Original Article

A nomogram for predicting the risk of residual stone fragments after ureteroscopy

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Background: The residual stone fragment is a tremendous issue after ureteroscopic lithotripsy and requires urologists to evaluate the condition of patients comprehensively. Our study aimed to construct a nomogram to make a personalized prediction of postoperative residual stone rate (RSR).

Methods: We implemented a retrospective cohort study in the Department of Urology, Shanghai General Hospital. A total of 277 patients undergoing ureteroscopy (URS) were enrolled in our study. Among them, 186 patients were included in the training group and the remaining 91 patients comprised the testing group. We utilized stepwise forward algorithm and logistic regression analysis to build predictive models and selected the best model based on Akaike's information criterion (AIC). The model was assessed by receiver operating characteristic (ROC) curves and the Hosmer-Lemeshow (HL) test. We also conducted decision curve analysis (DCA) to demonstrate the net benefit of the model. The independent testing group was used to validate the practicability of the nomogram.

Results: The severity of hydronephrosis, stone location, the transverse diameter of stone, hypertension, and white blood cell (WBC) were found to be significant predictive variables for RSR after URS. The area under the curve (AUC) of the training group was 0.7203 and that of the testing group was 0.7280. Besides, the nomogram also presented great calibration and accepted net benefit in a wide range of probabilities.

Conclusions: Our study achieved a predictive nomogram with excellent application value for urologists to assess RSR and make personalized treatment decisions.

Keywords: Nomogram; residual stone rate (RSR); ureteroscopic lithotripsy; predictive model; urolithiasis

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Introduction

Urolithiasis is becoming a significant worldwide source of morbidity with prevalence rates varying from 1% to 20% (1). Rapid technological and surgical advancements have granted urologists with more mini-invasive treatment choices to remove stones in urological tracts, such as extracorporeal shock-wave lithotripsy (ESWL), ureteroscopy (URS), and retroperitoneal laparoscopic ureterolithotomy (RPLU) (2,3). URS is a convenient, efficient, and minimally invasive surgical procedure for the management of urolithiasis and is widely adopted in the removal of urinary tract stones (4,5). After these active monitoring procedures, unsatisfactory outcomes needing further management are still possible, with a possibility of 10.1–15.4%, especially postoperative residual stone fragments (6,7). If left untreated, patients with residual stone fragments may experience stone-related events such as stone growth, obstruction, or urinary tract infections and have to eventually undergo secondary surgical intervention (8-10).

To deal with postoperative stone burdens, predictive tools distinguishing high-risk patients who are likely to face residual stone fragments preoperatively are essential in practical clinical scenarios. Nomograms can provide excellent individualized disease-related risk estimations due to their high accuracy and satisfactory discriminating characteristics, and they are widely used in estimating cancer prognosis or other health outcomes (11,12). Imamura *et al.* established the first nomogram to predict the clinical postoperative outcomes of URS and compare the nomogram with ESWL nomograms (13). De Nunzio *et al.* further constructed a new nomogram based on data from a Mediterranean population (14).

Based on the previous studies, we aimed to establish a new nomogram to make a personalized prediction of the possibility of residual stone fragments after URS in Asian countries, especially in the Chinese population, and to attempt to incorporate new variables to improve the performance of the model in the aspects of discrimination and calibration. We present the following article in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-609/rc).

Highlight box

Key findings

- We successfully constructed a nomogram including 5 factors to evaluate the risk of residual stone fragments after ureteroscopic lithotripsy with superior discrimination, excellent calibration abilities, and great clinical benefit.

What is known and what is new?

- Several factors including hydronephrosis, length of stones, stone location, and number of stones were found to be correlated with the risk of residual stone fragments after ureteroscopic lithotripsy;
- A novel predictive nomogram based on the Chinese population was constructed and validated. We also found that 5 factors had statistical links to the risk of residual stone fragments.

What is the implication, and what should change now?

- With further improvement and validation, the nomogram has high application potential to identify high-risk patients who may experience postoperative stone burden in advance and improve stone management in the future.

Methods

Study population

The data of 277 patients with urolithiasis treated with URS from September 2021 to May 2022 were collected. All patients had accepted normative and professional clinical care in Shanghai General Hospital, Shanghai Jiao Tong University (Shanghai, China). According to the radio of 7:3, these patients were randomly divided into a training group including 186 cases and an independent testing group including 91 cases. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was granted a waiver from approval by the Ethical Committee of the Shanghai General Hospital and informed consent was provided by all the patients. The diagnosis of ureteral stones was confirmed by non-contrast computed tomography (NCCT).

We collected the base information of all cases, including age, gender, body mass index (BMI), body temperature, hypertension, and diabetes mellitus. Patients underwent a series of detailed preoperative examinations including blood routine tests, complete urine tests, and urine cultures. The imaging parameters of stones were calculated from the preoperative NCCT by well-experienced uroradiologists. We measured the length of transverse and longitudinal diameters of the stones to calculate the stone size. Ureteral wall thickness (UWT) was defined as the maximum thickness of the ureteral wall and was obtained by measuring the thickness of the low-density soft tissue around the calculi. The location of stones was categorized by 0 = ureteropelvic junction, 1 = proximal ureter, 2 = middle ureter, and 3 = distal ureter. We also distinguished patients with single and multiple calculi. The severity of hydronephrosis was graded according to computed tomography (CT) image features. Grade 1 represented splitting of the renal pelvis only or not, grade 2 represented uniform dilation of the major and minor calyces, and grade 3 represented uniform dilation of the major and minor calyces accompanied with renal parenchymal thinning (15). Surgery-related variables were also recorded, such as the preoperative placement of double-J stents, the choice between rigid or flexible ureteroscope, and the operation time. Residual stone fragments were defined as remnant fragments bigger than 2 mm, which might need further intervention.

Procedures

All surgical procedures were monitored and implemented by the same professional urologist who had more than 15 years of ureteroscopic lithotripsy experience. Under general anesthesia, the URS was carried out in the lithotomy position. The rough distance between the stones and opening of ureters were evaluated according to the pre-operative examinations and body surface location. In the beginning, a safe guidewire was placed into the ureter to gain access to the stone through the bladder for stone localization. Then, a rigid ureteroscope was placed into the ureter at the lower end of the stones over the sensor guidewire, which was subsequently removed. We tended to utilize flexible ureteroscope and ureteral access sheaths to deal with upper ureteral calculi or renal calculi. Before the insertion of flexible ureteroscope, coaxial ureteric access sheaths were routinely placed into the ureter to gain access to the upper urinary tract. In the ureteroscopic field of view, the appearance of calculi, the situation of the ureteral wall, and the degree of urine opacity were observed and subsequently the lithotripsy was performed. The power was generated from a holmium laser generator (Lumenis company, San Jose, CA, USA) and transmitted through a 200/250 µm laser fiber. The power was usually set at 1.2–2.0 W and the frequency was set at 24–40 Hz, with flexible adjustment as necessary. Physiologic saline was used for irrigation to maintain a clear field of view during operation. Subsequently, the stone pieces were broken into fragments in the ureteral lumen for removal from the urinary system with a stone extractor. Procedures were completed with the retrograde dwelling of a double-J stent which would be removed through cystoscopy under local anesthesia on postoperative week 4. The record of the operation started at the beginning of general anesthesia and ended at successful placement of the catheters. All patients underwent NCCT on postoperative week 4 to examine for the presence of the residual stone fragments.

Statistical analysis

Out of all 277 cases, 186 were randomly identified as a training group to establish the nomogram, whereas the other 91 cases served as an independent dataset to validate the model. To explore the significant differences of variables between the patients with residual stone fragments and those without fragments, the Wilcoxon rank-sum test and Fisher's exact test were adopted. To assess the significance of each variable, *t*-test was used for continuous variables and Fisher's exact test for categorical variables.

We then conducted multivariate stepwise logistic regression analysis under the threshold of $P<0.1$ to select valuable predictive factors of stone-residual in the training group and also recorded the odds radio (OR) and 95% confidence interval (CI). Akaike's information criterion (AIC) was calculated and compared between each factor. We hypothesized that the model which had the minimal AIC value with the fewest number of variables was the final model. Receiver operating characteristic (ROC) curves were plotted to assess the discrimination of the model. The Hosmer-Lemeshow (HL) test was utilized to evaluate the calibration of the model. We further drew calibration plots to show the predictive probability and decision curve analysis (DCA) was conducted to demonstrate the net benefit of the model.

Based on previous analysis, we successfully formulated a nomogram to predict the risk of residual stone fragments. All statistical analysis was conducted with Stata 15.0 software (Stata Corp., College Station, TX, USA). A P value <0.05 was considered statistically significant. The process of our statistical analysis is shown in *Figure 1*.

Results

Among the 277 enrolled patients, including 200 (72.2%) males and 77 (27.8%) females, 87 (31.4%) cases had residual stone fragments after URS and the remaining 190 (68.6%) patients were confirmed as stone-free. Among them, diabetes occurred in 20 (7.2%) patients and hypertension occurred in 38 (13.7%) patients. We used median and interquartile range [IQR] to describe the distribution trends of quantitative variables, such as age 49.1 [38, 61] years, white blood cell (WBC) 6.91 [5.53, 9.07] $\times 10^9$/L, and transverse diameter of stones 7.07 [5.59, 9.33] mm. The characteristics of all variables are shown in *Table 1*. There

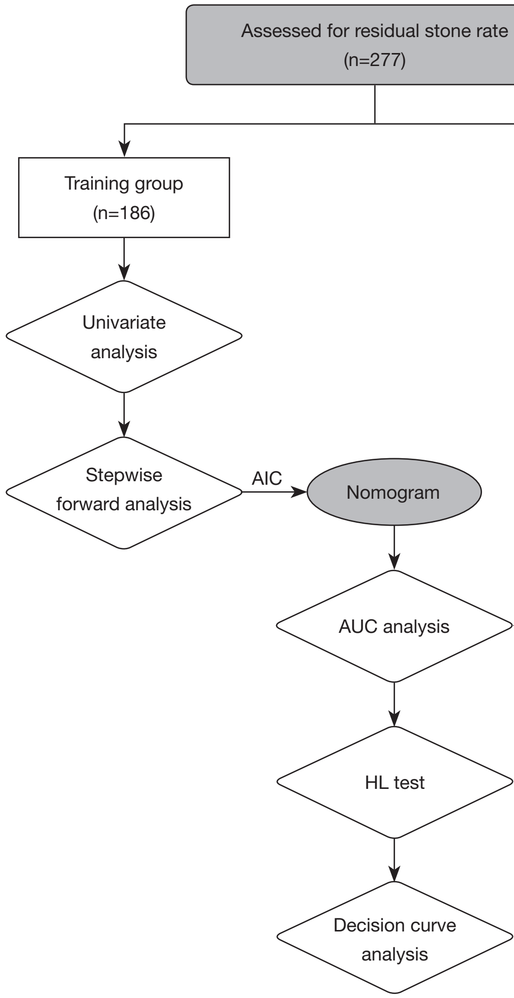

Figure 1 Characteristics of enrolled patients and analysis process of the study. AIC, Akaike's information criterion; AUC, area under the curve; HL, Hosmer-Lemeshow.

were no statistically significant differences between the training and the testing group.

The numbers of stone-free cases and stone-residual cases in the training group were 128 (68.8%) and 58 (31.2%), respectively, and in the testing group were 62 (68.1%) and 29 (31.9%), respectively. According to the univariate Cox regression analysis, 11 variables with P≤0.05 were recognized as being associated with residual stone rate (RSR). The results are shown in *Table 2*. The logistic model which had the minimal AIC value of 213.734 was identified as the final model (*Table 3*). It included 5 variables: WBC (P=0.061), hypertension (P=0.068), transverse diameter of stones (P=0.048), stone location (P=0.074), and hydronephrosis (P=0.021).

Based on the final model, we constructed a nomogram to predict the RSR. ROC analysis demonstrated that it had a great predictive accuracy of 0.7203 (95% CI: 0.6437–0.8051) (*Figure 2A*) and HL test revealed that it had strong calibration ability (P=0.34) (*Figure 2B*). In addition, the nomogram presented a net benefit in a range of probability between 20% and 80% through the DCA (*Figure 2C*). We further assessed the nomogram with an independent external dataset of which area under the curve (AUC) was 0.7280 (95% CI: 0.6054–0.8507) (*Figure 3A*) and the P value of the HL test was 0.65 (*Figure 3B*). It also presented a benign net benefit of 20% to 70% (*Figure 3C*). The

Table 1 Clinical characteristics of study sample statistics

Variables	Overall (n=277)	Stone-free (n=190, 68.6%)	Stone-residual (n=87, 31.4%)	P value
Gender				0.19
Male	200 (72.2)	142 (74.7)	58 (66.7)	
Female	77 (27.8)	48 (25.3)	29 (33.3)	
Age (years)	49.1 [38, 61]	46.5 [37, 59]	52 [39, 62]	0.25
BMI (kg/m²)	24.8 [22.8, 26.5]	24.9 [22.8, 26.4]	24.4 [22.8, 26.5]	0.95
Diabetes				0.024
No	257 (92.8)	181 (95.3)	76 (87.4)	
Yes	20 (7.2)	9 (4.7)	11 (12.6)	
Hypertension				0.14
No	239 (86.3)	168 (88.4)	71 (81.6)	
Yes	38 (13.7)	22 (11.6)	16 (18.4)	
Preoperative temperature (℃)	36.7 [36.5, 36.8]	36.7 [36.5, 36.8]	36.7 [36.5, 36.9]	0.24
White blood cell (×10^9/L)	6.91 [5.53, 9.07]	6.51 [5.47, 8.95]	8.00 [5.66, 9.49]	0.024
Neutrophils (×10^9/L)	4.68 [3.47, 6.59	4.26 [3.45, 6.58]	5.34 [3.69, 6.71]	0.078
Lymphocytes (×10^9/L)	1.67 [1.34, 2.11]	1.65 [1.35, 2.11]	1.82 [1.30, 2.14]	0.51
Platelets (×10^9/L)	218 [191, 258]	218 [190, 254]	223 [192, 263]	0.43
Creatinine (μmol/L)	80.6 [67.8, 99.1]	80.4 [67.5, 101.3]	81.0 [70.1, 98.3]	0.89
Uric acid (μmol/L)	381.0 [298.2, 449.3]	381.0 [297.2, 447.2]	380.5 [302.7, 460.6]	0.39
Urine leukocytes				0.064
0	147 (53.1)	106 (55.8)	41 (47.1)	
1	46 (16.6)	34 (17.9)	12 (13.8)	
2	60 (21.7)	39 (20.5)	21 (24.1)	
3	24 (8.7)	11 (5.8)	13 (14.9)	
Microscopic leucocyte				0.002
0	127 (45.8)	90 (47.4)	37 (42.5)	
1	110 (39.7)	83 (43.7)	27 (31.0)	
2	25 (9.0)	12 (6.3)	13 (14.9)	
3	13 (4.7)	5 (2.6)	8 (9.2)	
4	2 (0.7)	0 (0.0)	2 (2.3)	
Urine culture				0.81
Negative	254 (91.7)	175 (92.1)	79 (90.8)	
Positive	23 (8.3)	15 (7.9)	8 (9.2)	
Transverse diameter (mm)	7.07 [5.59, 9.33]	6.71 [5.30, 8.49]	8.26 [5.97, 11.75]	<0.001
Longitudinal diameter (mm)	10.00 [8.00, 13.75]	10.00 [7.50, 12.50]	12.00 [8.75, 18.75]	<0.001
Hounsfield units of stones	1,051.00 [731.00, 1,261.00]	985.25 [709.00, 1,209.67]	1,143.14 [854.80, 1,362.00]	0.005

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Overall (n=277)	Stone-free (n=190, 68.6%)	Stone-residual (n=87, 31.4%)	P value
UWT (mm)	3.52 [2.88, 4.32]	3.52 [2.93, 4.35]	3.50 [2.79, 4.25]	0.59
Left or right				0.60
Left	154 (55.6)	108 (56.8)	46 (52.9)	
Right	123 (44.4)	82 (43.2)	41 (47.1)	
Numbers of stones				<0.001
Single	193 (69.7)	148 (77.9)	45 (51.7)	
Multiple	84 (30.3)	42 (22.1)	42 (48.3)	
Stone location				<0.001
UPJ	21 (7.6)	7 (3.7)	14 (16.1)	
Proximal	158 (57.0)	105 (55.3)	53 (60.9)	
Middle	60 (21.7)	48 (25.3)	12 (13.8)	
Distal	38 (13.7)	30 (15.8)	8 (9.2)	
Hydronephrosis				<0.001
1	182 (65.7)	136 (71.6)	46 (52.9)	
2	66 (23.8)	44 (23.2)	22 (25.3)	
3	29 (10.5)	10 (5.3)	19 (21.8)	
Ureteral stenting				0.60
No	231 (83.4)	160 (84.2)	71 (81.6)	
Yes	46 (16.6)	30 (15.8)	16 (18.4)	
Operation procedures				0.16
Rigid	216 (78.0)	153 (80.5)	63 (72.4)	
Flexible	61 (22.0)	37 (19.5)	24 (27.6)	
Operation times (min)	35 [25, 45]	35 [25, 45]	35 [25, 60]	0.027

Data shown are number (%), or median [interquartile range]. BMI, body mass index; UWT, ureteral wall thickness; UPJ, ureteropelvic junction.

nomogram is presented in *Figure 4*.

Discussion

Our primary aim in the study was to establish a personal predictive nomogram for RSR and evaluate the performance of the nomogram from aspects of discrimination and calibration with an independent dataset. Briefly, our nomogram included 5 variables: WBC, hypertension, transverse diameter of stone, stone location, and hydronephrosis.

Estimating stone burden is a critical component of the management of renal stone disease, which can consistently and significantly affect decision-making. In general, the size of stones has a negative correlation with stone clearance effectiveness (16). In this study, we evaluated stone burden through measuring the length of diameters of stones and found the transverse diameter of calculi had a significant relationship with RSR (P=0.048), which agreed with previous studies (17,18). More severe stone burden frequently incurred longer operation time, more complex operation procedures, and eventually lead to higher RSR.

Previous studies have reported that hypertension is associated with the incidence of urolithiasis. Vodanović

Table 2 Univariate analysis predicting the risk of RSR

Variables	B	SE	P value
White blood cell	0.103	0.053	0.050
Urine leukocytes	0.308	0.147	0.036
Microscopic leucocyte	0.362	0.172	0.036
Transverse diameter	0.143	0.044	0.001
Longitudinal diameter	0.068	0.025	0.006
HU of stones	0.001	0.000	0.020
Numbers	0.679	0.337	0.044
Stone location	−0.604	0.219	0.006
Hydronephrosis	0.766	0.242	0.002
Operation times	0.028	0.009	0.002
Hypertension	−0.938	0.430	0.029

RSR, residual stone rate; HU, Hounsfield units; B, regression coefficient; SE, standard error.

et al. confirmed that arterial hypertension was an independent predictor of current urolithiasis (P<0.05) (19). Several cohort studies have revealed possible bidirectional associations between hypertension and nephrolithiasis (20-22). Stone disease influenced the level of blood pressure through multiple pathophysiological mechanisms like inflammation and oxidative stress. Thus, we attempted to unearth any potential connection between the risk of residual stone fragments and hypertension. Our analysis implied that patients with hypertension were more likely to have residual stone fragments after URS (P=0.068). Though no clear evidence of less satisfactory treatment results of patients with hypertension was found, enrolling hypertension in the final nomogram would improve clinical management and primary prevention of urolithiasis patients with hypertension.

Compared with proximal stones, the stone free rate

Table 3 Logistic regression of the final model

Variables	Coef.	SE	P value	95% CI	Sig.	AIC	BIC
White blood cell	0.107	0.057	0.061	−0.005 to 0.220	*	213.734	233.088
Hypertension	0.828	0.454	0.068	−0.061 to 1.718	*		
Transverse diameter	0.095	0.048	0.048	0.001 to 0.189	**		
Stone location	−0.434	0.244	0.074	−0.912 to −0.043	*		
Hydronephrosis	0.601	0.259	0.021	0.092 to 1.109	**		
Constant	−2.895	0.831	0.001	−4.524 to −1.267	–		

*, P<0.1; **, P<0.05. AIC, Akaike's information criterion; BIC, Bayesian information criterion; CI, confidence interval; Coef., coefficient; SE, standard error; Sig., significance.

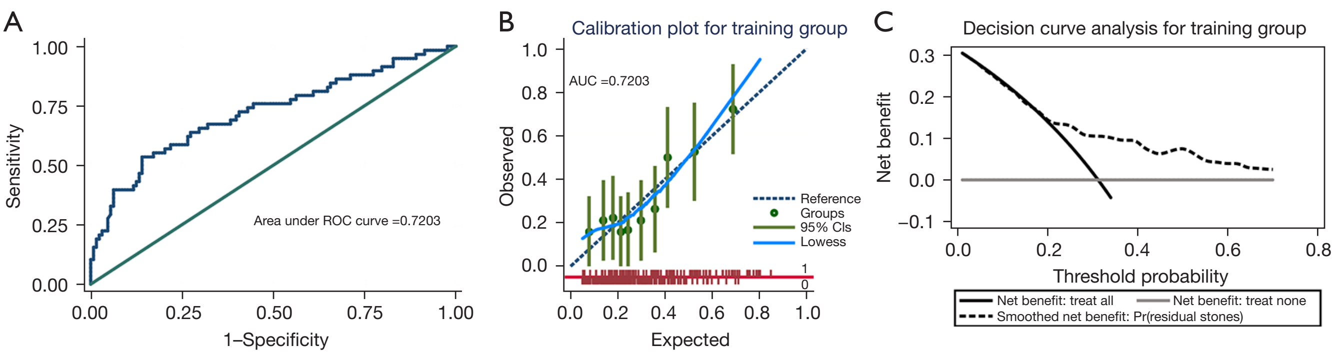

Figure 2 Performances of the predictive model on the training group. (A) ROC curves of the nomogram in the training group. The nomogram had good discriminative power with an area under the ROC curve of 0.7203. (B) Calibration plots with local regression non-parametric smoothing lines of the present nomogram in the training group. (C) DCA demonstrated the model presented a net benefit in a range of probability between 20% to 80% in the training group. ROC, receiver operating characteristic; AUC, area under the ROC curve; DCA, decision curve analysis; CI, confidence interval; Pr, probability.

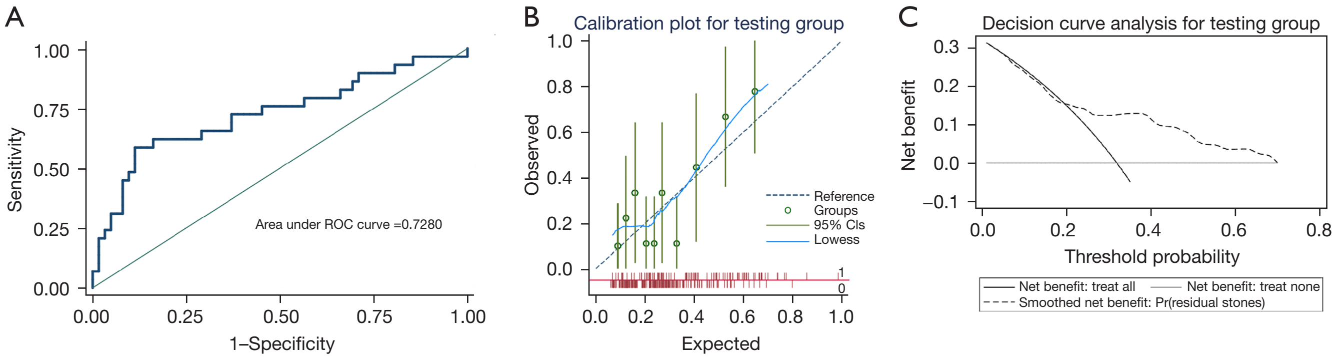

Figure 3 Performances of the predictive model on the testing group. (A) ROC curves of the nomogram in the testing group. The nomogram had good discriminative power with an area under the ROC curve of 0.7280. (B) Calibration plots with local regression non-parametric smoothing lines of the present nomogram in the testing group. (C) DCA demonstrated the model presented a net benefit in a range of probability between 20% and 70% in the testing group. ROC, receiver operating characteristic; DCA, decision curve analysis; CI, confidence interval; Pr, probability.

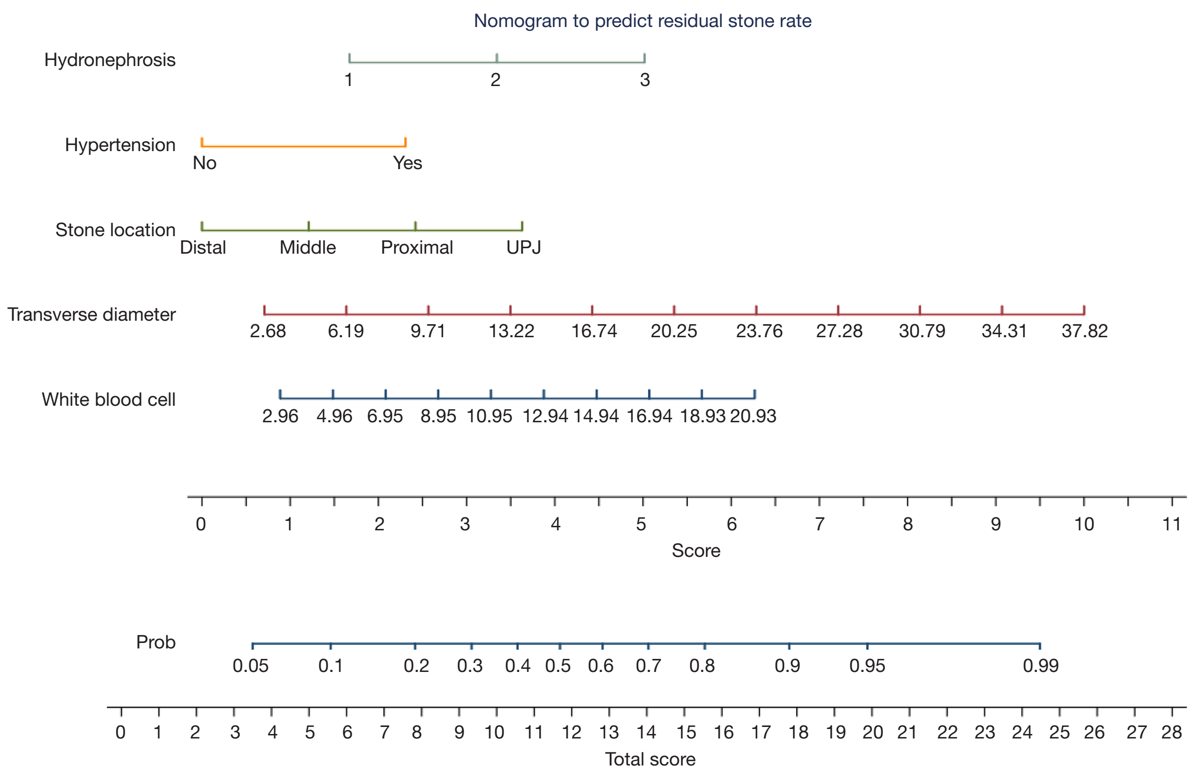

Figure 4 Nomogram predicting RSR after ureteroscopic lithotripsy. UPJ, ureteropelvic junction; RSR, residual stone rate.

was higher in distal stones (23). In our study, 78.9% of distal stones were removed clearly whereas only 66.5% of proximal stones had no residual fragments. Although the rate was somewhat lower than the treatment outcomes published in the European Association of Urology (EAU) Guidelines, which could be explained by the limitations of treatment options, we still certified that the location of stones obviously influenced the RSR, with statistical differences (P=0.006). Although some previous studies have remained suspicious of the relationship between the degree of hydronephrosis and RSR (24,25), hydronephrosis was identified as a significant factor for predicting RSR in a range of other surgical outcome predictive models (26,27). Overall analysis in our study indicated a significant difference in the role of hydronephrosis for RSR and retreatment rate (P=0.002). For surgical outcomes of ESWL, Abe *et al.* considered that pyuria served as an independent predictive factor (28). In our univariate analysis and logistic regression analysis, infectious-related factors such as WBC also showed great importance. No certain association between positive infectious-related factors and poor surgical outcomes has been found yet. Our findings can be explained by that the turbid urine related to serious infection can interfere surgical field and affect the stone-free rate. Besides, it is worth noting that severe hydronephrosis was often accompanied by impacted stones and increased the risk of urinary tract infection (29,30).

In clinical scenarios, rigid and flexible URS were both feasible options for the treatment of ureteral stones. Galal *et al.* concluded that flexible URS contributed to longer operative time and higher stone-free rate (31). Similarly, Yoshida *et al.* considered that high UWT was associated with poor endoscopic findings and adverse surgical outcomes in patients undergoing URS (32). However, our cohort study found no statistically significant difference between these factors and postoperative RSR, which may be explained by the discrepancy in the data source.

When evaluating the predictive accuracy of a model, discrimination, calibration, clinical benefit, and internal and external validity were significant aspects (33). Large numbers of nomograms have been developed to serve as predictive models in urology, especially in the oncological and cancer fields (34,35). Certainly, models to predict RSR after URS are also important (36). Imamura *et al.* constructed the first nomogram including the length, number, location of the stone, and the presence of pyuria based on a Japanese population (13), but the model showed plain discrimination abilities and poor calibration and lacked clinical net benefits with subsequent validation (37). De Nunzio *et al.* established another predictive model which included the following factors: hydronephrosis, length of stones, stone location, and number of stones (14); the model still needs further validation before actual clinical application. With the independent validation dataset, we examined the performance of our nomogram by ROC curves, HL test, and DCA. The results illustrated that our nomogram had great discrimination, favorable calibration, benign clinical benefit, and a convenient model presentation. It has been widely accepted that the predictive accuracy of a nomogram is inevitably affected by the general characteristics of the population (33). Thus, we aimed to construct a nomogram based on the Chinese population to achieve better application abilities. Our nomogram could distinguish high-risk patients who would have residual stone fragments and require secondary surgical intervention after URS. The nomogram could also offer auxiliary guidance for urologists with excellent clinical application value preoperatively.

Our study had some limitations. Firstly, the simple presentation of the nomogram sometimes limited its application; more flexible app- or web-based tools are required for further dissemination. Secondly, the single-center data source somewhat influenced the reliability of the model, more validation data from other institutions is necessary to enhance the predictive value in our further study. Nonetheless, our study established a nomogram to identify high-risk patients of stone residual fragments who still require secondary intervention.

Conclusions

We successfully constructed a nomogram including 5 factors to evaluate the risk of RSR after URS with superior discrimination, excellent calibration abilities, and great clinical benefit. With further improvement and validation, the nomogram has high potential application to pre-emptively identify high-risk patients who may experience postoperative stone burden and improve stone management in the future.

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Footnote

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Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-22-609/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-609/coif). The authors have no conflicts of interest to declare.

Ethical Statement: 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 study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was granted a waiver from approval by the Ethical Committee of the Shanghai General Hospital and informed consent was provided by all participants.

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