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An internally validated prognostic nomogram model predicts the stone-free rate following endoscopic combined intrarenal surgery for renal stones

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Abstract

Background Here, we aim to develop and validate a viable prognostic nomogram model for predicting a stone-free rate of kidney stones patients based on retrospective cohort analysis.

Methods This is a retrospective study that obtained a continuous cohort from the databases of two hospitals (General Hospital of Southern Theater Command, and Guangdong Second Provincial General Hospital), including 522 patients with kidney stones who underwent Endoscopic Combined Intrarenal Surgery (ECIRS) from January 2015 to December 2022.The characteristics of the primary cohort between the SF (stone-free) and SR (stone residue) groups were identified using single factor and multivariate logistic regression analyses. Factors in the main cohort were identified using minimal absolute shrinkage and selective operator regression. A nomogram was then constructed using these factors for subsequent analyses. Finally, a calibration curve, a receiver operating characteristic curve (ROC), and a decision curve analysis (DCA) curve were analyzed and plotted, and then used to test the predictive value of the nomogram in both calibration and discrimination.

Results Hydronephrosis, Renal Infundibular Length (RIL), Renal Infundibular Width (RIW), stone burden, and number of calyces involved were revealed to be significant factors in the prediction of stone-free rate after ECIRS. These five factors were used to develop a nomogram with good calibration and differentiation. The area under the curve (AUC) was 0.811 (95% CI: 0.766–0.856). The DCA demonstrated that the nomogram has clinical utility.

Conclusions Hydronephrosis, renal infundibular length, renal infundibular width, stone burden, and number of involved calyces were all significantly linked with residual stone after ECIRS. A nomogram created with these five factors showed good calibration, differentiation, and clinical usefulness.

Keywords Kidney stones, ECIRS, Nomogram, Stone free rate, LASSO regression

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Introduction

Kidney stones are a common urological illness. They are a recurring disease, and the pain caused by kidney stones always has a devastating impact on patients. Nephrolithiasis has been associated with an increased risk of chronic kidney disease (CKD) [1]. It is a major risk factor for end-stage renal failure [2].

With advances in endoscope miniaturization, disposable ureteroscopes, and the introduction of the holmium laser, more efficient procedures have been devised to diagnose and treat kidney stones. The majority of urologists prefer percutaneous nephrolithotomy (PCNL) for the treatment of renal calculi [3, 4]. Thus, many nephrolithometry scoring systems such as S.T.O.N.E, the Guy's stone score, and the S-ReSC predict stone-free rates after PCNL. [5–7]. However, as experience with PCNL grows, an increasing number of urologists are turning to Endoscopic combined intrarenal surgery (ECIRS) to treat complicated renal calculi. For larger and more complex renal stones, ECIRS has been shown to have higher stone clearance rates, fewer complications, and lower transfusion rates [8–10].

There is currently no scoring system for the stone-free rate following ECIRS. In clinical practice, effective prediction tools are useful for surgeon preoperative planning and preparation. In this study, patients with ECIRS were divided into Stone-free (SF) and Stone residue (SR) groups based on whether they had more than 4 mm of residual stones after surgery. The preoperative clinical data of the two groups of patients were then retrospectively reviewed to determine the factors influencing the stone-free rate of kidney stones. Consequently, nomogram models were developed and validated to predict patients with stone clearance after surgery. These models could help surgeons in their preparation for surgery.

Methods

Patients and data

This study was conducted between January 2015 and December 2022. A total of 522 patients with kidney stones from the Departments of Urology at General Hospital of Southern Theater Command, and Guangdong Second Provincial General Hospital underwent ECIRS. All patients had Computed Tomography (CT) scans before and after surgery. The stone burden was calculated in mm^2 using the formula: Σ (0.785*length (max) * width (max)). The number of calyces involved was split into three grades using the S.T.O.N.E scoring system (1 renal calyx involved in 1 grade, 2 grades in 2 to 3 renal calyces involved, and 3 grades in complete staghorn calculi)[5]. Renal infundibular width (RIW), the stone involves the narrowest width of the lower calyx. We split RIW into two categories: ≤ 5 mm for grade 1 and > 5 mm for grade 2. The Renal Infundibular Length (RIL) of the kidney measures the distance between the tip of the calyx with stones and the midpoint of the lower lip of the kidney. There are two levels of RIL: ≤ 3 mm for level 1 and > 3 mm for level 2.

Hydronephrosis, renal infundibular length, renal infundibular width, stone burden, and number of involved calyces were significantly associated with residual stone after ECIRS. A nomogram created using these five factors demonstrated good calibration, differentiation, and clinical usefulness[11]. Table 1 shows the features of each variable. Hydronephrosis is graded into three levels: none or light, moderate, and severe for levels 1, 2, and 3, respectively.

Inclusion and exclusion criteria

The inclusion criteria were: (1) preoperative CT findings are amenable to interrogation; (2) within a month after the operation, a KUB or CT scan was performed, and the findings may be interrogated, and (3) the maximum remaining single stone diameter is less than 4 mm, according to the SF Group standard.

The exclusion criteria were: (1) patients with urinary tract malformations; (2) patients with renal and ureteral calculi; (3) patients with incomplete clinical data; (4) patients who did not return to the outpatient ward within a month postoperatively;(5) minors or vulnerable groups.

ECIRS procedure

Experienced urologists (Achieved the title of associate chief physician in China and have been performing urological stone surgery for over 5 years.) performed all the procedures. All patients were first put under general anesthesia and placed in the contralateral Galdakao-modified supine Valdivia (GMSV) position. A 0.035-inch hydrophilic wire was introduced into the upper urinary tract while the patients were under general anesthesia. On the guidewire, an F12-14 ureteral sheath was then pushed forward. To observe the distribution of stones, an F8 flexible ureteroscope was inserted into the ureteral sheath. An F18 or F20 percutaneous lithotomy was performed simultaneously with sequential fascia expanders and an endoscopic ultrasound-guided matching stripping sheath. The holmium laser used in the transdermal pathway lithotripsy. Under a flexible ureteroscope, nickel-titanium lithotripsy baskets or lithotripsy tongs were to be used if necessary. However, due to differences in techniques and requirements, it was impossible to do both anterior and retrograde lithotripsy. Consequently, a nephrostomy fistula and F6 double J stent were successfully placed.

Table 1 Descriptive statistics for study variables

	Stone Free (419)	Stone Residue (103)	t/χ^2	P
Age	45.02 ± 18.05	47.04 ± 19.49	1.023	0.307
Gender				
Male	221(52.7%)	46(44.7%)	2.163	0.141
Female	198(47.3%)	57(55.3%)		
BMI	28.00 ± 6.57	28.62 ± 6.19	0.875	0.382
History of surgery				
absent	302(72.1%)	78(75.7%)	0.557	0.456
present	117(27.9%)	25(24.3%)		
Stone Side				
Left	176(42.0%)	59(57.3%)	9.795	0.005
Right	243(58.0%)	44(42.7%)		
Hydronephrosis				
None or Light	106(25.3%)	44(42.7%)	12.296	0.002
Moderate	202(48.2%)	39(37.9%)		
Severe	111(26.5%)	20(19.4%)		
IPA				
< 45°	199(47.5%)	39(37.9%)	3.091	0.079
≥ 45°	220(52.5%)	64(62.1%)		
Average Hounsfield unit				
≤ 950	215(51.3%)	44(42.7%)	2.443	0.118
> 950	204(48.7%)	59(57.3%)		
RIL				
< 30mm	268(64.0%)	45(43.7%)	14.153	0.000
≥ 30mm	151(36.0%)	58(56.3%)		
RIW				
< 5mm	155(37.0%)	50(48.5%)	4.625	0.032
≥ 5mm	264(63.0%)	53(51.5%)		
Hospitalization	7.10 ± 1.38	7.20 ± 1.45	6.709	0.152
Stone Burden	504.69 ± 108.32	605.83 ± 137.63	8.021	0.000
Skin to stone distance	9.88 ± 2.93	9.77 ± 2.71	0.351	0.726
Operative time	121.92 ± 31.29	118.23 ± 30.73	0.783	0.434
Number of calyces involved				
1, 2	232(55.4%)	14(13.6%)	75.069	0.000
3	135(32.2%)	45(43.7%)		
≥ 4	52(12.4%)	44(42.7%)		

Statistical analysis

Risk factors were identified using SPSS software (Version 26.0). For the continuous and categorical variables, the *t*-test and chi-square test were used. To further filter out factors affecting the stone-free rate, logistic regression was used. Additionally, the Lasso regression was simultaneously used with Logistic regression analysis to rescreen variables. A nomogram model was subsequently constructed using the filtered parameters. Calibration, ROC curve and DCA curve were used to assess the efficacy of the model. Two-sided $P < 0.05$ was considered statistically significant.

Results

Patient clinical characteristics

This study comprised 522 patients with kidney stones who underwent ECIRS and achieved successful outcomes. with 318 from the General Hospital of Southern Theater Command and 204 from Guangdong Second Provincial General Hospital. Based on radiographic findings within one month of surgery, the patients were divided into stone-free and stone-residual groups. Table 1 shows the clinical statistics of the patients, of which 19.7% had residual calculi postoperatively, and 80.3% had no residual calculi after surgery. The average age of patients in the SF (stone free) group was (45.02 ± 18.05) years.

The average age of patients in the SR (stone residue) group was (47.04 ± 19.49) years. The average stone burden for the SF group was found to be (504.69 ± 108.32) mm^3. In contrast, the SR group had a higher average stone burden of (605.83 ± 137.63) mm^3. Within the SF group 232 patients (55.4%) were involved in 1 calyx, 135 patients (32.2%) were implicated in 2 ~ 3 calyces, and 52 patients (12.4%) were implicated in ≥ 3 calyces. In the SR group there were 14 patients (13.6%) involved in 1 calyx, 45 patients (43.7%) patients involved in 2 ~ 3 calyces and 44 patients (42.7%) involved in ≥ 3 calyces. In the SF group 36.0% of patients had a RIL ≥ 30 mm. Conversely, in the SR group, 58 of patients had a RIL ≥ 30 mm (56.3%). In the SF group, 37.0% of patients had a RIW ≤ 5 mm; whereas in the SR group, 48.5% of patients had a RIW ≤ 5 mm. In the SF group, the proportion of patients with none or light hydronephrosis was 106(25.3%), the proportion of patients with moderate hydronephrosis was 202 (48.2%), and the proportion of patients with severe hydronephrosis was 111 (26.5%). On the other hand, in the SR group, the proportion of patients with none or light hydronephrosis was 44 (42.7%), the proportion of patients with moderate hydronephrosis was 39 (37.9%), and the proportion of patients with severe hydronephrosis was 20 (19.4%). Compared to patients in the SR group, we found that patients in the SF group had smaller stone burdens, more serious hydronephrosis, shorter RIL, and wider RIW. We also discovered no significant differences in age, sex, or other variables. Table 1 details the patient characteristics.

Building predictive models

To filter the variables, we used logistic regression and subsequently tested the results against each other. Significant differences were seen in variables such as Hydronephrosis, RIL, RIW, stone burden, and number of calyces involved. Table 2 shows the specific outcomes of variable screening.

The results of Logistic regression were then validated with Lasso regression, and the same variable was found to have a significant effect on Stone free rate. To screen for traits, the LASSO regression technique ["glmnet" package (13) in R software] was used in the primary cohort. The LASSO regression analysis selected variables based on non-zero coefficients from all 15 variables collected from patients. The lambda.1se was 0.01, and selected five variables (Fig. 1). In this study, prognostic factors were selected by the lambda.1se criteria and the five predictors included Hydronephrosis, RIL, RIW, stone burden, and number of calyces involved. A multivariate

Table 2 Predictive factors of stone-free rate in univariate and multivariate analyses

	Univariate analysis			Multivariate analysis		
	Odd Ratio	**Confidence interval 95% Lower ~ Upper**	***p* value**	**Odd Ratio**	**Confidence interval 95% Lower ~ Upper**	***p* value**
Age	0.994	0.982 ~ 1.006	0.306			
Gender	0.723	0.290 ~ 1.156	0.142			
BMI	0.986	0.953 ~ 1.018	0.382			
History of surgery	1.209	0.710 ~ 1.707	0.456			
Stone Side	1.851	1.415 ~ 2.287	0.006	0.991	0.481 ~ 1.502	0.974
Hydronephrosis						
None or Light	2.150	1.659 ~ 2.641	0.002	1.504	0.931 ~ 2.077	0.036
Moderate	2.304	1.712 ~ 2.896	0.006	1.686	1.017 ~ 2.355	0.026
IPA	0.674	0.232 ~ 1.116	0.080			
Average Hounsfield unit	0.708	0.273 ~ 1.142	0.119			
RIL	0.437	0.000 ~ 0.875	< 0.001	0.519	0.011 ~ 1.028	0.012
RIW	1.607	1.172 ~ 2.041	0.032	1.443	0.961 ~ 1.950	0.017
Hospitalization	0.946	0.790 ~ 1.101	0.479			
Stone Burden	0.993	0.991 ~ 0.995	< 0.001	0.995	0.993 ~ 0.998	< 0.001
Ski to stone distance	1.014	0.939 ~ 1.089	0.725			
Operative time	1.003	0.996 ~ 1.010	0.433			
Number of calyces involved						
1	2.538	2.014 ~ 3.063	< 0.001	1.280	0666 ~ 1.894	0.031
2	14.022	13.350 ~ 14.694	< 0.001	7.079	6.337 ~ 7.820	< 0.001

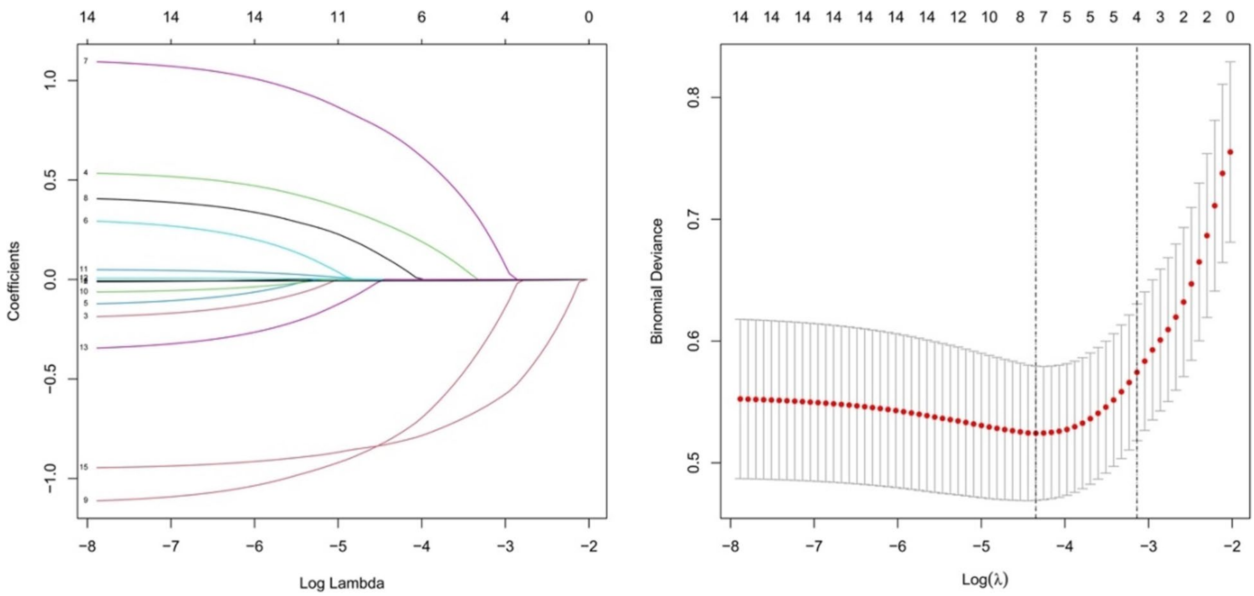

Fig. 1 LASSO regression analysis for variables. **A** Selection of the tuning parameter (λ) using ten-fold cross-validation via the minimum and 1-SE criteria in the LASSO regression analysis. **B** Selection of non-zero coefficients using ten-fold cross-validation, while the optimal λ (1-SE criteria, the right line) selected five non-zero coefficients (Hydronephrosis, RIL, RIW, stone burden, and number of calyces involved)

logistic regression model was built using these five factors and developed into the nomogram shown in Fig. 2 using "rms" package (14) in the R software. The probability score of stone-free rate was calculated by summarizing the scores of all the selected factors (Fig. 1 and Fig. 2).

Validating prediction models

We plotted the calibration and discrimination curves using the "rms" (14) and "pROC" (15) packages in R software to validate the performance of the nomogram in predicting the probability of post-ECIRS SF (Fig. 3 and 4). The results indicated good accuracy and calibration. The AUC values for ROC curves were (AUC = 0.913, CI = 0.880–0.946). The joint indicators showed a high predictive ability.

Discussion

The agonizing pain experienced by patients during the development of kidney stones greatly impacts their physical and mental well-being. Moreover, kidney stone patients incur substantial direct and indirect economic costs every year [12]. Consequently, there is a pressing need for timely and effective treatment of kidney stones, particularly in complex cases involving renal stone clearance. Endoscopic Combined Intra Renal Surgery (ECIRS) has emerged as an effective means of mitigating this issue, as studies have shown improved stone-free rate and a reduced incidence of complications after ECIRS [8, 13]. However, due to the complexity of the pelvic structure, and the size and the hardness of the stones, surgeons often struggle to predict the probability of successful stone removal before surgery. Therefore, the development of a computationally tractable model could greatly improve physicians' understanding of the difficulty of removing stones before surgery.

In this study, we used logistic regression and lasso regression to establish the key variables influencing the stone-free rate after ECIRS. The results showed hydronephrosis, RIL, RIW, stone burden, and number of calyces involved as the main factors affecting the stone-free rate. Traditional factors such as average Hounsfield unit and skin-to-stone distance, considered to influence stone clearance, were excluded from the study. Using the five identified parameters, we developed a nomogram to predict stone clearance rates. We then validated the effectiveness of the model using the calibration, DCA, and ROC curves. Furthermore, the DCA curves were plotted, showing a significant probability of range threshold, demonstrating that the nomogram had excellent predictive accuracy and that patients would benefit significantly from its use.

The stone burden is historically believed to be an independent factor in the kidney stones' free rate [14]. However, there is no universal standard for stone burden. It is not even explicitly addressed in parts of the literature. Therefore, the first question concerning the definition of stone burden is how to measure it. Clinics usually conduct Kidney-ureter-bladder radiography (KUB) or renal

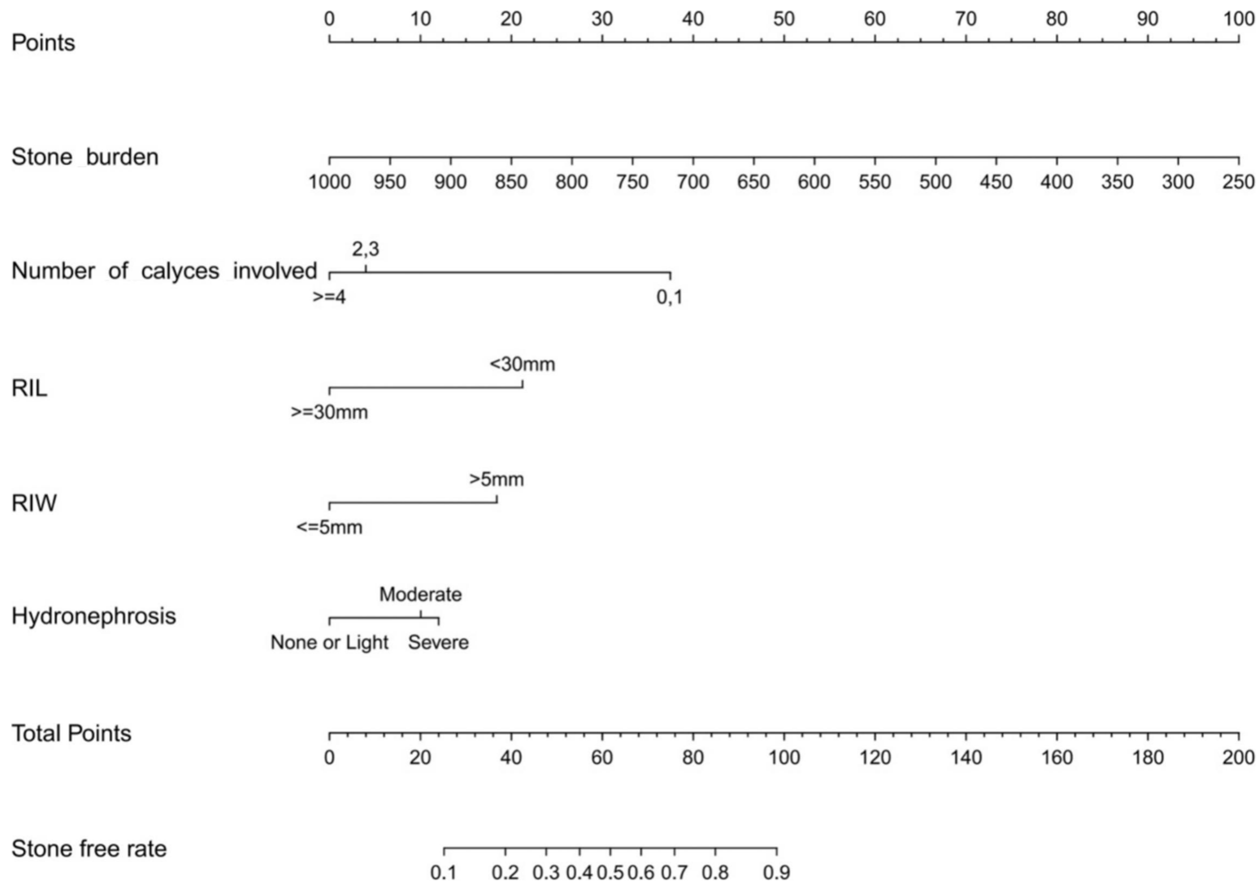

Fig. 2 Presentation of the prognostic nomogram template. The nomogram was built using five factors (Hydronephrosis, RIL, RIW, stone burden, and number of calyces involved) identified through LASSO regression analysis within the primary cohort. The nomogram simplifies output calculations based on a set of input variable values and shows the relative contribution of each factor to the overall score. Each input variable is plotted as a vertical line up to the first scale (individual score), and the tally of these outputs is used to compute the probability of a stone-free rate from the bottom scale (total score)

ultrasound (KUS). However, when a patient has symptoms or plans to undergo surgery, then Non-contrast-enhanced CT (NCCT) screening may be considered. The KUS technique is commonly used in outpatient settings and has the advantage of being radiation-free. Moreover, it can be checked multiple times. Studies have revealed that ultrasonography (US) is 45% sensitive and 88% specific to kidney stones [15]. However, KUS findings are largely operator-influenced, and results can vary widely among experienced sonographers. Consequently, KUS is only used typically as a preliminary exam. Although the NCCT is considered the most accurate diagnostic test, it does carry some radiation exposure risks. This risk can, however, be mitigated by low-dose CT, which has demonstrated a combined sensitivity of 93.1% and specificity of 96.6% in diagnosing urolithiasis [16]. As a preoperative test, we used low-dose CT to confirm stone size, location, and other associated details of renal stones. The sensitivity and specificity of KUB x-rays were estimated at 57% and 76%, respectively [17]. In addition, we used CT images as a reference and defined stone burden as Σ (0.785*length (max)* width (max)). In the process, we dropped the three-dimensional calculus size and adopted the planar calculation approach, mainly designed for surgeons to estimate quickly. We also opted not to use the longest path of stones, commonly used in clinics, because this calculation method is inaccurate for assessing alien stones. In this study, the stone burden was found to be a significant prognostic factor, showing a strong association with residual stone rates after ECIRS (OR = 0.995, $p < 0.001$). Moreover, the predictive ability of stone burden as a variable exhibited a high level of accuracy (AUC = 0.727, CI = 0.668–0.785). Based on the experience of the surgeons in this study, patients with larger stone burden are more likely to produce larger stone fragments and disperse them into the surrounding calyces intraoperatively. If the surgeon can confirm the presence of stones by ultrasound before perfecting the operation,

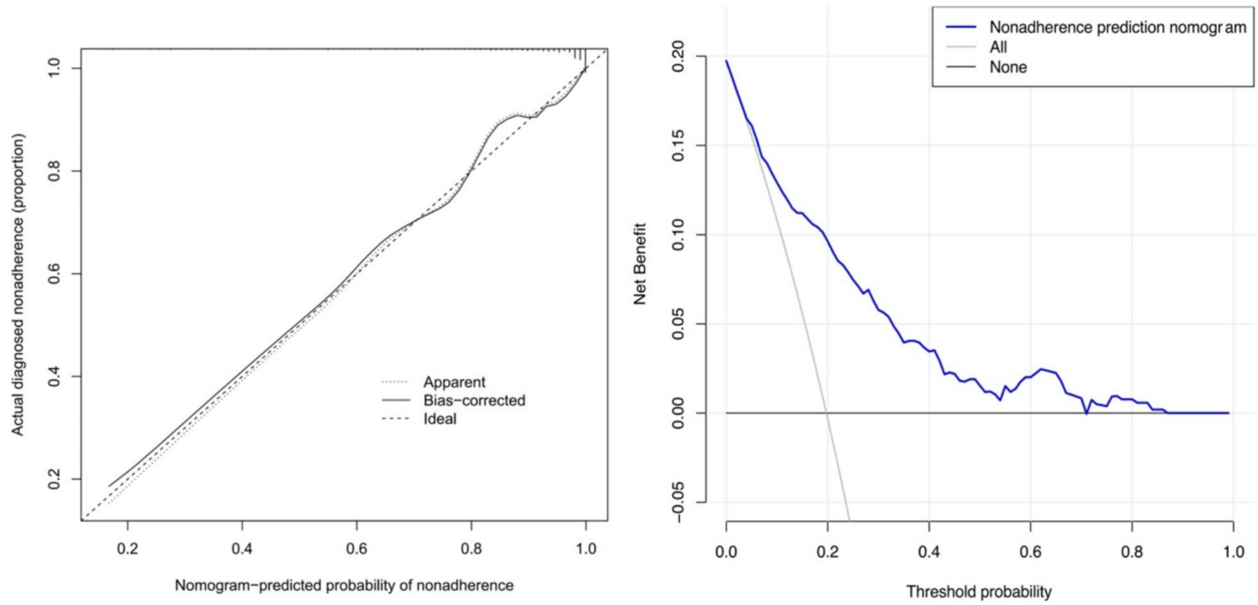

Fig. 3 **A** Calibration and discrimination curves of the predictive nomogram template. The X-axis scale represents the prediction values generated by the nomogram template, and the Y-axis scale represents the actual value probability of the stone-free rate. The grey dashed line represents the prediction performance of the nomogram, whereas the black solid line represents a perfect model. **B** The Y-axis is the degree of benefit to the patient, and the X-axis represents probability thresholds

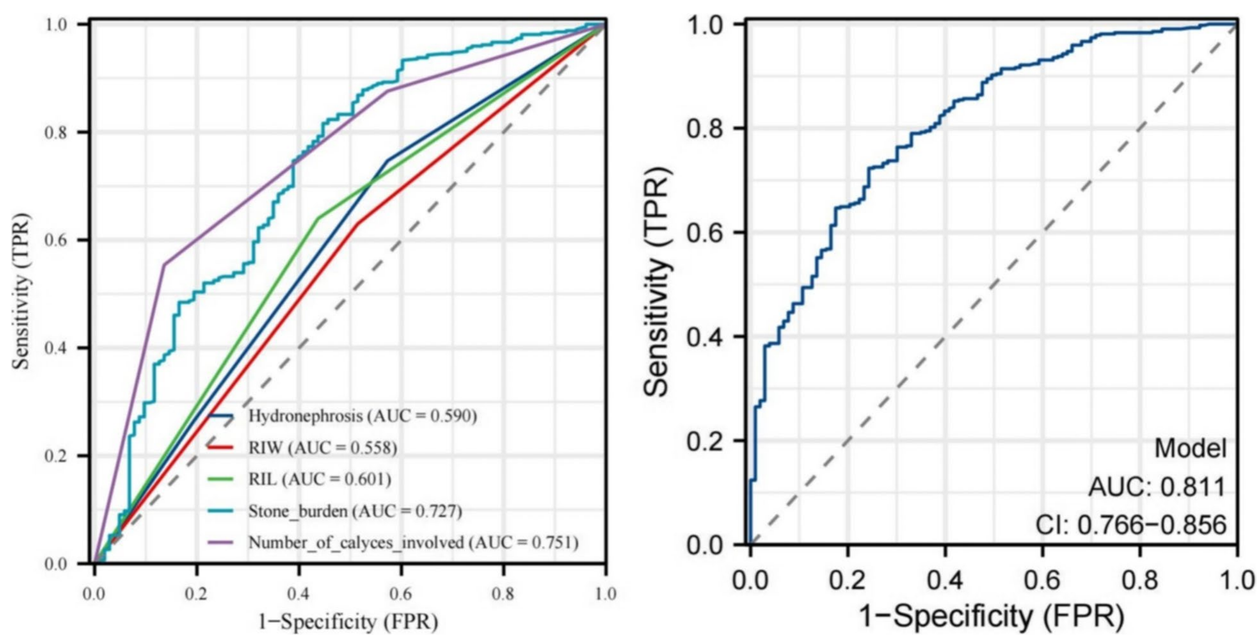

Fig. 4 **A** Receiver operating characteristic curves of hydronephrosis, RIL, RIW, stone burden, and number of calyces involved. The variables stone burden and number of calyces involved both showed highly accurate predictive abilities of (AUC = 0.727, CI = 0.668–0.785), and (AUC = 0.751, CI = 0.703–0.798), respectively. On the other hand, the variables RIL, RIW, and hydronephrosis showed less accurate predictive abilities of (AUC = 0.601, CI = 0.548–0.655), (AUC = 0.558, CI = 0.504–0.611), and (AUC = 0.590, CI = 0.531–0.650) respectively. **B** Receiver operating characteristic curves of the Joint index. The joint indicators showed a highly accurate predictive ability (AUC = 0.811, CI = 0.766–0.856)

the stone clearance rate will be greatly improved and the pain of patients with recurrent kidney stones will be better alleviated. This is an area where we believe further improvements can be made. Recent relevant studies have also mentioned that the Urologist should carefully evaluate patients with multiple calyceal stones and consider routine use of flexible nephoscopy to retrieve migrated fragments in order to improve their prediction of SFS.

In previous studies examining stone removal rates, hydrocephalus was classified into only two categories: with or without hydronephrosis. Consistent with other studies [18], our results suggested that hydronephrosis is a favorable factor for stone removal. We also discovered that different grades of hydronephrosis had varying effects on stone clearance. In our study, hydrocephalus as a prognostic factor had a strong positive association with the stone-free rate after ECIRS. However, the predictive ability of hydronephrosis as a variable showed a low level of accuracy (AUC = 0.590, CI = 0.531–0.650).

As commonly observed in various studies, the anatomy of the inferior pole of the kidney is an important factor affecting the stone removal rate. The characteristics of IPA, RIL and RIW are often analyzed to understand their effect on the stone clearance rate following retrograde intrarenal surgery (RIRS) [1, 19]. Studies have shown that IPA has a significant effect on the stone clearance rate of lower pole stones after RIRS. When reviewing the literature, we also found that IPA is measured differently. In this study, we used the inner angle formed at the intersection of ureteropelvic axis and the central axis of the lower pole infundibulum as IPA measurement[20]. An IPA < 45° is generally considered to significantly impact renal stone clearance after RIRS [1]. When doing an RIRS surgery on lower Renal Pelvic Stones, surgeons often encounter the anomaly of being able to see stones but not the impact of the holmium laser. However, in our study, IPA did not differ significantly between the SF and SR groups. Because of the ECIRS approach, we suggest that smaller IPA stones can be removed more effectively using PCNL. For RIL and RIW several standards exist [1, 11, 21]. We discovered that stone residue is more likely to occur when RIL ≥ 30 mm and RIW < 5 mm., which can be linked to the difficulty in passing PCNL endoscopes and RIRS ureteroscopes through the neck of calyces. These findings are consistent with other studies as RIL ≥ 30 mm significantly correlated with stone residue rate after ECIRS (OR = 0.205, p = 0.000). However, the predictive accuracy of the RIL variable was low (AUC = 0.601, CI = 0.548–0.655). On the other hand, RIW < 5 mm showed a negative and significant correlation with stone residue rate following ECIRS (OR = 0.519, p = 0.012). However, this scoring scheme may not be appropriate in all situations, such as when IPA is too small, RIL is too long, and RIW is too narrow for ECIRS. Furthermore, the predictive ability of the variable RIW demonstrated poor accuracy (AUC = 0.558, CI = 0.504–0.611).

In our clinical studies, we discovered that as the number of stones increased, the likelihood of being stone-free reduced. In the score of stone removal following PCNL, the S.T.O.N.E. score also highlighted the number of calyces involved as a factor in the surgical removal of stones [22, 23]. Although not explicitly stated, Guy's stone score grades also suggested that stone clearance rates are associated with the number of calyces occupied by stones [24, 25]. The number of calyces involved as a prognostic factor was significantly associated with the stone-free rate after ECIRS in our study. Additionally, the predictive ability of the variable number of calyces involved showed high accuracy (AUC = 0.751, CI = 0.703–0.798).

This study has several limitations. Firstly, it is retrospective, which introduces gaps in patient data collection and clinical variables such as the patient's history of urolithiasis surgery. Secondly, the study population was limited to patients from only two hospitals; hence the sample size was relatively small. As a result, the outcomes of this study have only been internally validated, with a significant number of procedures requiring external validation in subsequent studies. Lastly, this study's nomogram may not apply to patients with anatomic renal anomalies.

Conclusions

In summary, we used Logistics regression and Lasso regression to screen for factors affecting kidney stone clearance. We found that hydronephrosis, RIL, RIW, stone burden, and number of calyces involved were all significant for stone clearance. Based on these five variables, we constructed and validated a nomogram model. Our Nomogram model may help guide ECIRS treatment options. Additionally, when used in conjunction with PCNL's scoring system, it may help urologists choose which surgery to perform.

Clinical trial number

Not applicable.

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Not applicable.

Authors' contributions
A.B: Writing- Reviewing and Editing,Software, Validation. C: Investigation, Conceptualization, Supervision. D: Visualization, Methodology, Software. E, F, G, H, I : Validation. All authors reviewed the manuscript.

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Data availability
Data can be provided upon reasonable request from the author. Data supporting the results of this study can be obtained from the first author, Kaiqiang Wang.

Declarations

Ethics approval and consent to participate
The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The procedures used in this study adhere to the tenets of the Declaration of Helsinki (as revised in 2013). Approval was obtained from the Research Ethics Committee of General Hospital of Southern Theater Command (No. NZLLKZ2022168) and Guangdong Second Provincial General Hospital (No. 2022-KY-KZ-256–02). Individual consent for this retrospective analysis was waived.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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