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ARTICLE

Development and Validation of a Preoperative Prediction Model for Neoplastic Gallbladder Polyps

Yanning Zhang[1], Jinyong Hao[1], Pengfei Wang[1], Shaoce Xu[2], Xiong Zhou[3], Jingzhe Wang[4], Xiaojun Huang[1,*]

[1]Department of Gastroenterology, Lanzhou University Second Hospital, Lanzhou, Gansu, China
[2]Department of Pathology, Lanzhou University Second Hospital, Lanzhou, Gansu, China
[3]Department of Gastroenterology, Dingxi People's Hospital, Dingxi, Gansu, China
[4]Department of Gastroenterology, Wuwei People's Hospital, Wuwei, Gansu, China
*Correspondence: huangxj@lzu.edu.cn (Xiaojun Huang)

Abstract

Aims/Background The primary goal in evaluating gallbladder polypoid lesions (GPLs) is to identify neoplastic polyps (NP). Numerous studies have investigated risk factors for NP. This study aimed to develop a practical preoperative prediction model for NP using simple and easily accessible clinical variables.

Methods We retrospectively analyzed clinical data from patients with GPLs who underwent cholecystectomy at Lanzhou University Second Hospital between January 2018 and September 2022. A total of 621 cases were included and randomly assigned into a training set (70%) and an internal validation set (30%). An external validation set was established using data from 117 patients treated at other centers between January and December 2023. Univariate logistic analyses were performed, followed by backward stepwise multivariate logistic regression analysis for variables with $p < 0.2$ to identify significant variables associated with NP. These predictors were included in the final logistic regression model and visualized as a nomogram model. The discrimination, calibration, and clinical utility of the model were evaluated.

Results Age (odd ratio (OR) = 1.06, 95% CI = 1.03–1.09, $p = 0.0001$), polyp size (OR = 19.01, 95% CI = 6.48–55.79, $p < 0.0001$), polyp number (OR = 0.25, 95% CI = 0.12–0.56, $p = 0.0006$), gallbladder wall thickness (OR = 1.57, 95% CI = 1.02–2.41, $p = 0.0385$), and polyp echo characteristics (OR = 0.41, 95% CI = 0.19–0.85, $p = 0.0169$) were identified as independent influencing factors for NP. The area under the curve (AUC) of the nomogram model in the training, internal validation, and external validation sets were 0.886 (95% CI, 0.841–0.930), 0.836 (95% CI, 0.753–0.919), and 0.867 (95% CI, 0.743–0.978), respectively. Calibration curves for the three datasets showed Brier scores of 0.079, 0.092, and 0.070, all below 0.25, indicating good calibration. Decision curve analysis (DCA) and clinical impact curve (CIC) analysis suggested that a threshold probability of 0.6 provided the most significant clinical benefit.

Conclusion This prediction model, incorporating easily accessible variables, demonstrated excellent performance in the identification of NP and contributed to clinical decision-making in GPL management.

Key words: gallbladder neoplasms; neoplastic polyps; nomogram; prediction model; clinical decision-making

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Introduction

With the advancement and widespread adoption of imaging techniques, the detection rate of biliary system abnormalities has significantly improved, including

gallbladder polypoid lesions (GPLs). GPLs encompass all non-calculous lesions with polypoid growth into the gallbladder wall. In 1970, Christensen and Ishak proposed the initial pathological classification of GPLs, distinguishing between malignant and benign lesions (Christensen and Ishak, 1970). The most prevalent malignant lesion is gallbladder adenocarcinoma. Benign lesions are categorized as non-neoplastic polyps (NNP) or neoplastic polyps (NP). NNP can be further classified into cholesterol, inflammatory, hyperplastic, and adenomyomatosis polyps. NP, most commonly adenomas, are precancerous lesions that may progress to gallbladder adenocarcinoma (Chou et al, 2017; Maciejewski and Strzelczyk, 2014). The incidence of GPLs varies by region and ethnicity, ranging from 0.9% to 12.1% (Wang et al, 2024a). Although gallbladder carcinoma is relatively rare, ranking 25th among the most common malignancies worldwide (Sung et al, 2021), its prognosis remains poor, with a 5-year survival rate below 5% for advanced disease (Pavlidis et al, 2024). Consequently, clinicians often adopt aggressive treatment strategies for GLP patients.

Current management guidelines for gallbladder polyps primarily focus on polyp size, recommending cholecystectomy for polyps $\geq$10 mm (Wiles et al, 2017). However, studies have shown that approximately 70% of NNP cases undergo cholecystectomy, with any polyps $\geq$10 mm being benign (Elmasry et al, 2016; Lee et al, 2019). Despite advancements in imaging techniques, including computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasonography, preoperative identification of neoplastic gallbladder polyps remains challenging (Obmann et al, 2021; Takahashi et al, 2024; Zhou et al, 2024).

In this study, we retrospectively analyzed 5 years of data from patients with pathologically confirmed GPLs who underwent cholecystectomy at Lanzhou University Second Hospital. The study aimed to identify risk factors for NP and develop a preoperative prediction model. This model will support GPL management, minimize unnecessary cholecystectomies, and optimize the treatment strategies.

Methods

Study Subjects and Data Collection

Data were collected from patients with GPLs who underwent cholecystectomy at Lanzhou University Second Hospital between January 2018 and September 2022 for a retrospective case-control study. The inclusion criteria were as follows: (1) individuals with pathological examination after cholecystectomy confirmed NNP or NP, (2) individuals with complete clinical baseline data and laboratory findings, and (3) clear and detectable GPLs on ultrasound imaging performed within 8 weeks pre-cholecystectomy. The exclusion criteria included: (1) individuals with preoperative diagnosis of gallbladder carcinoma, (2) individuals with acute cholecystitis, (3) individuals with incomplete description of polyp characteristics, and (4) malignant tumors in other organs.

Experienced pathologists conducted postoperative gallbladder histopathology. Polyp types were classified into NNP and NP based on the most atypical histological finding in cases with multiple histopathological diagnoses. NP cases were

further classified into gallbladder adenomas and adenocarcinomas. A total of 621 patients were included in the analysis, with cases randomly divided in a 7:3 ratio into training and internal validation sets. Additionally, an external validation set comprising 117 patients from Dingxi People's Hospital and Wuwei People's Hospital was constructed from January to December 2023.

The study was conducted following the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Lanzhou University Second Hospital (approval No.: 2024A-797). The study was a retrospective analysis of anonymized data, and therefore, informed consent was not required.

The evaluation indicators in this study included: (1) General patient data: Age, sex, body mass index (BMI), diabetes, and hypertension; (2) laboratory data: Fasting blood glucose (FBG); liver function parameters (alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP)); blood lipids (total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)); and kidney function parameters (blood urea nitrogen (BUN), serum uric acid (SUA) and serum creatinine (Scr)); (3) Ultrasonic data: Polyp size, polyp number, polyp shape, polyp echo characteristics, gallbladder wall thickness, and presence of coexisting gallstones.

Statistical Methods

The Kolmogorov-Smirnov test was used to assess data normality. Variables following normal distribution were expressed as mean ± standard deviation (SD) ($\bar{x} \pm s$), and group comparisons were made using the *t*-test. Non-normally distributed variables were expressed as median (interquartile range) [M (QL, QU)] and compared using the non-parametric Mann-Whitney U test. Categorical data were expressed as frequencies and percentages, with comparisons conducted using the chi-square (χ^2) test. For comparisons among the three groups, one-way analysis of variance (ANOVA) was applied for normally distributed variables, while the Kruskal-Wallis test was used for non-normally distributed variables. Categorical variables were compared using chi-square (χ^2) or Fisher's exact tests.

Univariate logistic regression analyses were first performed on the training set, followed by backward stepwise multivariate logistic regression analysis for variables with $p < 0.2$ to identify significant predictors of NP. These predictors were included in the final logistic regression model, and visualized as a nomogram model. The discrimination of the model was evaluated using the area under curve (AUC) of the receiver operating characteristic (ROC) curve. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test and calibration curves. The clinical utility of the model was examined through decision curve analysis (DCA) and clinical impact curves (CICs), which evaluated the net benefit across different threshold probabilities. Bilateral statistical tests were performed, with α set as 0.05. A *p*-value < 0.05 was considered statistically significant. All analyses were conducted using the R software (version 4.3.2, R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline Characteristics

Based on postoperative pathological findings, 621 patients were divided into NNP and NP groups. Among the 519 cases of NNP, cholesterol polyps were the most prevalent subtype (476 cases, 76.7%), followed by hyperplastic polyps (24 cases, 3.9%), inflammatory polyps (12 cases, 1.9%), and adenomyosis (7 cases, 1.1%). The NP group included 84 cases of gallbladder adenoma (13.5%) and 18 cases of adenoma with high-grade intraepithelial neoplasia or severe heterogeneous hyperplasia (2.9%). The pathological distribution of the 621 patients is shown in Fig. 1.

The dataset was randomly divided into a training set (434 cases) and an internal validation set (187 cases) in a 7:3 ratio. The training set comprised 362 NNP cases and 72 NP cases, while the internal validation set included 157 NNP cases and 30 NP cases. Statistical analysis revealed no significant differences ($p > 0.05$) in baseline characteristics between the two datasets, as illustrated in Table 1.

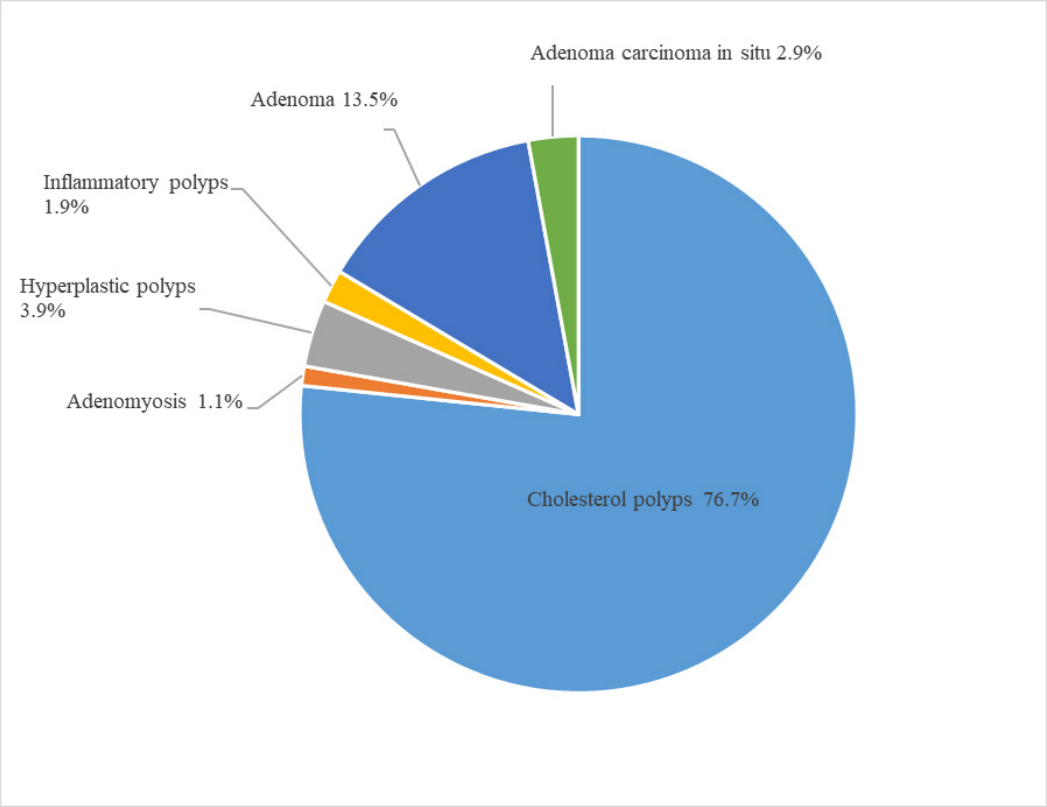

Fig. 1. Postoperative pathological findings of 621 cases of gallbladder polypoid lesions (GPLs).

Univariate Logistic Analysis of NP in the Training Set

Univariate analysis of the training set revealed statistically significant differences between the NP and NNP groups in polyp size, age, gallbladder wall thickness, and the presence of coexisting gallstones ($p < 0.05$). Additionally, the propor-

Table 1. Comparison of general characteristics between the training set and internal validation.

Variables	Training set (n = 434)	Internal validation set (n = 187)	Statistic	*p*-value
Age (years)	49.64 ± 12.33	50.05 ± 11.96	$t = 0.38$	0.701
Sex			$\chi^2 = 1.18$	0.277
Female (%)	256 (58.99)	119 (63.64)		
Male (%)	178 (41.01)	68 (36.36)		
BMI (kg/m^2)	23.97 ± 2.52	23.95 ± 2.70	$t = –0.08$	0.937
Hypertension			$\chi^2 = 0.28$	0.594
No (%)	376 (86.64)	159 (85.03)		
Yes (%)	58 (13.36)	28 (14.97)		
Diabetes			$\chi^2 = 0.23$	0.634
No (%)	409 (94.24)	178 (95.19)		
Yes (%)	25 (5.76)	9 (4.81)		
FBG (mmol/L)	4.91 (4.37, 5.35)	4.97 (4.40, 5.50)	Z = –0.73	0.468
TBIL (μmol/L)	15.70 (11.40, 20.45)	15.10 (11.40, 21.40)	Z = –0.07	0.945
ALT (U/L)	24.00 (14.00, 41.00)	28.00 (15.00, 40.00)	Z = –0.83	0.408
AST (U/L)	26.00 (20.00, 37.00)	25.00 (20.00, 38.00)	Z = –0.45	0.654
GGT (U/L)	30.50 (18.00, 59.00)	33.00 (18.00, 64.50)	Z = –0.78	0.433
ALP (U/L)	85.00 (65.00, 106.75)	84.00 (62.50, 113.00)	Z = –0.25	0.806
TC (mmol/L)	4.33 ± 1.07	4.29 ± 1.16	$t = –0.45$	0.652
TG (mmol/L)	1.32 (0.92, 1.83)	1.35 (1.00, 1.85)	Z = –0.86	0.388
HDL-C (mmol/L)	1.26 ± 0.37	1.25 ± 0.36	$t = –0.16$	0.873
LDL-C (mmol/L)	2.59 ± 0.72	2.61 ± 0.77	$t = 0.32$	0.747
BUN (mmol/L)	5.10 (4.20, 6.10)	5.10 (4.25, 6.00)	Z = –0.07	0.943
Scr (μmol/L)	63.45 ± 18.61	64.57 ± 14.21	$t = 0.73$	0.463
SUA (μmol/L)	302.26 ± 84.22	301.80 ± 93.09	$t = –0.06$	0.952
Gallbladder wall thickness (mm)	3.10 (2.80, 3.40)	3.10 (2.70, 3.40)	Z = –0.68	0.495
Polyp size (cm)	0.80 (0.60, 1.00)	0.80 (0.60, 1.00)	Z = –0.44	0.662
Polyp number			$\chi^2 = 1.24$	0.266
Single (%)	76 (17.51)	26 (13.90)		
Multiple (%)	358 (82.49)	161 (86.10)		
Polyp shape			$\chi^2 = 0.68$	0.410
Pedunculate (%)	11 (2.53)	7 (3.74)		
Sessile (%)	423 (97.47)	180 (96.26)		
Polyp echo characteristics			$\chi^2 = 0.02$	0.893
Low/moderate echo (%)	160 (36.87)	70 (37.43)		
High-level echo (%)	274 (63.13)	117 (62.57)		
Coexisting gallstones			$\chi^2 = 0.58$	0.445
No (%)	274 (63.13)	112 (59.89)		
Yes (%)	160 (36.87)	75 (40.11)		

Abbreviations: BMI, body mass index; FBG, fasting blood glucose; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, serum total bilirubin; GGT, gamma-glutamyl transpeptidase; ALP, alkaline phosphatase; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; BUN, blood urea nitrogen; SUA, serum uric acid; Scr, serum creatinine.

tions of multiple polyps, hyperechoic polyps, and sessile polyps were significantly lower in the NP group compared to the NNP group ($p < 0.05$), as detailed in Table 2.

Table 2. Comparison of variables between the NP and NNP groups in the training set.

Variables	NNP (n = 362)	NP (n = 72)	Statistic	*p*-value
Age (years)	48.36 ± 12.69	56.07 ± 7.64	$t = -6.88$	<0.001
Sex			$\chi^2 = 0.15$	0.700
Female (%)	215 (59.39)	41 (56.94)		
Male (%)	147 (40.61)	31 (43.06)		
BMI (kg/m^2)	23.97 ± 2.50	23.98 ± 2.62	$t = -0.06$	0.952
Hypertension			$\chi^2 = 2.76$	0.097
No (%)	318 (87.85)	58 (80.56)		
Yes (%)	44 (12.15)	14 (19.44)		
Diabetes			$\chi^2 = 3.45$	0.063
No (%)	345 (95.30)	64 (88.89)		
Yes (%)	17 (4.70)	8 (11.11)		
FBG (mmol/L)	4.93 (4.39, 5.34)	4.84 (4.35, 5.42)	Z = –0.26	0.791
TBIL (μmol/L)	15.45 (11.40, 20.28)	16.35 (12.07, 21.42)	Z = –0.86	0.389
ALT (U/L)	24.00 (14.00, 42.00)	24.00 (15.75, 34.00)	Z = –0.01	0.994
AST (U/L)	26.00 (20.00, 37.00)	26.00 (20.00, 36.50)	Z = –0.06	0.956
GGT (U/L)	30.00 (17.00, 61.75)	31.00 (19.00, 52.00)	Z = –0.44	0.659
ALP (U/L)	86.00 (65.25, 106.75)	82.00 (62.75, 103.25)	Z = –0.98	0.325
TC (mmol/L)	4.36 ± 1.08	4.21 ± 1.02	$t = 1.08$	0.281
TG (mmol/L)	1.32 (0.92, 1.84)	1.31 (0.92, 1.80)	Z = –0.31	0.757
HDL-C (mmol/L)	1.27 ± 0.38	1.21 ± 0.35	$t = 1.33$	0.184
LDL-C (mmol/L)	2.59 ± 0.72	2.63 ± 0.69	$t = -0.43$	0.666
BUN (mmol/L)	5.10 (4.20, 6.10)	5.30 (4.57, 6.23)	$t = -1.554$	0.120
Scr (μmol/L)	63.29 ± 18.98	64.25 ± 16.72	$t = -0.40$	0.691
SUA (μmol/L)	301.64 ± 83.12	305.38 ± 90.13	$t = -0.34$	0.731
Gallbladder wall thickness (mm)	3.10 (2.70, 3.40)	3.30 (2.90, 4.03)	Z = –3.26	0.001
Polyp size (cm)	0.70 (0.60, 0.90)	1.20 (0.90, 1.42)	Z = –8.58	<0.001
Polyp number			$\chi^2 = 74.32$	<0.001
Single (%)	38 (10.50)	38 (52.78)		
Multiple (%)	324 (89.50)	34 (47.22)		
Polyp shape			$\chi^2 = 39.71$	<0.001
Pedunculate (%)	1 (0.28)	10 (13.89)		
Sessile (%)	361 (99.72)	62 (86.11)		
Polyp echo characteristics			$\chi^2 = 62.07$	<0.001
Low/moderate echo (%)	104 (28.73)	56 (77.78)		
High-level echo (%)	258 (71.27)	16 (22.22)		
Coexisting gallstones			$\chi^2 = 12.95$	<0.001
No (%)	242 (66.85)	32 (44.44)		
Yes (%)	120 (33.15)	40 (55.56)		

Abbreviations: NNP, non-neoplastic polyps; NP, neoplastic polyps.

Table 3. Stepwise logistic regression analysis for predicting the presence of NP.

Variable	β	SE	Wald	p-value	OR (95% CI)
Intercept	–7.5196	1.3621	30.475	<0.0001	
Polyp number = Multiple	–1.3700	0.4002	11.719	0.0006	0.25 (0.12–0.56)
Polyp echo = High-level	–0.8985	0.3762	5.705	0.0169	0.41 (0.19–0.85)
Polyp size	2.9449	0.5493	28.738	<0.0001	19.01 (6.48–55.79)
Gallbladder wall thickness	0.4528	0.2188	4.285	0.0385	1.57 (1.02–2.41)
Age	0.0589	0.0155	14.374	0.0001	1.06 (1.03–1.09)

Abbreviations: OR, odd ratio.

Logistic Regression Model for NP

Variables with $p < 0.2$ in the univariate analysis were included in a backward stepwise multivariate logistic regression analysis. This analysis identified age, polyp size, polyp number, polyp echo characteristics, and gallbladder wall thickness as independent risk factors for NP diagnosis. The results of the logistic regression analysis are presented in Table 3.

Development of the Prediction Nomogram Model

A logistic regression equation was formulated based on the identified predictors as follows: Ln(p/1-p) = –7.5196 + 0.0589 × age + 0.4528 × gallbladder wall thickness + 2.9449 × polyp size – 0.8985 × polyp echo – 1.3700 × number of polyps. A nomogram was constructed using R software to visualize the logistic regression model, as shown in Fig. 2.

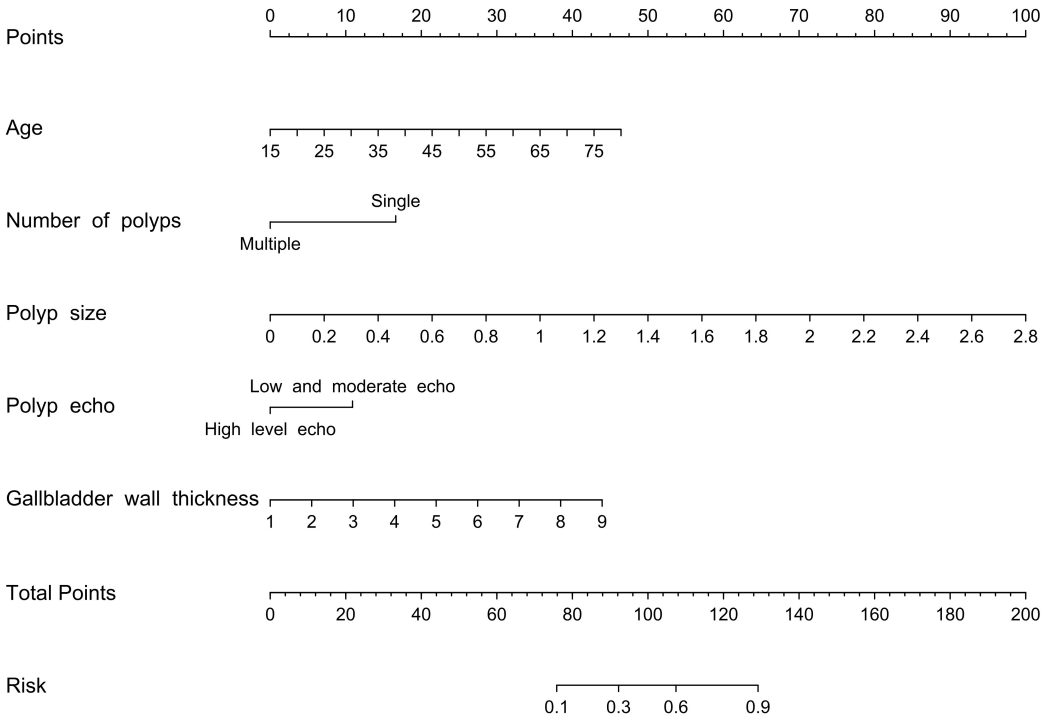

Fig. 2. Nomogram model for predicting neoplastic polyps (NP).

Evaluation and Validation of the Prediction Nomogram Model

Discrimination Evaluation

The nomogram demonstrated excellent discriminatory performance. The AUC value for the training set was 0.886 (95% CI: 0.841–0.930, $p < 0.0001$), with a sensitivity of 0.736 and specificity of 0.878. For The internal validation set, the AUC was 0.836 (95% CI: 0.753–0.919, $p < 0.0001$), with a sensitivity of 0.766 and specificity of 0.751. The external validation set showed an AUC of 0.867 (95% CI: 0.743–0.978, $p < 0.0001$), with sensitivity of 0.789 and specificity of 0.928. These findings indicate robust discriminatory capability for the prediction model (Fig. 3).

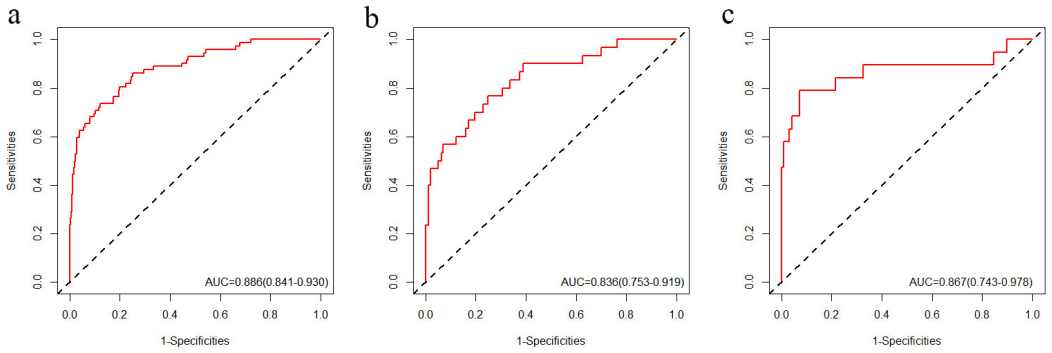

Fig. 3. Receiver operating characteristic (ROC) curves of the prediction nomogram model. (a) ROC curve for the training set. (b) ROC curve for the internal validation set. (c) ROC curve for the external validation set. AUC, area under curve.

Calibration Evaluation

Calibration analysis revealed no significant differences between predicted and observed probabilities in the training set ($\chi^2 = 4.073$, $p = 0.254$), internal validation set ($\chi^2 = 0.322$, $p = 0.956$), external verification set ($\chi^2 = 12.24$, $p = 0.058$). Calibration curves showed that the Brier scores for the training, internal validation and external validation sets were 0.079, 0.092, and 0.070, respectively, all below 0.25, suggesting that the model had a superior calibration capability (Fig. 4).

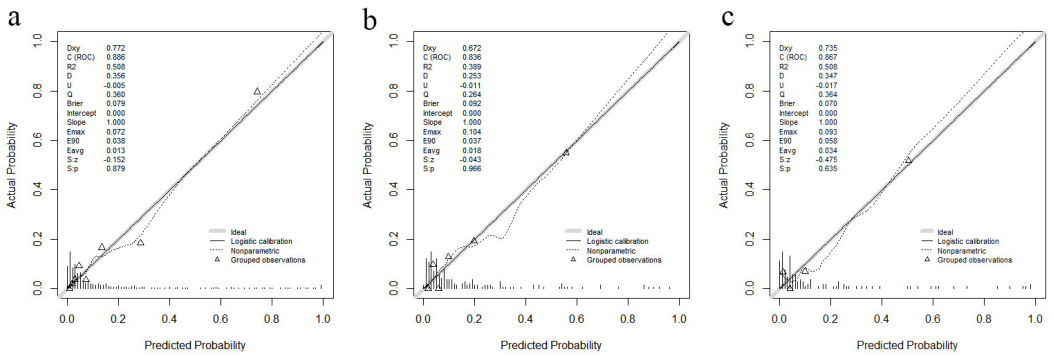

Fig. 4. Calibration curves of the prediction nomogram model. (a) Calibration curve for the training set. (b) Calibration curve for the internal validation set. (c) Calibration curve for the external validation set.

Clinical Adaptability Evaluation

The clinical utility of the nomogram was assessed using DCA. When the threshold probability across the three datasets was below 90%, the DCA curve demonstrated a higher net value compared to the two extreme values. These findings indicate that the model effectively identifies high-risk groups and supports clinical decision-making within this threshold range, highlighting its clinical utility and benefit (Fig. 5).

The model was used to predict the risk stratification of 1000 individuals, and clinical impact curves (CICs) were constructed to illustrate the proportions of losses and benefits across probability thresholds. The solid red line represents the number of individuals classified as high risk (or positive) by the prediction model, while the solid blue line indicates the actual number of individuals experiencing the outcome event at each threshold probability. Notably, when the threshold probability of the prediction model across all three datasets was approximately 0.6, the number of true positives closely corresponded to the number of individuals identified as high-risk by the model (Fig. 6).

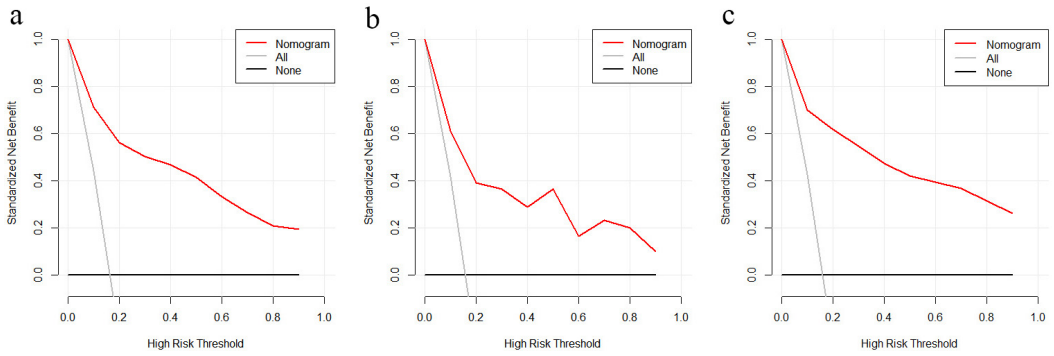

Fig. 5. Decision curve analysis (DCA) curves of the prediction nomogram model. (a) DCA curve for the training set. (b) DCA curve for the internal validation set. (c) DCA curve for the external validation set.

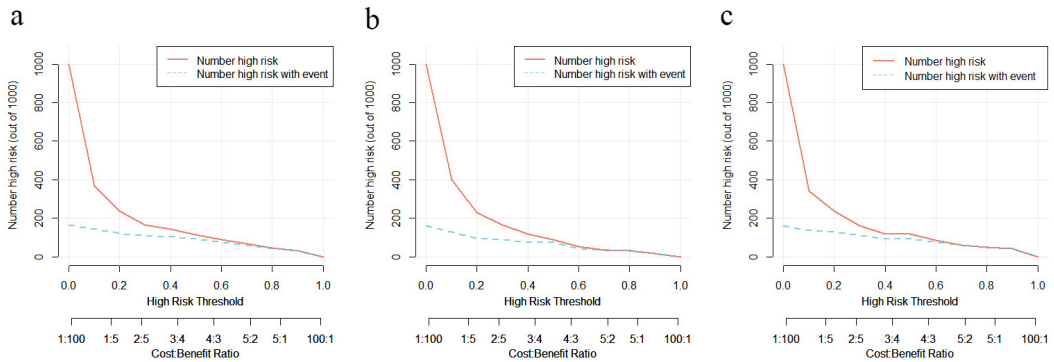

Fig. 6. Clinical impact curve (CIC) of the prediction nomogram model. (a) CIC for the Training set. (b) CIC for the internal validation set. (c) CIC for the external validation set.

Discussion

Approximately 95% of gallbladder carcinomas originate from epithelial cells, with adenocarcinoma accounting for over 90% of cases (Roa et al, 2021). The progression of gallbladder carcinoma typically follows a sequence of pathological events: metaplasia, dysplasia, adenoma or carcinoma *in situ*, and ultimately invasive carcinoma (Jang and Ahn, 2016). In our study, 102 NP cases were identified in the baseline dataset of 621 cases, with 18 cases (2.9%) classified as adenoma-carcinoma *in situ*. Further investigation revealed these cases to be incidental post-operative gallbladder carcinoma. According to the current guidelines, patients with carcinoma *in situ* or T1a gallbladder based on tumor node metastasis (TNM) staging can be treated with a simple cholecystectomy without the need for additional surgical intervention (Balakrishnan et al, 2023). These observations underscore the importance of making informed clinical decisions for patients diagnosed with GPLs.

Numerous predictive and diagnostic models have been established to guide clinical decision-making for GPLs. Given the complex nature of tumor biology, previous studies have incorporated diverse factors, such as the cross-sectional area (CSA) of polyps, bile viscosity, forward blood flow, and tumor markers (Kim and Hong, 2020; Li et al, 2023; Ma et al, 2022). However, ultrasonography remains the optimal initial screening and follow-up modality for gallbladder disease due to its accessibility, cost-effectiveness, and dynamic monitoring capabilities (Branch of Biliary Surgery et al, 2020). In our study, we used ultrasonography as the primary tool and identified one clinical factor (age) and four ultrasound features (polyp size, polyp number, polyp echogenicity, and gallbladder wall thickness) as independent risk factors for NP. These were incorporated into a multivariate logistic regression model to develop a predictive nomogram.

Age is a risk factor associated with the risk for malignancy in GPLs. In our study, the mean age of NP patients was 56.07 $\pm$ 7.64 years, significantly higher than NNP patients. While the optimal age threshold varies across studies, thresholds of 50, 60, and 65 years have been proposed for identifying high-risk cases (Riddell et al, 2023). Polyp morphology and number also play an important role in risk stratification. A large-scale case series involving 2704 patients undergoing cholecystectomy reported that NPs are more likely to be single and sessile, while NNPs are likely multiple and pedunculated (Liu et al, 2021). Polyp size is also recognized as a predictor of malignancy. Polyps $\geq$10 mm are considered high-risk for NP (Foley et al, 2022). However, Taskin et al (2024) found that nearly a third of NPs measured less than 10 mm. These findings challenge the reliability of size alone as an indicator for guiding clinical decision-making in GPL management.

Gallbladder wall thickness has also been identified as a significant factor. A retrospective analysis of data from 4119 patients reported that the normal human gallbladder wall thickness averages 2.6 $\pm$ 1.6 mm, with a thickness $\geq$3 mm considered pathological (Matcuk et al, 2014). Studies have shown that NP cases often exhibit greater wall thickening than NNP and that malignant polyps are associated with thicker walls compared to precancerous polyps (Wennmacker et al, 2019; Björk et

al, 2021). Interestingly, adenomatous polyps have been reported to have thinner gallbladder walls than cholesterol polyps (Wang et al, 2024a; Zhang et al, 2021).

Polyp echogenicity has been shown to correlate with pathological characteristics. Most NPs are hypoechoic or display moderate echogenicity, while cholesterol polyps tend to be hyperechoic (Kim et al, 2015; Wang et al, 2024b). These findings are consistent with our results. Nevertheless, the validity and generalizability of these observations require further verification through larger-scale multicenter studies.

Univariate analysis in our study revealed a statistically significant difference between NP combined with gallstones and NNP. Gallstones are a significant risk factor for gallbladder carcinoma, with studies indicating that gallbladder carcinoma is more likely to be present when the stone diameter exceeds 1.95 cm. Additionally, gallstones are an independent risk factor for gallbladder carcinoma in patients with cholelithiasis (Ryu et al, 2016; Zhu et al, 2023). Tumor markers were excluded in our study due to their low detection rate among patients considered NNP. In most cases, tumor marker levels were within the normal range, limiting their utility in large-scale clinical applications. However, tumor markers, primarily carbohydrate antigen 19-9 (CA 19-9), are valuable in early diagnosis and recurrence monitoring in gallbladder carcinoma. CA 19-9 has demonstrated a sensitivity of 79.1% and a specificity of 97.2% in detecting recurrence (Agrawal and Saxena, 2023).

Dyslipidemia correlates with the prevalence of GPLs, with elevated LDL levels posing a more significant risk factor than decreased HDL, elevated total cholesterol, or increased triglycerides (Zheng et al, 2020). Dyslipidemia increases the malignancy risk in GLPs by 2.674-fold (Deng et al, 2021). Additionally, the progression of GPLs is strongly associated with overweight or obesity. Advanced age, excessive body weight, and abnormal blood lipid profiles elevate the risk of cholesterol polyps (Yu et al, 2021). A higher BMI correlates with an increased prevalence of GLPs, with a 5 kg/m^2 BMI increase resulting in a 47% higher risk of gallbladder carcinoma in women, while the risk increase is less pronounced in men (Saeed et al, 2023).

A previous Chinese predictive model, including age, cholelithiasis, carcinoembryonic antigen (CEA), polyp size, and sessile morphology as independent predictors of NP, demonstrated strong diagnostic performance, with AUC of 0.846 in the training set and 0.835 in the validation set (Zhang et al, 2022). Recently, a Bayesian network model for predicting the risk of neoplastic gallbladder polyps >10 mm identified independent risk factors such as single polyp, polyp CSA ≥ 85 mm^2, broad-based polyps located at the fundus, and medium echogenicity (Li et al, 2023). This model exhibited superior diagnostic accuracy, with an AUC exceeding those developed by the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS), the European Society of Gastrointestinal and Abdominal Radiology (ESGAR), ultrasound-reported diagnoses (US-reported), and the Chinese Committee of Biliary Surgeons (CCBS) models (Li et al, 2023). In comparison, our nomogram model demonstrated excellent diagnostic performance with AUCs of 0.886, 0.836, and 0.867 across the three datasets. The model also exhibited high calibration ability and provided practical advantages, including cost-effectiveness and the use of

easily obtainable variables. The model achieved maximum clinical benefit when the threshold probability was approximately 0.6.

Our findings suggest that patients classified as low-risk by the nomogram model can safely continue with regular follow-up, while high-risk patients can be advised to undergo surgical treatment. Preoperative CT scans can be used to confirm the diagnosis and assess the presence of gallbladder abdominal metastasis. Compared to previous models, the primary strengths of our model are its simplicity, cost-effectiveness, and high diagnostic accuracy. Moreover, the external validation demonstrated its strong generalizability, making it suitable for application in broader populations.

The present study has several limitations. First, the study employed a retrospective design, and the number of NP cases included was relatively small. Larger, more diverse datasets from additional medical centers are needed for prospective external validation to confirm the generalizability of the model. Second, although ultrasound findings were thoroughly reviewed, the diagnostic accuracy of ultrasound remains susceptible to operator subjectivity, which could influence the reliability of the data. Third, the analysis did not include certain potential variables, such as tumor markers, polyp growth rate, alcohol consumption, surface antigens, family history, dietary habits, and a history of primary sclerosing cholangitis. The preoperative diagnosis of NP remains a significant clinical challenge. Despite these limitations, our study presents a model that provides practical and effective support for clinical decision-making in patients with GPLs.

Conclusion

We developed a preoperative prediction model based on easily accessible clinical and ultrasound parameters to improve the preoperative identification of NP. This model holds promise for optimizing clinical decision-making for patients with GPLs.

Key Points

- The independent influencing factors of neoplastic polyps were explored in homology data.
- A preoperative prediction model for NP was constructed using readily accessible clinical and ultrasound variables.
- The prediction model was rigorously evaluated and validated on homologous and non-homologous data using ROCs, calibration curves, DCA, and CICs.
- This study provides a reference for the evaluation, management and clinical decision-making of gallbladder polypoid lesions.

Availability of Data and Materials

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

Author Contributions

YNZ, JYH and XJH conceived and designed the study, YNZ, SCX, XZ, and JZW collected patients' samples and medical information, YNZ and JYH performed the literature search and wrote the manuscript, YNZ and PFW conducted statistical analysis of the data, JYH and XJH received funding. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Lanzhou University Second Hospital (approval No.: 2024A-797) and all patients were exempt from informed consent. The study strictly adheres to the principles of the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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