

# A Nomogram for Predicting the Risk of Common Bile Duct Stones Based on Preoperative Laboratory Tests and Ultrasonography

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## Research Article

**Keywords:** Nomogram, Prognosis, Common bile duct, Stones

**Posted Date:** March 11th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-265606/v1>

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# **A nomogram for predicting the risk of common bile duct stones based on preoperative laboratory tests and ultrasonography**

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## **Abstract**

**Objective:** The objective of this study was to determine the predictive factors for common bile duct (CBD) stone and establish a nomogram model based on the preoperative laboratory tests and imaging findings.

**Methods:** A total of 1701 patients who underwent laparoscopic cholecystectomy (LC) combined with common bile duct exploration (CBDE) for suspected choledochlithiasis from November 2014 to October 2020 were eligible for this analysis. All patients were divided into the training set (from November 2014 to November 2019, n=1,453) and validation set (from November 2019 to October 2020, n=248) based on the admission time. The predictive factors for CBD stone were determined by the univariate and multivariate logistic regression model. A nomogram model for predicting the presence of CBD stone was developed based on significant variables, and receiver operating characteristic (ROC) curve, calibration plot and decision curve analysis (DCA) were used to assess the predictive performance of the nomogram.

**Results:** The results of multivariate logistic regression analysis demonstrated that multiple gallbladder stones (OR: 7.463, 95%CI: 5.437-10.243, P<0.001), the maximal diameter of CBD stone measured by preoperative ultrasonography (OR for 0.8-1.5 cm: 4.756, 95%CI: 3.513-6.438, P<0.001; OR for 1.5-2.0 cm: 9.597, 95%CI: 4.621-19.931, P<0.001; OR for >2.0 cm: 24.473, 95%CI: 2.809-213.207, P<0.001), preoperative GGT level (OR for 90-225 U/L: 2.828, 95%CI: 1.898-4.214, P<0.001; OR for 225-450 U/L: 9.994, 95%CI: 4.668-21.403, P<0.001; OR for >450 U/L: 12.535, 95%CI: 4.452-35.292, P<0.001) and DB/TB ratio (OR: 394.329, 95%CI: 79.575-1954.064, P<0.001) were independent predictive factors for CBD stone. The nomogram model for predicting the presence of CBD stone was developed based on the above-

mentioned variables. ROC curve showed that the C-index of the nomogram model for the training set and validation set was 0.875 (95% CI: 0.857-0.893) and 0.834 (95% CI: 0.784-0.883), which were better than that of MRCP for preoperative diagnosis of CBD stone. The calibration curve and DCA curve demonstrated that the nomogram model had a good clinical utility for predicting the presence of CBD stone .

**Conclusion:** The nomogram based on preoperative laboratory tests and ultrasonography had an excellent predictive power for CBD stone, and it might provide useful information for making treatment strategies.

**Keywords:** Nomogram; Prognosis; Common bile duct; Stones

## **Introduction**

It has been reported that the prevalence of secondary common bile duct (CBD) stone was approximately 15-18% in patients with gallbladder stones [1]. CBD stone could further result in hepatic injury, pain, cholangitis, and even acute obstructive cholangitis or biliary pancreatitis [2]. In the past, CBD stone was mainly diagnosed by endoscopic retrograde cholangiopancreatography (ERCP), but the diagnostic method had a relatively high risk of acute pancreatitis and hemorrhage [3]. On the other hand, laparoscopic cholecystectomy (LC) combined with endoscopic retrograde cholangiopancreatography (ERCP) or laparoscopic common bile duct exploration (LCBDE) had been performed to determine the presence of CBD stone during the operation [4,5]. LCBDE largely preserved the integrity of the common bile duct, and avoided unnecessary choledochotomy and preserved the function of the Oddi sphincter [6,7]. With the advancement in the diagnostic technique and equipment, a variety of non-invasive imaging examinations such as abdominal ultrasonography (US), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography (EUS), and abdominal CT scan were widely applied to identify the presence of CBD stone before surgery. To date, abdominal ultrasound usually was considered as the primary imaging examination followed by MRCP [8]. It has been shown that the diagnostic sensitivity and specificity of MRCP for CBD stone was more than 95%, with a high degree of accuracy [9,10]. However, MRCP examination was more expensive and its diagnostic accuracy was easily affected by several subjective conditions. Therefore, it is urgent to develop a simple, non-invasive and efficient tool to precisely predict the presence of CBD stone before surgery.

Recently, the nomogram model, which was a graphical computational scale, was proposed by many studies to predict the possibility of interest events [11,12]. In the present study, patients who underwent surgical treatment for suspected choledocholithiasis were reviewed and predictive factors for CBD stone were analyzed. We aimed to construct a nomogram model for predicting the presence of CBD stone according to the preoperative laboratory test and imaging findings in order to help clinicians make therapeutic strategies.

## **Methods**

### ***Patient***

In this study, a total of 1701 consecutive patients who underwent surgical treatment for suspected choledocholithiasis at the department of general surgery, Beijing Friendship Hospital from November 2014 to October 2020 were analysed retrospectively. Eligibility criteria required: (1) All patients suffering from cholangitis had definitive imaging examinations, including MRCP and abdominal ultrasonography, before surgery; (2) complete laboratory findings at the time of first presentation to the hospital. The exclusion criteria were: (1) patients without bile duct exploration; (2) contraindications to laparoscopic surgery; (3) clinical data were incomplete.

### ***Clinical information***

The positive findings of imaging examination were defined as visible stones diagnosed by preoperative magnetic resonance cholangiopancreatograph (MRCP) or ultrasonography (US). CBDD was described as the maximal value of CBD diameter on US imaging. All routine biochemical indicators, including alanine aminotransferase (ALT), aspartate aminotransferase

(AST), alkaline phosphatase (ALP), glutamyl transpeptidase (GGT), direct bilirubin (DB) and total bilirubin (TB), were systematically collected.

In our laboratory, ALT>40U/L, AST>35U/L, ALP>100U/L, GGT>45U/L, TB>17.1umol/L, DB>6.84umol/L were considered as abnormal value, respectively. The patients were divided into two groups according to the presence of CBD stone.

### ***Statistical analysis***

Statistical analysis was conducted with SPSS software (version 26) and R software (version 4.0.2). Continuous variables were presented as mean±SD and the differences between research groups were compared using a Student's t-test if they followed a normal distribution; otherwise, they were recorded as the medium (P<sub>25</sub>, P<sub>75</sub>) and were compared using Mann-Whitney U test. Categorical variables were shown as frequency or percentage and were compared using chi-square test or Fisher's exact test. The cut-offpoint for CBDD measured by preoperative ultrasonography was determined by receiver operating characteristics (ROC) curve. Univariate and multivariate logistic regression were used to determine the predictive factors for CBD stone, and relevant results were reported as odds ratio (OR) and its 95% confidence intervals (CIs).

In the present study, the nomogram model for predicting the presence of CBD stone before surgery was developed according to the regression coefficients estimated by multivariate logistic regression model.

The predictive performance of the nomogram model was assessed by the ROC curve. Calibration curves were plotted to evaluate the association between predicted probabilities and actual observations. A two-sided P-value of <0.05 indicated a significantly statistical

significance.

## **Results**

### ***The baseline characteristics of patients***

From November 2014 to October 2020, a total of 1701 patients with suspected choledochlithiasis were eligible for this analysis. Of these patients, 773 were male (45.4%) and 928 were female (54.6%), and the mean age was  $57.95 \pm 14.81$  years. In terms of surgical methods, 1560 patients (91.7%) underwent LC plus LCBDE, 106 patients (6.2%) underwent choledocholithotomy, and 30 patients (1.8%) underwent partial hepatectomy owing to the presence of intrahepatic bile duct stone. After performing laparoscopic common bile duct exploration, 968 patients (56.9%) were intraoperatively diagnosed with CBD stone and 633 patients (43.1%) did not show any positive finding. Baseline characteristics, imaging examinations and biomarker variables are shown in Table 1. There were significant differences between patients with and without CBD stone for imaging examinations and laboratory characteristics.

For the development and validation of the nomogram model for predicting the presence of CBD stone, all patients were divided into the training set (from November 2014 to November 2019, n=1,453) and validation set (from November 2019 to October 2020, n=248) based on the admission time.

### ***Univariate and multivariate analysis of predictive factor for CBD stone***

Univariate analysis of predictive factor for CBD stone was performed in the training set, and the results revealed that the presence of CBD stone was significantly associated with multiple

gallbladder stones ( $P<0.001$ ), elevated levels of TB ( $P<0.001$ ), DB ( $P<0.001$ ), cholestatic liver enzymes (ALP and GGT,  $P<0.001$ ) and hepatocellular liver enzymes (ALT and AST,  $P<0.001$ ). In addition, the presence of CBD stone was more likely to be detected by preoperative ultrasonography ( $P<0.001$ ) and was associated with larger diameter of CBD stone measured by ultrasonography ( $P<0.001$ ) (Table 2).

Based on the results of the univariate analysis, the variables with  $P<0.05$  were further analyzed by the multivariate logistic regression model. The results demonstrated that multiple gallbladder stones (OR: 7.463, 95%CI: 5.437-10.243,  $P<0.001$ ), the maximal diameter of CBD stone measured by preoperative ultrasonography (OR for 0.8-1.5 cm: 4.756, 95%CI: 3.513-6.438,  $P<0.001$ ; OR for 1.5-2.0 cm: 9.597, 95%CI: 4.621-19.931,  $P<0.001$ ; OR for  $>2.0$  cm: 24.473, 95%CI: 2.809-213.207,  $P<0.001$ ), GGT level (OR for 90-225 U/L: 2.828, 95%CI: 1.898-4.214,  $P<0.001$ ; OR for 225-450 U/L: 9.994, 95%CI: 4.668-21.403,  $P<0.001$ ; OR for  $>450$  U/L: 12.535, 95%CI: 4.452-35.292,  $P<0.001$ ) and DB/TB ratio (OR: 394.329, 95%CI: 79.575-1954.064,  $P<0.001$ ) were independent predictive factors for CBD stone.

### ***Construction and validation of nomogram for the prediction of CBD stone***

Next, we developed a nomogram model for the prediction of CBD stone according to the results of multivariate logistic regression analysis in the training set (Table 3 and Table 4). As shown in the Figure 1, four variables, including the number of gallbladder stones (multiple vs single), the maximal diameter of CBD stone measured by preoperative ultrasonography ( $<0.8$ , 0.8-1.5, 1.6-2.0 and  $>2.0$  cm), GGT level ( $<90$ , 90-225, 226-450 and  $>450$  U/L) and DB/TB ratio, were used. The risk of CBD stone was predicted by scoring each variables and counting total points (Table 5) . Higher total points in the nomogram model, higher risk of CBD stone in these

patients. ROC curve demonstrated that the C-index of the nomogram model for the prediction of CBD stone was 0.875 (95% CI: 0.857-0.893), and the sensitivity and specificity of 81.7% and 57.6%, which was better than that of MRCP for preoperative diagnosis of CBD stone (Fig. 2A). Meanwhile, the calibration curves showed a good consistency between predicted and observed outcomes in the training set and validation set (Fig. 2B and C). In addition, the decision curve analyses (DCA) indicated that the clinical applicability of the nomogram model was comparable to that of MRCP for the diagnosis of CBD stone (Fig. 2D).

## **Discussion**

In 2010, the American Society for Gastrointestinal Endoscopy (ASGE) published a proposed guideline for predicting the risk of choledocholithiasis. The patients were categorized into low (<10%), intermediate (10%–50%) and high (>50%) risk for CBD stone according to the clinical symptoms, abdominal ultrasound (US) and laboratory tests . The guideline recommended that endoscopy or surgery should be performed for high-risk patients to remove stones, while those patients with intermediate risk should further make a definite diagnosis by EUS or MRCP [14]. However, several studies showed unsatisfactory diagnostic accuracy of ASGE guideline for predicting CBD stones [15, 16]. MRCP is widely accepted as a non-invasive diagnostic method with high sensitivity and specificity, but it is time-consuming, relatively expensive, and its diagnostic accuracy mainly depends on the image quality and radiologist's experience.

Therefore, to develop a simple, non-invasive and efficient model for predicting the presence of CBD stone was useful to make a rapid diagnosis and guide therapeutic strategies before surgery.

The nomogram enables the assessment of the probability of clinical events through

individual patient characteristics, and its visual and iconic results provide a more intuitive representation for risk assessment of disease than other predictive models. In this study, we used the univariate and multivariate logistic regression analysis to determine the predictive factors for CBD stone. Our results revealed that multiple gallbladder stones, the maximal diameter of CBD stone measured by preoperative ultrasonography, preoperative GGT level and DB/TB ratio were independent predictors of CBD stone, which had been reported by previous studies [17-19]. Based on these variables, we developed a nomogram model and the results showed that the AUC of ROC curve for the training set was 0.875, with a sensitivity and specificity of 83.1% and of 76.1% for the prediction of CBD stone, respectively. More importantly, the predictive performance of the nomogram model was further validated by an internal dataset, suggesting that it had an excellent predictive capability for CBD stone. To date, few prediction models for CBD stone were proposed. Recently, Kadah A [20] developed the scoring model for predicting CBD stone based on patient age, GGT and CBDD, and the results showed an AUC of 0.729, the sensitivity and specificity of 81.7% and 57.6%, respectively. Compared with the scoring model, our nomogram had a better predictive value for the diagnosis of CBD stone. On the other hand, our results demonstrated that the nomogram model had a better clinical utility than MRCP according to the DCA curves for predicting the presence of CBD stone. These findings supported that the nomogram could provide a clinical benefit for patients in terms of the diagnosis of CBD stone.

The current study had several limitations. First, all data of patients were obtained from a single institution and the sample size was limited, which might result in the selection bias. Therefore, further investigations need to involve a larger sample size as well as multicenter

external cohorts to validate the predictive power of the nomogram. Second, the imaging characteristics mainly relied on manual measurements by radiologists and their individual experience. Finally, clinical characteristics included in this analysis was still limited, and the stratification of patients with different ages or severity of disease should be further refined in subsequent studies.

## **Conclusion**

In conclusion, we developed and validated a simple, non-invasive nomogram to predict the risk of CBD stone based on preoperative laboratory tests and ultrasonography. The results showed that the nomogram had an excellent predictive power and clinical utility for CBD stone. The nomogram might be an useful tool to make a diagnosis and guide treatment strategies for CBD stone.

## **Funding**

This study was supported by National Key Technologies R&D Program (No. 2015BAI13B09), Research Foundation of Beijing Friendship Hospital, Capital Medical University (No. yyqdk2018-10), Wu Jieping Medical Foundation (No. 320.6750.19089-37) and Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support (XMLX202102).

## **Acknowledgements**

Not applicable

## **Ethical approval**

The ethical approval for the present study was obtained from the Beijing Friendship Hospital

ethics committee, and the informed consent was obtained from all participants.

### **Availability of data and materials**

The datasets used during the current study are available from the corresponding author on reasonable request

### **Consent for publication**

Not applicable

### **Authors' contributions**

Wei Guo and Kai Wu designed the study; Dong Wang, Kai Wu, Jiegao Zhu, Hongwei Wu, Kun Liu, and Jun Liu performed the acquisition, analysis, and interpretation of the data; Dong Wang and Kai Wu drafted the manuscript; and Wei Guo revised the manuscript. The authors read and approved the final manuscript.

### **Conflict of interest**

The authors declare no conflict of interest

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**Table 1**

Baseline demographic data and clinical characteristics

Variables	CBD stone		$\chi^2/t/Z$	P-value	
	Positive(n=968)	Negative(n=733)			
Sex	male	447(46.2)	326(44.5)	0.488	0.485
	female	521(53.8)	407(55.5)		
Age(years)		58.95±15.121	56.62±14.296	2.363	0.001
MRCP	Positive	614(63.4)	76(10.4)	487.125	<0.001
	Negative	354(36.6)	657(89.6)		
US	Positive	226(23.3)	33(4.5)	114.766	<0.001
	Negative	742(76.7)	700(95.5)		
Gallbladder stones	Multiple	764(78.9)	320(43.7)	224.474	<0.001
	Single	204(21.1)	413(56.3)		
CBDD (cm)		1.0(0.8,1.4)	0.7(0.5,0.9)	-20.045	<0.001
ALT(U/L)		30(17,79)	21(14,42.5)	-7.541	<0.001
AST(U/L)		25.6(19.8,47.1)	21(17,30.2)	-8.962	<0.001
ALP(U/L)		112(83,174)	80(63,107)	-14.248	<0.001
GGT(U/L)		126(38,279)	38(20,100.5)	-14.271	<0.001
TB (umol/L)		17.63(12.65,27.86)	14.69(11.54,20.39)	-7.01	<0.001
DB (umol/L)		4.83(2.8,11.98)	2.83(2.01,4.03)	-14.538	<0.001
DB/TB ratio		0.271(0.201,0.492)	0.192(0.157,0.251)	-15.982	<0.001

Variables	Training Set(n=1453)			Validation Set(n=248)			
		Positive for CBD stone(n=807)	Negative for CBD stone(n=646)	P-value	Positive for CBD stone(n=161)	Negative for CBD stone(n=87)	P-value
Sex	male	370(45.8)	295(45.7)	0.944	77(47.8)	31(35.6)	0.062
	female	437(54.2)	351(54.3)		84(52.2)	56(64.4)	
Age(years)		59.7±14.676	56.99±14.397	0.073	60.07±16.159	52.45±15.256	0.099
MRCP	Positive	502(62.2)	60(9.3)	<0.001	112(69.6)	16(18.4)	<0.001
	Negative	305(37.8)	586(90.7)		49(30.4)	71(81.6)	
US	Positive	191(23.7)	29(4.5)	<0.001	35(21.7)	4(4.6)	<0.001
	Negative	616(76.3)	617(95.5)		126(78.3)	83(95.4)	
Gallbladder stones	Multiple	647(80.2)	281(43.5)	<0.001	117(72.7)	39(44.8)	<0.001
	Single	160(19.8)	365(56.5)		44(27.3)	48(55.2)	
CBDD (cm)		1.0(0.8,1.4)	0.7(0.5,0.9)	<0.001	1.0(0.8,1.35)	0.7(0.6,0.9)	<0.001
ALT(U/L)		30(17,74)	21(13,42)	<0.001	29(16.5,107)	25(15,63)	0.303
AST(U/L)		25(19.8,47)	21(17,29)	<0.001	25(19.75,55.8)	22.4(18.2,36.8)	0.11
ALP(U/L)		111(83,175)	79(61,102)	<0.001	113(81,170.5)	103(73,139)	0.077
GGT(U/L)		128(42,282)	35.5(20,94.25)	<0.001	99(26,250.5)	55(21,175)	0.045
TB (umol/L)		17.49(12.65,27.48)	14.69(11.59,20.38)	<0.001	18.31(12.63,31.45)	15.22(11.26,22.73)	0.009
DB (umol/L)		5.00(2.83,11.92)	2.79(2.01,3.97)	<0.001	4.03(2.34,12.45)	3.09(2.17,4.83)	0.001
DB/TB ratio		0.283(0.206,0.511)	0.192(0.156,0.251)	<0.001	0.226(0.188,0.379)	0.195(0.167,0.248)	<0.001

\* MRCP, Magnetic Resonance Cholangiopancreatograph; US, Ultrasonography; MRCP or US Positive indicates that imaging examination revealed CBD stone; CBDD, the value of maximal CBD diameter measured on the Ultrasonography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, glutamyl transpeptidase; TB, total bilirubin; DB, direct bilirubin; P-value<0.05 indicates statistical significance.

Variables		Trianing set(n=1453)	Validation Set(n=248)	P-value
Sex	male	665(45.8)	108(43.5)	0.517
	female	788(54.2)	140(56.5)	
Age(years)		58.04±14.56	57.4±16.23	0.527
US	Positive	220(15.1)	39(15.7)	0.813
	Negative	1233(84.9)	209(84.3)	
Gallbladder stones	Multiple	928(63.9)	156(62.9)	0.770
	Single	525(36.1)	92(37.1)	
CBDD(cm)		0.9(0.6,1.2)	0.9(0.7,1.1)	0.478
ALT(U/L)		25.0(15.0,58.0)	28.0(16.0,90.5)	0.057
AST(U/L)		23.1(18.5,36.0)	24.2(18.8,40.9)	0.082
ALP(U/L)		92.0(72.0,138.5)	109.0(78.0,156.8)	0.002
GGT(U/L)		79.0(25.0,193.0)	85.0(24.0,228.0)	0.456
TB(umol/L)		16.14(12.14,23.07)	17.36(11.83,27.38)	0.298
DB(umol/L)		3.55(2.41,7.56)	3.61(2.26,7.76)	0.937
DB/TB ratio		0.230(0.179,0.355)	0.216(0.177,0.321)	0.153

\* MRCP, Magnetic Resonance Cholangiopancreatograph; US, Ultrasonography; MRCP or US Positive indicates that imaging examination revealed CBD stone; CBDD, the value of maximal CBD dimeter measured on the Ultrasonography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, glutamyl transpeptidase; TB, total bilirubin; DB, direct bilirubin; P-value<0.05 indicates statistical significance.

**Table 2**

Univariate analysis of variables associated with CBD stone.

Variables		Positive for CBD stone(n=807)	Negative for CBD stone(n=646)	$\chi^2/Z$	P-value
Sex	male	370	295	0.005	0.944
	female	437	351		
Age(years)		59.7±14.676	56.99±14.397	1.254	0.073
US	Positive	191	29	102.642	<0.001
	Negative	616	617		
Gallbladder stones	Multiple	647	281	208.981	<0.001
	Single	160	365		
CBDD (cm)	<0.8	235	476	297.772	<0.001
	0.8-1.5	449	157		
	1.5-2.0	94	13		
	>2.0	28	1		
ALT(U/L)	<40	489	481	31.052	<0.001
	≥40	318	165		
AST(U/L)	<35	546	532	40.435	<0.001
	≥35	261	114		
ALP(U/L)	<100	333	477	146.563	<0.001
	100-200	305	127		
	200-500	137	39		
	>500	32	3		
GGT(U/L)	<90	288	480	165.972	<0.001

	90-225	259	117		
	225-450	158	30		
	>450	102	19		
TB (umol/L)	<17.1	397	400	38.464	<0.001
	17.1-34.2	264	198		
	≥34.2	146	48		
DB (umol/L)	<6.84	489	565	129.922	<0.001
	≥6.84	318	81		
DB/TB ratio		0.283(0.206,0.511)	0.192(0.156,0.251)	-15.787	<0.001

\* US, Ultrasonography; US Positive indicates that imaging examination revealed CBD stone; CBDD, the value of maximal CBD diameter measured on the Ultrasonography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, glutamyl transpeptidase; TB, total bilirubin; DB, direct bilirubin; P-value<0.05 indicates statistical significance.

**Table 3**

Multifactorial logistic regression analysis of CBD stone.

Predictors	B	S.E.	Wald	P-value	95% Confidence Interval	
					Lower Bound	Upper Bound
US	0.778	0.261	8.862	0.003	1.305	3.636
Gallbladder multiple stones	1.955	0.156	157.13	<0.001	5.203	9.589
CBDD	1.082	0.101	114.742	<0.001	2.421	3.598
ALT	-0.35	0.236	2.197	0.138	0.444	1.119
AST	-0.327	0.27	1.462	0.227	0.425	1.225
ALP	0.067	0.145	0.21	0.646	0.804	1.421
GGT	0.211	0.049	18.817	<0.001	1.122	1.358
TB	0.017	0.146	0.014	0.907	0.764	1.354
DB	-0.736	0.332	4.899	0.027	0.25	0.919
DB/TB ratio	6.23	0.808	59.427	<0.001	104.153	2474.186

\* US, Ultrasonography; US Positive indicates that imaging examination revealed CBD stone; CBDD, the value of maximal CBD diameter measured on the Ultrasonography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, glutamyl transpeptidase; TB, total bilirubin; DB, direct bilirubin; P-value<0.05 indicates statistical significance.

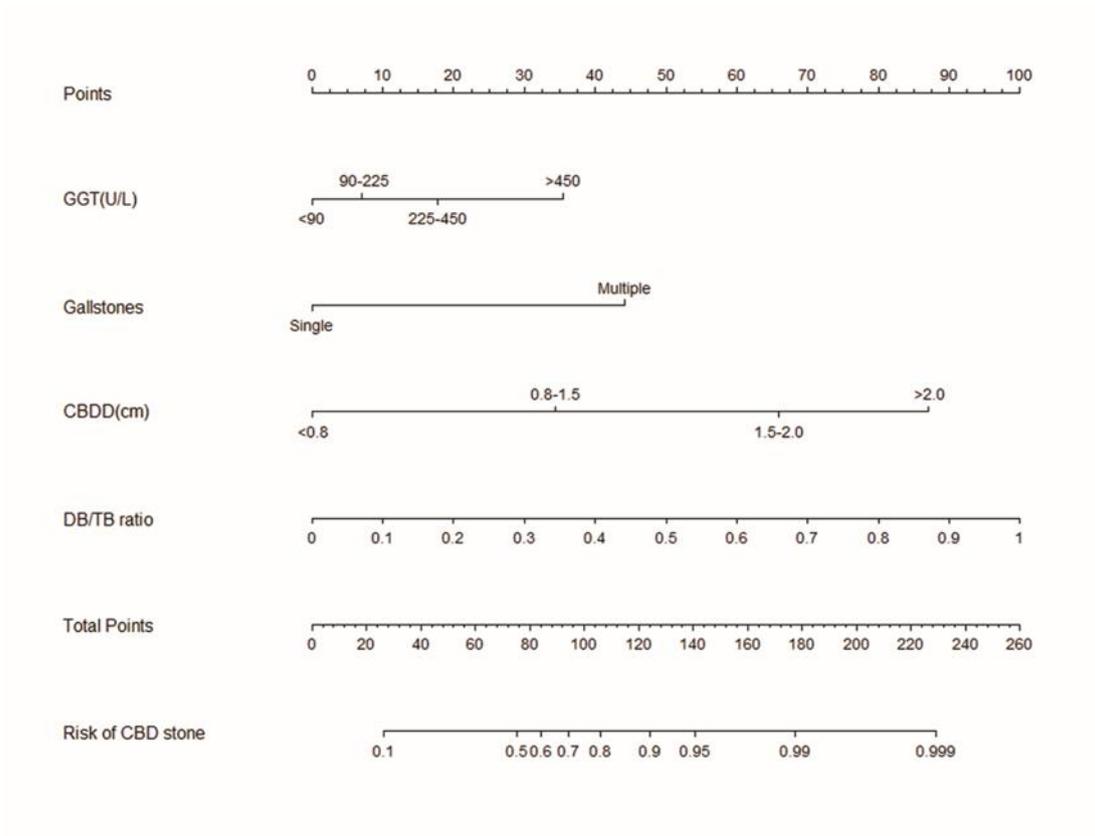
**Table 4**

Univariate and multivariate analysis of variables associated with CBD stone in training set.

Variables	Positive for CBD stone(n=807)	Negative for CBD stone(n=646)	Univariate analysis(P-value)	Multivariate analysis	
				HR(95%CI)	P-value
Sex			0.944		
male	370 (45.8)	295 (45.7)		-	-
female	437 (54.2)	351 (54.3)		-	-
Age(years)	59.7±14.676	56.99±14.397	0.073	-	-
US			<0.001		0.003
Negative	616 (76.3)	617 (95.5)		reference	
Positive	191 (23.7)	29 (4.5)		2.245(1.325-3.804)	
Gallbladder stones			<0.001		<0.001
Single	160 (19.8)	365 (56.5)		reference	
Multiple	647 (80.2)	281 (43.5)		7.463(5.437-10.243)	
CBDD (cm)			<0.001		<0.001
<0.8	235 (29.1)	476 (73.7)		reference	
0.8-1.5	449 (55.6)	157 (24.3)		4.756(3.513-6.438)	
1.5-2.0	94 (11.7)	13 (2.0)		9.597(4.621-19.931)	
>2.0	29 (3.6)	0 (0)		24.473(2.809-213.207)	
ALT(U/L)			<0.001		0.139
<40	489 (60.6)	481 (74.5)		reference	
≥40	318 (39.4)	165 (25.5)		0.515(0.314-0.845)	
AST(U/L)			<0.001		0.226
<35	546 (67.7)	532 (82.4)		reference	
≥35	261 (32.3)	114 (17.6)		0.799(0.460-1.386)	
ALP(U/L)			<0.001		0.634
<100	333 (41.3)	477 (73.8)		reference	
100-200	305 (37.8)	127 (19.7)		1.485(1.011-2.181)	
200-500	137 (17.0)	39 (6.0)		0.354(0.148-0.850)	
>500	32 (3.9)	3 (0.5)		0.646(0.111-3.750)	
GGT(U/L)			<0.001		<0.001
<90	288 (35.7)	480 (74.3)		reference	
90-225	259 (32.1)	117 (18.1)		2.828(1.898-4.214)	
225-450	158 (19.6)	30 (4.6)		9.994(4.668-21.403)	
>450	102 (12.6)	19 (3.0)		12.535(4.452-35.292)	

TB (umol/L)			<0.001		0.921
<17.1	397 (49.2)	400 (61.9)		reference	
17.1-34.2	264 (32.7)	198 (30.7)		1.152(0.822-1.614)	
≥34.2	146 (18.1)	48 (7.4)		0.914(0.440-1.898)	
DB (umol/L)			<0.001		0.028
<6.84	489 (60.6)	565 (87.5)		reference	
≥6.84	318 (39.4)	81 (12.5)		0.547(0.276-1.084)	
DB/TB ratio	0.283(0.206,0.511)	0.192(0.156,0.251)	<0.001	394.329(79.575-1954.064)	<0.001

\* US, Ultrasonography; US Positive indicates that imaging examination revealed CBD stone; CBDD, the value of maximal CBD diameter measured on the Ultrasonography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, glutamyl transpeptidase; TB, total bilirubin; DB, direct bilirubin; HR, hazard ratio; CI, confidence interval; P-value<0.05 indicates statistical significance.



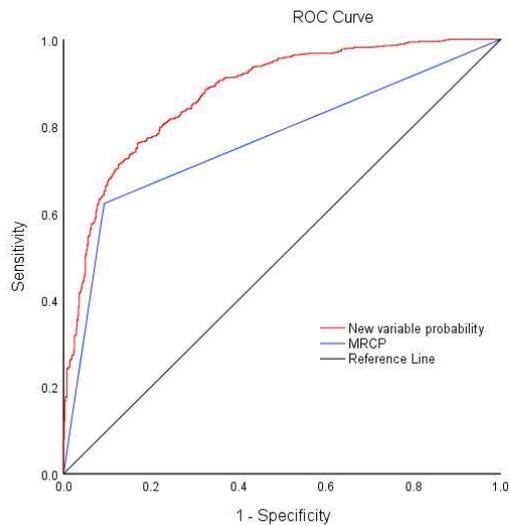
**Fig. 1** Nomogram model of CBD stone risk

**Table 5**

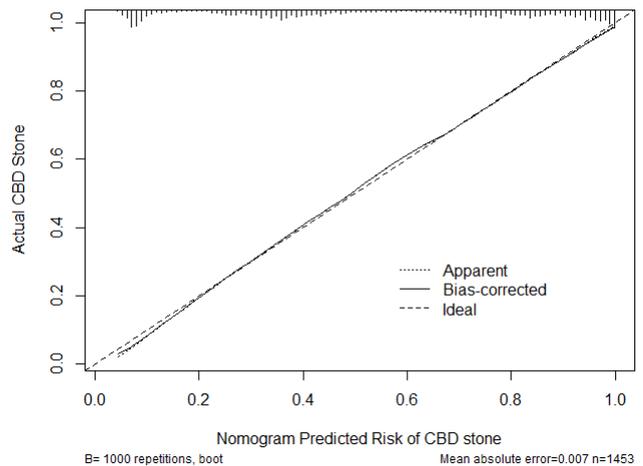
Score assignment for specific categories of variables included in the Nomogram

Prognostic factors		
Variables	Category	Score
GGT(U/L)	<90	0
	90-225	7
	225-450	18
	>450	25
Gallbladder stones	Single	0
	Multiple	44
CBDD (cm)	<0.8	0
	0.8-1.5	34
	1.5-2.0	66
	>2.0	87
DB/TB ratio	0.0	0
	0.1	10
	0.2	20
	0.3	30
	0.4	40
	0.5	50
	0.6	60
	0.7	70
	0.8	80
	0.9	90
1.0	100	
Total score	Risk of CBD stone	
10	0.050	
26	0.100	
44	0.200	
56	0.300	
66	0.400	
75	0.500	
84	0.600	
94	0.700	
106	0.800	
124	0.900	
141	0.950	
178	0.990	
229	0.999	

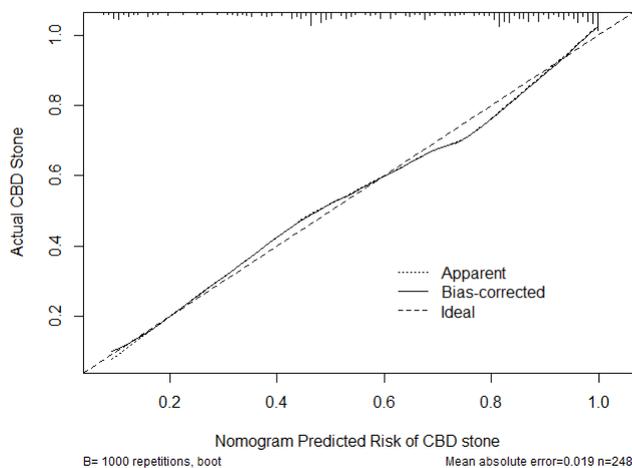
\* CBDD, the value of maximal CBD diameter measured on the Ultrasonography; GGT, glutamyl transpeptidase; TB, total bilirubin; DB, direct bilirubin; HR, hazard ratio; CI, confidence interval; P-value<0.05 indicates statistical significance.



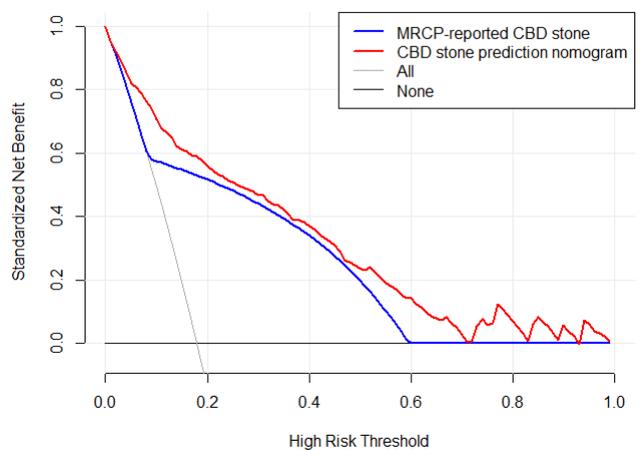
(A)



(B)



(C)



(D)

**Fig. 2** (A)ROC curve based on the nomogram compared with MRCP. Calibration curve based on the nomogram model in the training set(B) and the validation set(C), the dashed line represents the predictive performance of the nomogram, and the 45 straight lines represent the perfect match between the actual (y-axis) and the predicted probability of the nomogram (x-axis). The closer the distance between the two curves, the higher the prediction accuracy of the nomogram; (D)Decision curve analysis for MRCP-reported and the prediction nomogram in predicting CBD stone. The y-axis measures the net benefit. The net benefit is calculated by subtracting the proportion of all false positives and adding the proportion of true positives to weight the relative harms of forgoing treatment against the harms of unnecessary treatment [9]. The gray line represents the assumption that all patients have CBD stone. The black line represents the assumption that no patients have CBD stone. Using the prediction nomogram (red curve) to predict CBD stone adds more benefit for patients than predicting by MRCP.

# Figures

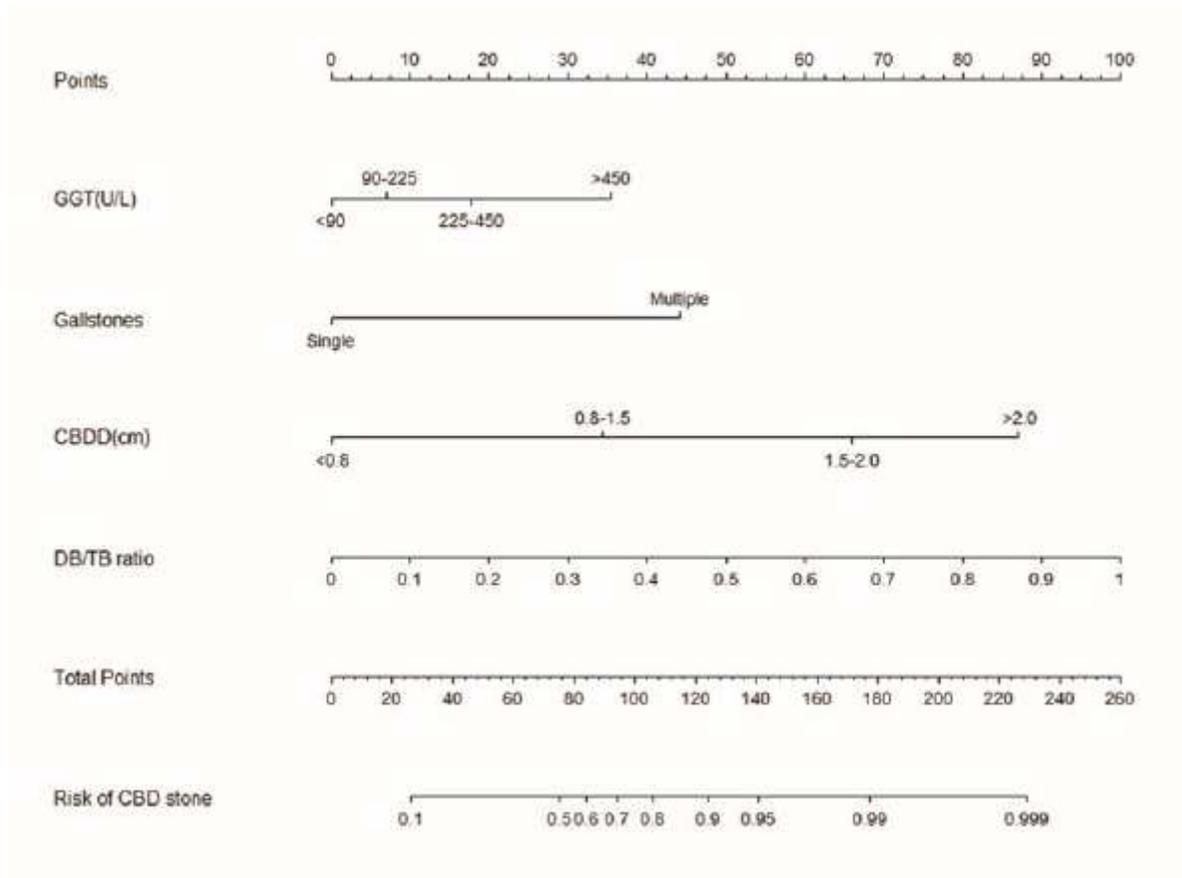
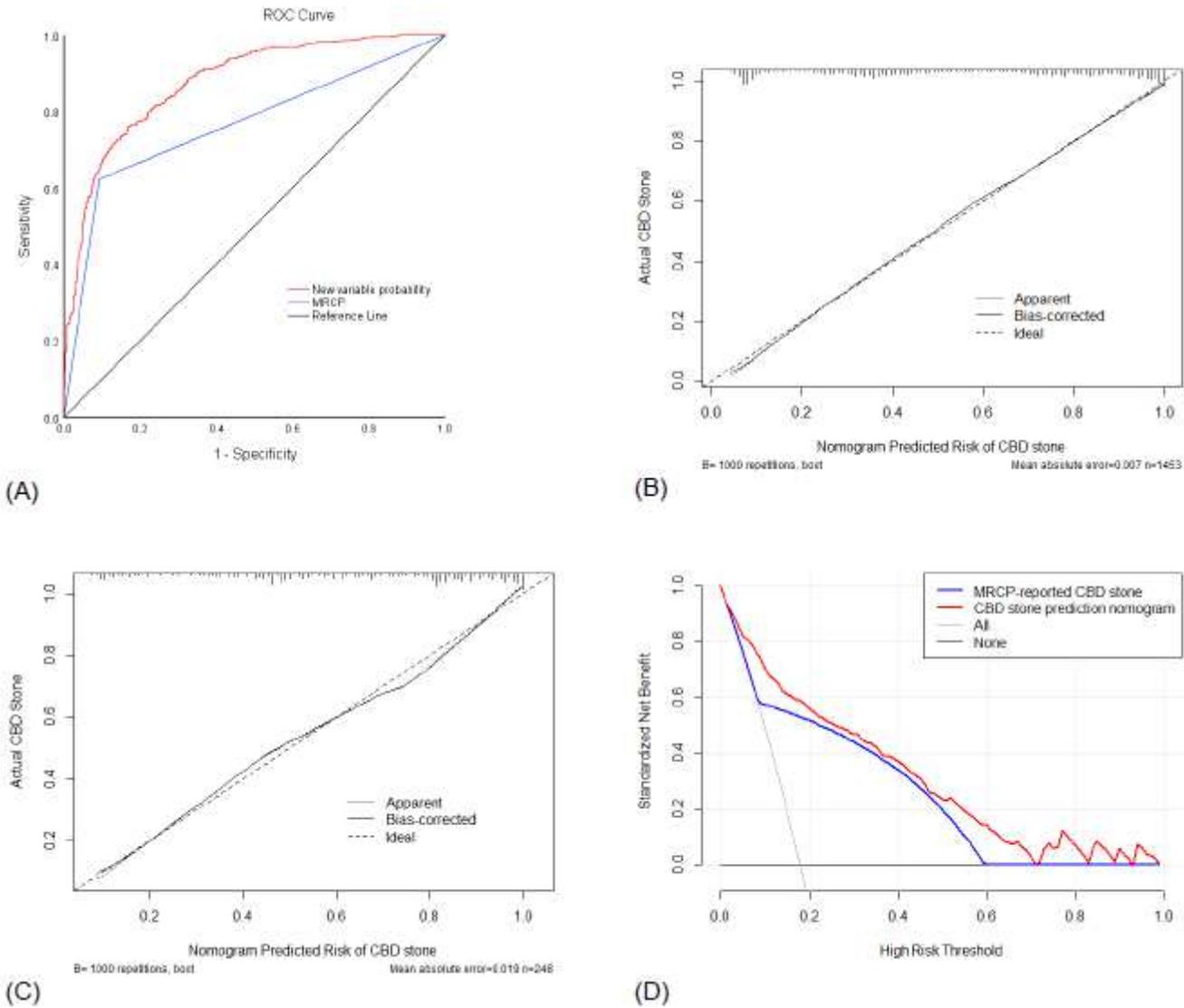


Figure 1

Nomogram model of CBD stone risk



**Figure 2**

(A) ROC curve based on the nomogram compared with MRCP. Calibration curve based on the nomogram model in the training set (B) and the validation set (C), the dashed line represents the predictive performance of the nomogram, and the 45 straight lines represent the perfect match between the actual (y-axis) and the predicted probability of the nomogram (x-axis). The closer the distance between the two curves, the higher the prediction accuracy of the nomogram; (D) Decision curve analysis for MRCP-reported and the prediction nomogram in predicting CBD stone. The y-axis measures the net benefit. The net benefit is calculated by subtracting the proportion of all false positives and adding the proportion of true positives to weight the relative harms of forgoing treatment against the harms of unnecessary treatment [9]. The gray line represents the assumption that all patients have CBD stone. The black line represents the assumption that no patients have CBD stone. Using the prediction nomogram (red curve) to predict CBD stone adds more benefit for patients than predicting by MRCP.