancreatography (ERCP) in the 1960s, it has become an essential diagnostic and therapeutic approach to CBDS because of its safety and fast postoperative recovery. ERCP can result in a number of complications like acute pancreatitis, cholangitis, and sepsis as an invasive procedure. Even if this were the case, it also has a risk of CBDS recurrence varying from 4% to 24% in different studies[4-6]. The risk of recurrence increases with each subsequent relapse: 23.4% after the first recurrence and up to 33.4% following two recurrences[7]. Factors, including stone characteristics, congenital, microbiological, and intervention, are considered to be associated with CBDS recurrence[8-10]. Debate continues about the best intervention strategies for preventing CBDS recurrence. In accordance with previous European population-based studies[11,12], gallbladder removal after ERCP helped to reduce biliary complications including CBDS recurrence. However, it remains controversial whether this conclusion is applicable for broader populations as cholesterol gallstone is a dominant type in European populations while pigment gallstones in Asian populations. In addition, we lack effective means of risk assessment for CBDS recurrence despite some known risk factors.

This study aims to compare the probability and related risk factors of CBDS recurrence in patients with different intervention strategies for gallbladder after ERCP, and to set up a model to predict the long-term risk of CBDS recurrence.

Patients and Methods

Patients

A total of 562 patients with firstly diagnosed choledocholithiasis were treated with ERCP from January 2015 to January 2018 at the Department of Gastroenterology, Zhongshan Hospital of Xiamen University (Xiamen, China). These patients were evaluated by complete preoperative clinical work-up like physical examination, medical history taking, blood tests and imaging studies. All ERCP procedures were carried out by experienced therapeutic endoscopists. After stone removal, the contrast agent was injected to confirm that the CBDS was cleaned up. Medical records of 355 patients selected based on the inclusion and exclusion criteria were retrospectively reviewed. Inclusion criteria: (1) a preoperative diagnosis of CBDS; (2) patients who received a complete cycle of treatment in the hospital; (3) complete clearance for CBDS can be achieved. Exclusion criteria: (1) a prior history of ERCP; (2) patients who had comorbidities of hepatobiliary and duodenal neoplasms; (3) congenital malformations of the biliary tract; (4) biliary stent placements; (5) postoperative residual stones; (6) patients lost to follow up. Taking the same approach, the clinical data of 100 patients from the Department of Endoscopy, Fujian Provincial Hospital (Fuzhou, China) were collected as an external validation set.

Follow-Up Evaluation

The follow-up duration was calculated from the date of initial endoscopic treatment until the date of CBDS recurrence, which was recorded as the primary endpoint (shown as non-recurrent duration). Patients were asked about symptoms including abdominal pain, jaundice, or fever if the recurrence was suspected, and CT or ultrasound was necessary for definitive diagnosis. Diagnostic criteria for CBDS recurrence[13-16]: diagnosed with CBDS more than six months after endoscopic stone retraction by ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP) or ERCP. If the outcomes event had not occurred, the last follow-up data was obtained by telephone surveys throughout January 1, 2021.

Statistical Analysis

Data were analyzed using IBM SPSS 24.0 (IBM Corp., Armonk, NY, USA) and R (version 3.6.3) software (Indianapolis, IN, USA). The Chi-square test or Fisher exact test was used for categorical variables. Continuous variables that followed a normal distribution were expressed as the mean ± SD, followed by the *t*-test; those that didn't were expressed as the median (lower quartile, upper quartile), followed by the U-test. The cut-off value from the receiver operating characteristic (ROC) curve was used to turn into categorical variables for subsequent analyses. $p < 0.05$ was considered statistically significant. The cumulative recurrence rate was determined using the Kaplan-Meier method. We used the ggplot2 (version 3.3.3) R package to draw the histogram of relapse rates between groups and generate the forest plots for subgroup analysis. Univariate and multivariate analyses were performed to identify the risk factors for recurrence using Cox regression. The rms (version 6.2) and survival (version 3.2) R packages were run to create the nomogram based on multivariate Cox regression analysis. The validity of the nomogram model was assessed through calibration plots, DCA (Decision Curve Analysis) and ROC curves.

Results

Univariate and Multivariable Analysis of Risk Factors for Choledocholithiasis Recurrence in Different Subgroups

The 355 patients were divided into three subgroups for separate analyses according to whether they underwent cholecystectomy: treated by cholecystectomy (E-CCY group) or without surgery (E-NCCY group) after ERCP (Table I), and with a prior history of cholecystectomy (PH-CCY group) (Table II).

There are 102 patients in the E-CCY group including both postoperative cases with recurrence (n=12) and nonrecurrence (n=90), between which there are significant differences in body mass index (BMI), drinking history and diabetes (Table I). Although the number and colors of common bile duct stones showed moderate correlations with stone recurrence, there is no significant difference in the results obtained using multivariate logistic regression analysis (Table III). Chi-square analysis also found that patients who received EST and EPBD combination therapy had a significantly higher recurrence rate. Of all independent risk factors, it's the leading risk factor for stone recurrence in the E-CCY group (OR=36.678, *p*=0.001).

Among 198 patients in the E-NCCY group, the rate of recurrence is 19.70% (39/198). As can be seen in Table I, the difference is statistically significant in age, gender, BMI, the anatomical features of bile duct, and multiple common bile duct stones between patients with and without recurrence. Multivariate logistic regression analysis (Table III) indicated that age > 67 years

Table I. Clinical characteristics of patients who underwent ERCP with or without cholecystectomy before ERCP.

	E-CCY			E-NCCY		
	Recurrence (12)	Non-recurrence (90)	*p*-value	Recurrence (12)	Non-recurrence (90)	*p*-value
Age (years)	61.8 ± 16.9	52.2 ± 16.1	0.058	73.0 (59.0,80.0)	59.5 (46.0, 70.0)	0.000*
> 67				26 (66.7)	49 (30.8)	0.000*
Gender (male/female)	9/3	48/43	0.156	16/23	95/24	0.035*
BMI (kg/m^2)	24.7 ± 3.6	22.6 ± 3.3	0.048*	23.3 (20.3, 26.4)	22.4 (19.5, 24.5)	0.028*
> 25.4	5 (41.7)	12 (13.3)	0.039*			
> 25.0				18 (46.2)	34 (21.4)	0.002*
Smoking	1 (8.3)	11 (12.2)	1.000	7 (17.9)	33 (20.8)	0.696
Alcohol consumption	5 (41.7)	8 (8.9)	0.006*	1 (2.6)	14 (8.8)	0.326
Hypertension	2 (16.7)	22 (24.4)	0.815	12 (30.8)	33 (20.8)	0.181
Diabetes	5 (41.7)	9 (10.0)	0.011*	5 (12.8)	23 (14.5)	0.792
Preoperative infection	10 (83.3)	50 (55.6)	0.127	23 (59.0)	74 (46.6)	0.164
Postoperative pancreatitis	2 (16.7)	17 (18.9)	1.000	2 (5.1)	19 (11.9)	0.342
Periampullary diverticulum	4 (33.3)	25 (27.8)	0.952	10 (25.6)	42 (26.4)	0.922
EST + EPBD	9 (75.0)	15 (16.7)	0.000*	14 (35.9)	54 (34.0)	0.820
Cholecystolithiasis				20 (51.3)	79 (49.7)	0.803
Number ≥ 2				11 (28.2)	52 (32.7)	0.652
Common bile duct						
Diameter (cm)	1.0 (0.8, 1.2)	0.8 (0.8, 1.0)	0.706	1.3 (1.0, 1.5)	1.0 (0.8, 1.2)	0.000*
> 0.9 cm				35 (89.7)	81 (50.9)	0.000*
Angulation	5 (41.7)	29 (32.2)	0.744	16 (41.0)	38 (23.9)	0.031*
Choledocholithiasis						
Diameter (cm)	0.6 (0.6, 1.0)	0.7 (0.5, 1.0)	0.492	0.8 (0.6, 1.0)	0.8 (0.6, 1.0)	0.108
Number > 2	8 (66.7)	24 (26.7)	0.013*	20 (51.3)	64 (40.2)	0.000*
Color (black/brown)	10 (83.3)	46 (51.1)	0.035*	22 (56.4)	81 (50.9)	0.540
Trait (mass)	11 (91.7)	74 (82.2)	0.680	38 (97.4)	139 (87.4)	0.126

ERCP: Endoscopic Retrograde Cholangiopancreatography; BMI: body mass index; EST: endoscopic sphincterotomy; EPBD: endoscopic papillary balloon dilation; E-CCY: the patient was treated by cholecystectomy after ERCP; E-NCCY: the patient was treated without surgery after ERCP; **p*-value < 0.05.

Table II. Clinical characteristics of patients who has a prior history of cholecystectomy.

	Recurrence (24)	Non-recurrence (31)	*p*-value
Age (years)	69.3 ± 8.9	58.9 ± 6.1	0.004*
> 67	21 (87.5)	13 (41.9)	0.001*
Time interval between cholecystectomy and ERCP (days)	926.83 ± 614.8	1,311.90 ± 413.6	0.010*
Gender (male/female)	13/11	9/22	0.059
Smoking	5 (20.8)	3 (9.7)	0.276
Alcohol consumption	1 (4.2)	1 (3.2)	1.000
Hypertension	11 (45.8)	7 (22.6)	0.068
Diabetes	5 (20.8)	3 (9.7)	0.436
Preoperative infection	12 (50.0)	12 (38.7)	0.402
Postoperative pancreatitis	1 (4.2)	4 (12.9)	0.519
Periampullary diverticulum	5 (20.8)	10 (32.3)	0.345
BMI (kg/m^2)	25.46 (21.7, 26.8)	20.9 (18.5, 23.6)	0.001*
> 23.1	17 (70.8)	8 (25.8)	0.001*
EST+EPBD	6 (25.0)	10 (32.3)	0.557
Common bile duct			
Diameter (cm)	1.6 ± 0.5	1.5±0.6	0.269
≥ 1.5 cm	14 (58.3)	15 (48.4)	0.464
Angulation	8 (33.3)	8 (25.8)	0.542
Common bile duct stones			
Diameter (cm)	1.2 (1.0, 1.6)	0.9 (0.6, 1.2)	0.048*
> 1.1 cm	17 (70.8)	9 (29.0)	0.002*
Color (black or brown)	6 (25)	9 (29.0)	0.627
Number (> 2)	18 (75)	14 (45.2)	0.026*
Trait (mass)	24 (100)	26 (83.9)	0.557

(*p*=0.014), BMI > 25 kg/m^2 (*p*=0.001), common bile duct diameter > 0.9 cm (*p*=0.003), number of common bile duct stones > 2 (*p*=0.013) are independent risk factors. In addition to that, cholecystolithiasis does not affect the risk of stone recurrences in patients who did not undergo cholecystectomy after ERCP.

In the PH-CCY group there are 55 patients with a previous history of cholecystectomy, 24 (43.64%) of whom experienced a second bile duct stone episode after ERCP. Using Chi-square test for correlation analysis, similar findings amongst the PH-CCY group were discovered compared to the E-NCCY group (Table II). In particular, the patients in the recurrent group have significantly larger diameter of choledocholithiasis, as opposed to the common bile duct diameter, than non-recurrent group. However, only the difference in age (> 61 years, OR=20.468, *p*=0.001) and BMI (> 23.1 kg/m^2, OR=14.643, *p*=0.002) remains statistically significant in multivariate analysis. On the whole, these three subgroups demonstrated significantly different features of risk factors distribution, and in the total study population high

Table III. Multivariate logistic regression analysis for independent risk factors.

E-CCY	Group	B	OR	*p*	95% CI
Alcohol consumption	1.942	6.971	0.076	0.818	59.426
Diabetes	2.228	9.278	0.030*	1.235	69.704
BMI > 25.4 (kg/m^2)	2.093	8.109	0.039*	1.109	59.298
EST+EPBD	3.602	36.678	0.001*	4.810	279.669
E-NCCY Group					
Age > 67 years	1.064	2.898	0.014*	1.246	6.744
BMI > 25.0 (kg/m^2)	1.526	4.601	0.001*	1.895	11.174
CBD diameter > 0.9 cm	1.751	5.763	0.003*	1.835	18.100
CBDS number	1.142	3.133	0.013*	1.278	7.682
PH-CCY Group					
Age > 61 years	3.019	20.468	0.001*	3.247	129.032
BMI > 23.1 kg/m^2	2.684	14.643	0.002*	2.758	77.757

PH-CCY: the patient who has a prior history of cholecystectomy; OR: odds ratio; CI: confidence interval.

BMI correlated with an increased risk of choledocholithiasis recurrence after ERCP.

Impact of Cholecystectomy for Choledocholithiasis Recurrence After ERCP

Figure 1A visually displays the comparisons in rate of stone recurrence among groups. The difference in recurrence rates between E-CCY and E-NCCY groups is not statistically significant, while the difference between E- and PH-groups is significant ($p < 0.001$). The recurrence curves in Figure 1B showed that the cumulative recurrence rate gradually increased with longer follow-up time. The median time to recurrence is 22 months in the E-CCY group, 18 months in the E-NCCY group, and 20 months in the PH-CCY group. The current clinical experience suggests that an important consideration for patients undergoing cholecystectomy after ERCP is choledocholithiasis combined with gallbladder stones. Therefore, we also investigated the effect of cholecystectomy after ERCP on the recurrence rate in 200 patients with both gallbladder stones

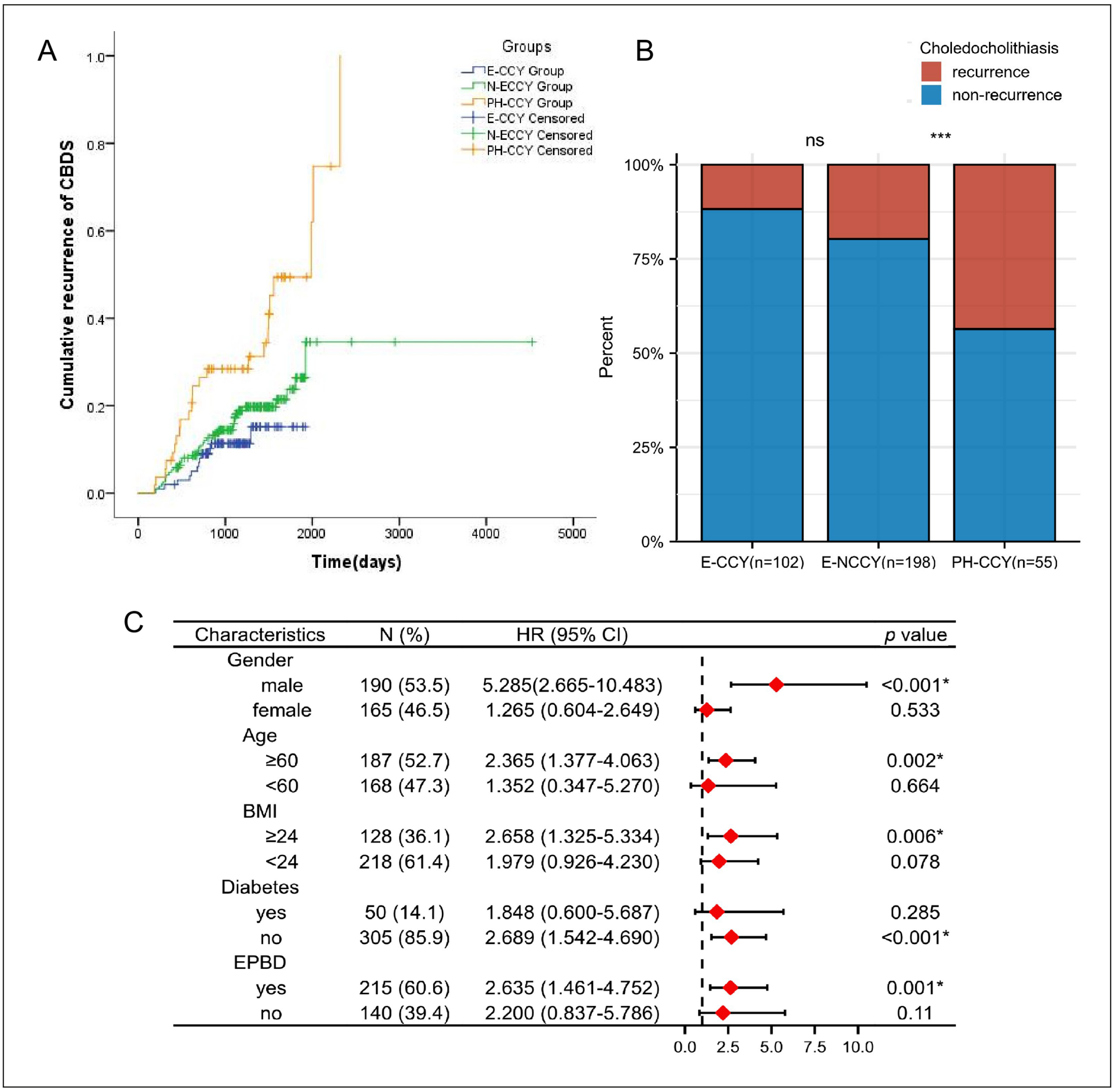

Figure 1. Comparisons of CBDS recurrence rates across groups. **A,** Kaplan-Meier cumulative incidence of relapse. **B,** Histogram of relapse rates among groups. **C,** Forest plot of univariable Cox proportional hazard ratios for the prior history of cholecystectomy before ERCP in key baseline subgroups. (ns: *p*-value > 0.05; **p*<0.01; ****p*<0.0001; HR: hazard rate).

and CBDS (**Supplementary Table I**). For 102 patients who received concomitant cholecystectomy, the recurrence rate of CBDS is 11.8%; for 98 patients who didn't, the recurrence rate is 20.4% (p=0.098). These results, taken together, indicated that cholecystectomy might not be beneficial for preventing CBDS recurrence, and a preexisting history of cholecystectomy suggested a higher risk of recurrence.

To provide further insight into the association between relapse rates and the prior history of cholecystectomy, we performed the Cox proportional hazard analysis in key baseline subgroups (Figure 1C). It is interesting to note that the prior history of cholecystectomy means a higher risk of CBDS recurrence in the male patient (HR=5.285, p<0.001) and the subset of patients older than 60 years (HR=2.365, p=0.002), with a BMI greater than 24 (HR=2.658, p=0.006), without diabetes (HR=2.689, p<0.001) or receiving ERCP combined with EPBD (HR=2.635, p=0.001). Apparently, the prior history of cholecystectomy is an indispensable factor that influences CBDS recurrence.

Construction of Prediction Model for Choledocholithiasis Recurrence After ERCP

To better predict choledocholithiasis recurrence after ERCP, univariate and multivariate Cox regression analyses were performed in all 355 patients, and all significant variables ($p \leq 0.05$) were shown in Table IV. It is worth mentioning that the results of multivariate Cox regression analysis revealed no statistically significant difference in preoperative biliary tract infection, a prior history of CCY or choledocholithotomy between the recurrent and non-recurrent groups. To account for this, we introduce the concept of gallbladder- or biliary tract-related events. The patients who experienced gallbladder- or biliary tract-related events before ERCP might have a prior history of CCY or choledocholithotomy, a preoperative biliary tract infection or the coexistence of cholecystolithiasis. It well reflected an elevated risk of CBDS recurrence in multivariate Cox regression analysis (HR=4.972, p=0.005).

Nomograms have been widely developed for various disease prognostics[17-19]. However, far too little attention has been paid to CBDS recurrence. Based on the above conclusion, we set up the nomogram model to predict the risk of long-term recurrence with the inclusion of age, BMI, CBD diameter, the number of CBDS>2, and the gallbladder- or biliary tract-related events (Figure 2A, **Supplementary Table II**). The C-index of the nomogram model is 0.749 (0.717-0.782), and the calibration plots, or ROC curves showed excellent predictive performance for internal validation (Figure 2 B, C) in 3- and 5-year follow-ups. The difference in recurrence rate between high-risk and low-risk groups was visualized by risk maps in Figure 2 D-E. To further test the validity of the above models, 100 patients were randomized from another clinical centers to perform a cross-validation study. The results are shown in Figure 3: the ROC AUC are 0.780 (3-year) and 0.714 (5-year) (Figure 3A); the decision curve plots NB for a range of relevant risk thresholds (Figure 3B); the C-index is 0.739 (0.685-0.792) (Figure 3C).

Discussion

Despite the fact that ERCP is has been a widely accepted therapy for CBDS, no definite risk factors for the recurrence of CBDS and intervention strategies for gallbladder after ERCP have been established. For patients with bile duct stones, prospective studies revealed that laparoscopic cholecystectomy after endoscopic sphincterotomy (EST) could reduce the incidence of biliary tract-related events including the recurrence of CBDS[11]. But some other studies obtained quite the opposite conclusions[20,21]. In this study, the approximate recurrence rate of CBDS between E-CCY and N-ECCY groups indicates that cholecystectomy after ERCP could not reduce the recurrence risk for patients with gallbladder stones and CBDS. In addition, gallbladder stone is not associated with recurrence in the N-ECCY group. These results confirmed that the decision-making about whether the gallbladder should be resected might not be based on CBDS recurrence considerations. That said, an aggressive resection in patients who underwent ERCP is just beneficial in the treatment of cholecystolithiasis.

CBDS can be primary and secondary stones based on the formation conditions. The former occurs mainly in the common bile duct, most of which are pigmented, while the latter migrate from the gallbladder, most of which consist of cholesterol. Therefore, it has been argued that cholecystectomy after ERCP can prevent cholesterol CBDS recurrence. On the other hand, Tanaka et al[22] pointed out that all of the recurrent stones were bilirubinate irrespective of the stone types intraoperatively. Moreover, Tazuma[2] also

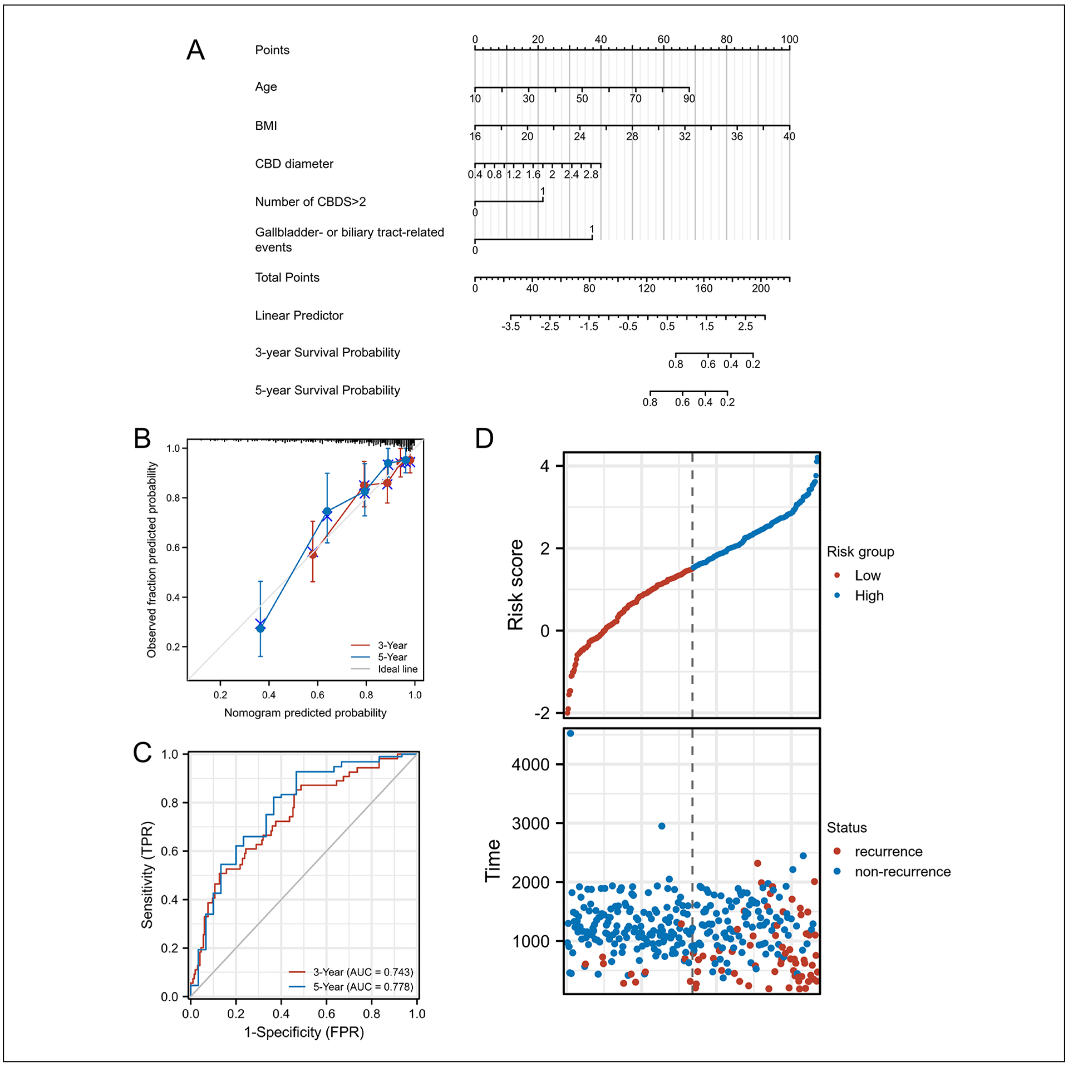

Figure 2. Construction of nomogram prognostic model. **A,** The nomogram based on age, BMI, CBD diameter, the number of CBDS>2, and the gallbladder- or biliary tract-related events. **B,** Calibration plot for the nomogram model. **C,** ROC curves for the nomogram model. **D,** Scatterplot of risk scores showing the recurrent outcomes.

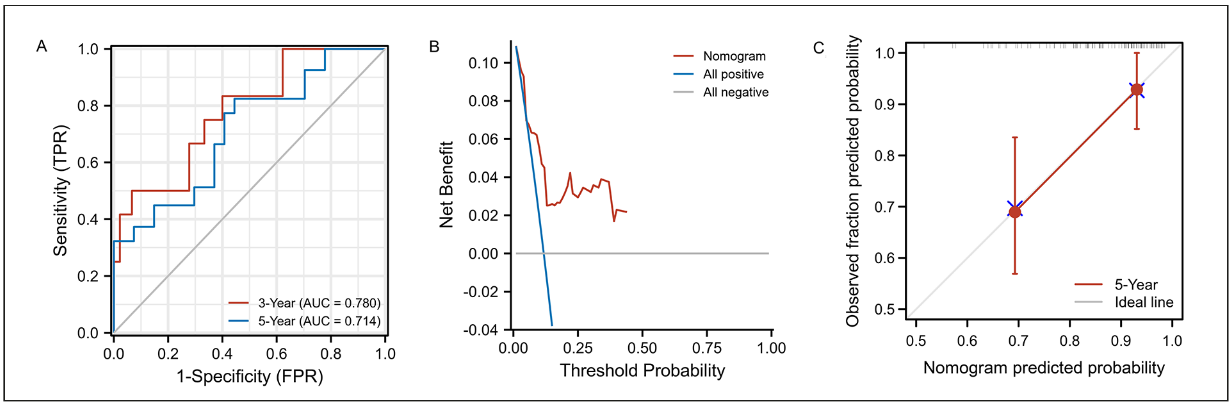

Figure 3. External validation cohort. **A,** Time dependent ROC curves at 3- and 5-year post-baseline. **B,** Decision curve analysis (DCA) for the nomogram model. **C,** Calibration plot in the validation cohort.

Table IV. Univariate and multivariate analyses for CBDS recurrence with the Cox proportional hazards regression model.

Characteristics	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*p*-value	Hazard ratio (95% CI)	*p*-value
Age	1.039 (1.022-1.056)	< 0.001	1.031 (1.011-1.051)	0.002*
BMI	1.108 (1.038-1.183)	0.002	1.173 (1.085-1.269)	< 0.001*
Hypertension	1.631 (1.006-2.646)	0.047	0.971 (0.538-1.750)	0.921
Diabetes	1.984 (1.118-3.523)	0.019	1.555 (0.838-2.884)	0.162
CBD diameter	2.642 (1.737-4.018)	< 0.001	1.630 (0.933-2.847)	0.086
Number of CBDS > 2	3.047 (1.767-5.253)	< 0.001	2.289 (1.287-4.071)	0.005*
CBDS diameter > 1 cm	1.780 (1.122-2.824)	0.014	0.986 (0.581-1.673)	0.960
Prior history of CCY	2.568 (1.565-4.213)	< 0.001	1.009 (0.487-2.090)	0.981
Prior history of choledocholithotomy	3.320 (1.630-6.764)	< 0.001	1.763 (0.751-4.142)	0.193
Preoperative biliary tract infection	1.703 (1.060-2.735)	0.028	0.889 (0.508-1.555)	0.680
Gallbladder- or biliary tract–related events	5.071 (2.043-12.590)	< 0.001	4.972 (1.628-15.185)	0.005*

suggested that bile pigments predominated in CBDS for European and Asian populations. This could explain why cholecystectomy could not reduce the recurrence rate of CBDS.

It is well known that bile stored in the gallbladder is excreted to flush the biliary tract so that the microlithiasis and sludge can be passed out. These effects of preventing stone formation are lost if the gallbladder is removed. Additionally, the gallbladder with normal function maintains a steady pressure of Oddi sphincter. Cholecystectomy decreases the pressure difference between both sides of Oddi sphincter and shortens the time of bile excretion, followed by an increased chance of retrograde bile duct infections due to intestinal fluid reflux. Park et al[23] reported that patients with a prior history of cholecystectomy exhibit a high rate of CBDS recurrence, which is consistent with our finding in PH-CCY group. They also found that prophylactic cholecystectomy was not required for preventing the recurrence of CBDS after ERCP in Asian populations.

However, these results do not mean that CCY makes no contribution to postoperative complications and gallbladder preservation is always chosen. In fact, UK and US guidelines suggested that CCY need to be considered when patients undergo therapeutic ERCP for CBDS[3,24]. More interestingly, a new laparo-endoscopic rendezvous has been recently proposed and put into operation[25], as it boasts a unique advantage of reducing the risk of recurrent biliary event or complications[26-28].

In the nomogram model, age and BMI are congenital factors of CBDS recurrence. Recent studies[29,30] have reported BMI is considered as the independent risk factor of CBDS recurrence in all patients. Two prospective studies[31,32] with large sample sizes have investigated the association between different lifestyle pattern and the risk of symptomatic gallstone disease. Our result is consistent with previous finding, in which a positive association between BMI and the risk of gallstones has been identified. The possible reason is that increased cholesterol crystallization formed by lipid accumulations often results in gallbladder stones or secondary CBDS. Another view is that patients with hypertriglyceridemia were insensitive to cholecystokinin, the postprandial release of which promotes gallbladder motility and is of great help in CBDS prevention[32]. Multiple studies[33,34] have shown that age was the risk factor of CBDS recurrence. It was reported that the recurrence rate of CBDS was as high as 30% in the elderly population (>65 years of age)[35]. Furthermore, Wang et al[36] conducted an observational study among 16,299 participants and demonstrated a positive association between gallstone disease and type 2 diabetes. However, the final model framework did not include the diabetes, probably due to its small case volume.

Conclusions

In summary, the purpose of this study was to evaluate the risk factors for recurrence of CBDS in patients with different intervention strategies for gallbladder after ERCP. Our study found that cholecystectomy does not help in the prevention of CBDS recurrence, and a prior history of cholecystectomy may indicate high risk of recurrence. A nomogram model for prediction of CBDS recurrence is established by identifying candidate predictors of recurrence. In the future, application to the wider population can be validated.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Authors' Contribution

XZ and YH: designed the study; JL and XW: collected and analyzed the data; JL, XW and ZY: wrote the manuscript; XL, LW, YZ and JZ: made the contribution for the data quality control and manuscript revision. All authors have read and approved the manuscript.

Ethics Approval

The studies involving human participants were reviewed and approved by the Ethics Committee of Zhongshan Hospital of Xiamen University and Shengli Clinical Medical College of Fujian Medical University (K2021-06-021).

Informed Consent

Written informed consent for participation was not required for the retrospective study in accordance with the national legislation and the institutional requirements.

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