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Original Article

Surgical outcomes and postoperative hemorrhage risk of percutaneous nephrolithotomy (PCNL) for deer horn shaped stones analyzed by Lasso regression

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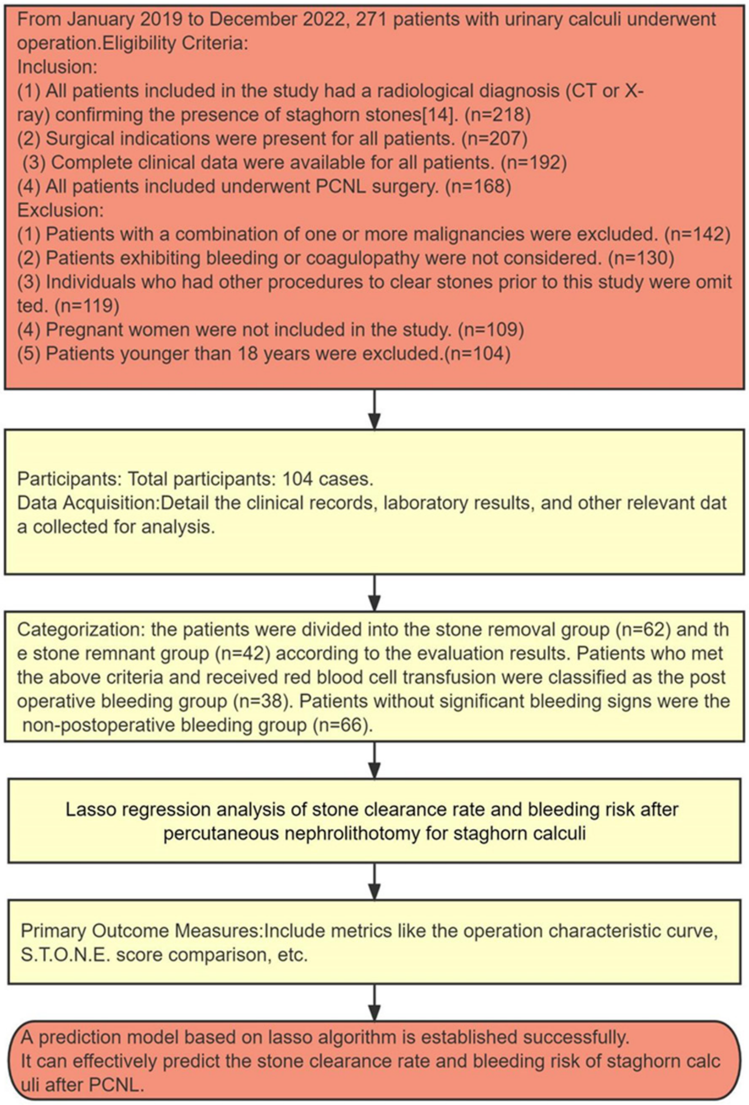
Abstract: Objective: To predict surgical outcomes and postoperative hemorrhage risk for percutaneous nephrolithotomy (PCNL) in cases of staghorn-shaped stones using lasso regression. Methods: We collected data from 104 patients with staghorn-shaped stones treated with PCNL between January 2019 and December 2022 at the Department of Urology Surgery, the Third People's Hospital of Gansu Province. Medical history, stone-related parameters, and lab test data were collected. Patients were categorized into stone clearance or residual groups based on postoperative stone status, and bleeding or non-bleeding groups based on post-surgery blood transfusion. The lasso model's predictive ability for post-PCNL Stone Free Rate (SFR) and hemorrhage risk was evaluated using ROC curves. The lasso model's predictive performance for post-PCNL SFR was compared to the S.T.O.N.E. score. Results: Overall stone clearance rate was 59.29%. The lasso model identified hypertension history, calyx count at stone location, prior calyx surgeries, age, operation duration, and pre-op creatinine level as SFR predictors. The AUC of lasso model (0.867) significantly surpassed the S.T.O.N.E. model (0.748) (P=0.006) in predicting post-PCNL SFR. In addition, the AUC of lasso model in predicting the risk of postoperative bleeding was 0.779, suggesting an ability in the prediction of bleeding occurrence. Conclusion: A predictive model utilizing lasso algorithm was successfully established. It effectively predicts stone clearance rate and bleeding risk after PCNL for staghorn shaped kidney stones.

Keywords: Lasso regression, staghorn shaped stones, percutaneous nephrolithotomy, surgical outcomes, postoperative hemorrhage risk

Introduction

Urinary tract stones are a common urological disease, with a global prevalence of 2-20% [1]. In China, the overall prevalence is between 1-5%, and in the southern region, it is as high as 5-10% [2]. The types of diseases include kidney stones, ureteral stones, bladder stones, and urethral stones, with upper urinary tract stones accounting for 99.5% of all cases [3, 4]. If urinary tract stones are not treated promptly and effectively, they can lead to urinary tract damage, obstruction, secondary infections, and even renal impairment and uremia [5]. The long-term irritation, infection, and hydronephrosis caused by stones can potentially lead to malignant changes in the epithelial cells of the renal collecting system [6], posing a serious threat to patients' health.

Staghorn calculi are a special type of kidney stone, classified as complex kidney stones, mainly located in the renal pelvis and branched into the calyx. If these branches occupy 80% or more of the volume of the renal pelvis and calyx, they are referred to as complete staghorn stones, otherwise as partial staghorn stones [7]. Patients with staghorn stones often have recurrent urinary tract infections and chronic renal failure, resulting in difficult stone extraction, low stone clearance rate, and recurrence after surgery [8]. In the past, we mainly treated staghorn stones through open surgery, but this type of surgery is traumatic, risky, and slow to recover [9]. With the development and improvement of endoscopic technology, percutaneous nephrolithotripsy (PCNL) has begun to replace open surgery and become the first choice for treating complex kidney stones. Compared with



From January 2019 to December 2022, 271 patients with urinary calculi underwent operation.Eligibility Criteria:
Inclusion:
(1) All patients included in the study had a radiological diagnosis (CT or X-ray) confirming the presence of staghorn stones[14]. (n=218)
(2) Surgical indications were present for all patients. (n=207)
(3) Complete clinical data were available for all patients. (n=192)
(4) All patients included underwent PCNL surgery. (n=168)
Exclusion:
(1) Patients with a combination of one or more malignancies were excluded. (n=142)
(2) Patients exhibiting bleeding or coagulopathy were not considered. (n=130)
(3) Individuals who had other procedures to clear stones prior to this study were omitted. (n=119)
(4) Pregnant women were not included in the study. (n=109)
(5) Patients younger than 18 years were excluded.(n=104)

Participants: Total participants: 104 cases.
Data Acquisition:Detail the clinical records, laboratory results, and other relevant data collected for analysis.

Categorization: the patients were divided into the stone removal group (n=62) and the stone remnant group (n=42) according to the evaluation results. Patients who met the above criteria and received red blood cell transfusion were classified as the postoperative bleeding group (n=38). Patients without significant bleeding signs were the non-postoperative bleeding group (n=66).

Lasso regression analysis of stone clearance rate and bleeding risk after percutaneous nephrolithotomy for staghorn calculi

Primary Outcome Measures:Include metrics like the operation characteristic curve, S.T.O.N.E. score comparison, etc.

A prediction model based on lasso algorithm is established successfully.
It can effectively predict the stone clearance rate and bleeding risk of staghorn calculi after PCNL.

Figure 1. Flow chart of the prediction model construction. S.T.O.N.E., Stone size, Tract length, Obstruction, Number of involved calices, and Essence or stone density; PCNL, percutaneous nephrolithotomy.

traditional open surgery, PCNL is less traumatic, recovers faster, and can perform multiple stone clearances. Many studies have proven that the effect of PCNL on treating complex kidney stones is better than that of open surgery [10].

Currently, there are various models to assess the complexity of renal stones and to predict the surgical outcome of PCNL, which helps in clinical decision making and patient communication [11]. However, existing tools demonstrate limited accuracy in predicting patient outcomes, for example, Atalay et al. [12] found that the area under the curve of the stone volume and the renal collecting system volume in predicting stone clearance in patients was 0.76. Therefore, it is particularly important to find new prediction tools. In addition, predicting postoperative complications such as bleeding remains a challenge. Bleeding after PCNL is one of the most common complications [13], with an incidence of 7-10%. Severe bleeding usually requires blood transfusion or vascular embolization, prolonging hospitalization. Therefore, predicting bleeding risk is valuable for surgical planning and consent.

In this study, we used Lasso regression to predict both the efficacy and postoperative bleeding risk of PCNL for staghorn stones. The model can aid clinical decision-making regarding this complex stone disease.

Methods and materials

Sample information

We collected data from 104 patients with staghorn stones who underwent PCNL surgery in Department of Urology Surgery, the Third People's Hospital of Gansu Province from January 2019 to December 2022. The study was conducted with the approval of the Medical Ethics Committee of the Third People's Hospital of Gansu Province, Ethics Approval Number: 202234L. To give the reader more about the flow of the article, we drew a flow chart (**Figure 1**). Inclusion criteria: (1) Patients with a radiological diagnosis (CT or X-ray) confirming the presence of staghorn stones [14]. (2) Patients with surgical indications. (3) Patients with complete clinical data. (4) Patients who underwent PCNL surgery. Exclusion criteria: (1) Patients with a combination of one or more malignancies. (2) Patients exhibiting bleeding or coagulopathy. (3) Individuals who had other procedures to clear stones prior to this study. (4) Pregnant women. (5) Patients younger than 18 years.

Data collection

We collected various information about the patient during their hospital stay by accessing the case management and imaging systems. This information includes gender, age, body mass index (BMI), history of hypertension or diabetes, stone features (stone type, stone burden and stone cross-sectional area), preoperative hemoglobin and creatinine levels, the duration of the operation, the number of renal puncture channels, intraoperative blood loss and postoperative flow.

Sample grouping

The stone remnants were determined according to the patients' CT scans within 1 week after surgery. The patients were assigned to a clearance group (n=62) if there was no residual stone in the calyx system at all, and others with any residual stone were assigned into the stone remnant group (n=42). The criteria for stone removal are recommended in the literature [15]. Postoperative bleeding was defined according to whether the patients had severe bleeding and received red blood cell infusion after surgery. The criteria for severe bleeding were referred to in the literature [16, 17], i.e., drainage volume > 1500 ml within 12 hours after surgery, or hemorrhagic shock manifestations such as decreased blood pressure and increased heart rate in the postoperative period. Patients who met the above criteria and received red blood cell transfusion were classified as the postoperative bleeding group (n=38). Patients without significant bleeding signs were classified as the non-postoperative bleeding group (n=66).

Observation indicators

We established receiver operating characteristic (ROC) curves to calculate the predictive ability of the Lasso model for postoperative SFR and postoperative bleeding risk of PCNL. In terms of predicting post-PCNL SFR, we compared the area under the ROC curve (AUC) of the Lasso model and the Stone size, Tract length, Obstruction, Number of involved calices, and Essence or stone density (S.T.O.N.E.) score to assess the predictive performance of the Lasso model for post-PCNL SFR in staghorn stones.

Statistical analysis

Data were analyzed using SPSS version 26.00 (IBM Corp., Armonk, NY). Metric data were analyzed and processed using SPSS 26.0 statistical software. Metric data that met the normal distribution and homogeneity of variance were expressed as mean ± standard deviation, and metric data were tested using independent samples t-test for intergroup comparison, and paired t-test for intragroup comparison. Count data were represented by the rate and were tested using the chi-square test. The effect of the various indicators on treatment efficacy (SFR) and postoperative bleeding was determined by Lasso regression analysis. The risk score was calculated by the following formula: Risk scores = $\sum_{i}^{n} Xi \times Yi$ (X: coefficient of each clinical factor, Y: expression of each clinical factor). The efficacy of the risk score in predicting treatment efficacy was analyzed using the receiver operating characteristic (ROC) curve. Differences in the AUC between the two models were compared using the DeLong-test. A *P*-value < 0.05 (two-sided) was considered statistically significant.

Results

Baseline data

A total of 104 patients with staghorn stones undergoing PCNL were included. There were 48 patients ≥ 55 years old and 56 patients < 55 years old. The cohort contained 53 male and 51 female patients. BMI was ≥ 25 kg/m^2 in 20 patients and < 25 kg/m^2 in 84 patients. Renal puncture was performed in 28 patients and not performed in 77 patients. A history of diabetes was present in 13 patients and absent in 91 patients. A history of hypertension was present in 24 patients and absent in 80 patients. Stones were located on the left side in 28 patients and the right side in 76 patients. Complete staghorn stones occurred in 56 patients, and partial staghorn stones occurred in 48 patients. Stone burden was ≥ 1000 mm^2 in 40 patients and < 1000 mm^2 in 64 patients. Preoperative hemoglobin was ≥ 120 g/L in 51 patients and < 120 g/L in 53 patients. Preoperative creatinine was ≥ 100 μmol/L in 31 patients and < 100 μmol/L in 73 patients. Stone cross-sectional area was ≥ 500

Table 1. Patient baseline data

Factor	Number	Factor	Number
Age		Preoperative hemoglobin levels	
≥ 55 years old	48	≥ 120 g/L	51
< 55 years old	56	< 120 g/L	53
Gender		Preoperative creatinine levels	
Male	53	≥ 100 umol/L	31
Female	51	< 100 umol/L	73
BMI		Stone cross-sectional area	
≥ 25 kg/m^2	20	≥ 500 mm^2	50
< 25 kg/m^2	84	< 500 mm^2	54
The number of renal puncture channels		The degree of hydronephrosis	
Yes	28	Mild	35
No	77	Moderate	35
History of diabetes		Severe	35
Yes	13	The number of renal puncture channels	
No	91	≥ 2	33
History of hypertension		< 2	71
Yes	24	Duration of the operation	
No	80	≥ 2 h	54
Affected side		< 2 h	50
Left	28	Postoperative transfusion situation	
Right	76	Transfusion	38
Stone type		No transfusion	66
Complete	56	Intraoperative bleeding	
Partial	48	≥ 100 mL	40
Stone burden		< 100 mL	64
≥ 1000 mm^2	40	Postoperative flow was induced	
< 1000 mm^2	64	≥ 1500 mL	38
Stone removal rate		< 1500 mL	66
Clean	62		
Uncleared	42		

Note: BMI, body mass index.

mm^2 in 50 patients and < 500 mm^2 in 54 patients. Hydronephrosis was mild in 35 patients, moderate in 35 patients, and severe in 35 patients. The number of renal puncture tracts was ≥ 2 in 33 patients and < 2 in 71 patients. Operation duration was ≥ 2 hours in 54 patients and < 2 hours in 50 patients. Postoperative transfusion was required in 38 patients and not required in 66 patients. Intraoperative bleeding was ≥ 100 mL in 40 patients and < 100 mL in 64 patients. Postoperative drainage was ≥ 1500 mL in 38 patients and < 1500 mL in 66 patients. Stone clearance rate was complete in 62 patients and residual in 42 patients (**Table 1**).

Predicting therapeutic effect

Based on CT assessment within one week after surgery, the stone-free rate (SFR) reached 59.61%. Patients were then divided into the stone clearance group (n=62) and stone residual group (n=42). Lasso regression on 17 factors identified that age, BMI, hypertension history, preoperative creatinine, stone cross-sectional area, number of tracts, and operation time were strongly correlated with SFR (all $P < 0.05$, **Figure 2A**, **2B**). Using lambda.1se, we constructed a risk score formula: -6.911030506 + Age × 0.02844913 + BMI × 0.061961767 + Hypertension History × 0.110416072 + Preoperative Creatinine × 0.002950637 + Stone Cross-Sectional Area × 0.00020067 + Number of Tracts × 0.254095422 + Operation Time × 0.022750267. The stone clearance group had significantly lower risk scores than the residual group ($P < 0.0001$, **Figure 3A**). ROC analysis found that the risk score AUC was 0.867 for predicting patient SFR (**Figure 3B**).

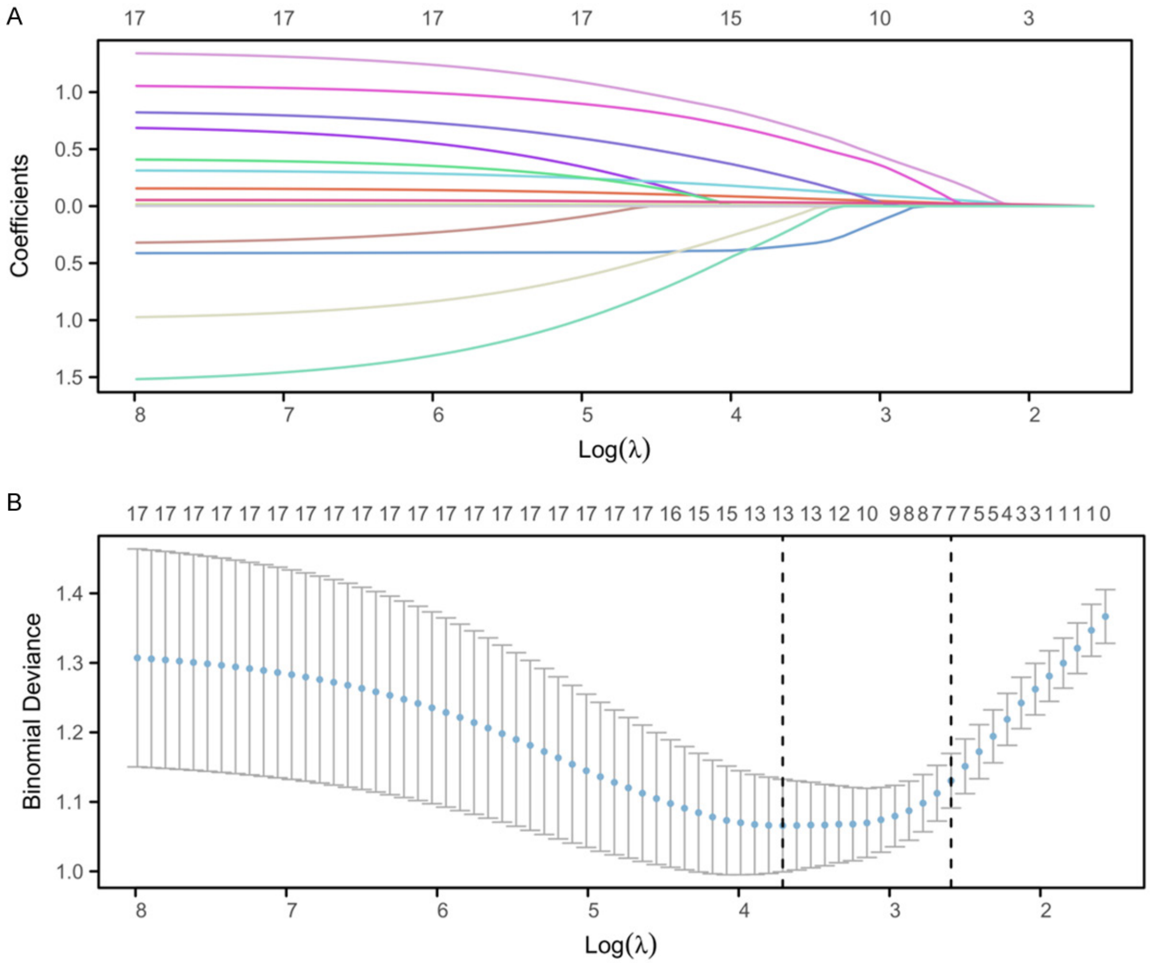


Figure 2. Risk model for the prediction of postoperative SFR by the Lasso regression model. A, B. Coefficient distribution of LASSO regression analysis and parameter adjustment calculation (lambda) based on 10-fold cross-validation deviances. SFR, stone free rate.

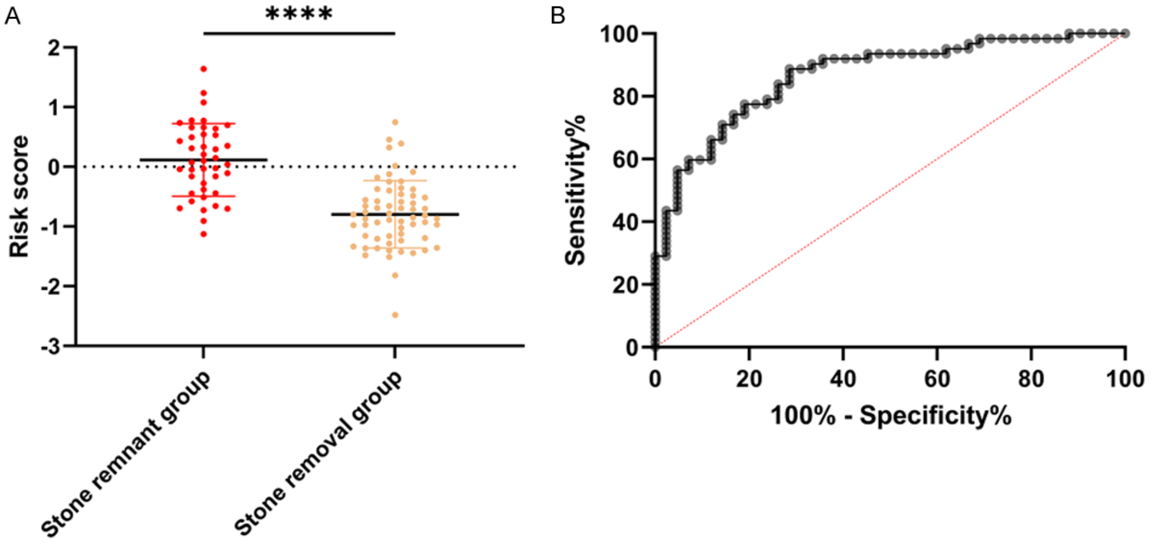


Figure 3. The level and area under the curve (AUC) of risk score in predicting patient SFR. A. Risk score in patients with or without stone residual. B. ROC curve of the risk score in predicting SFR. Note: SFR, stone-free rate; ROC, receiver operating characteristic; ****P < 0.0001.

Table 2. ROC parameter

Predictive Variable	Area under curve	Confidence interval	Sensitivity	Specificity	Youden's index
S.T.O.N.E. score	0.748	0.651-0.846	83.87%	52.38%	36.25%
Risk score	0.867	0.798-0.936	88.70%	71.42%	60.13%

Note: S.T.O.N.E., Stone size, Tract length, Obstruction, Number of involved calices, and Essence or stone density.

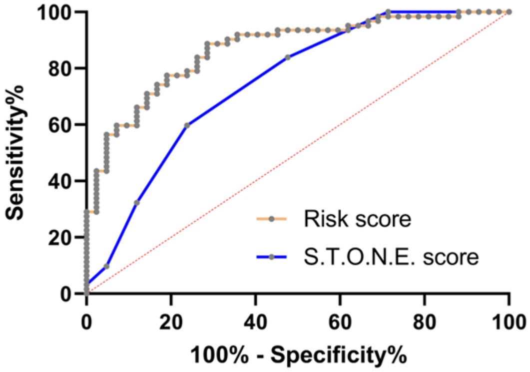


Figure 4. ROC curve of the risk score and S.T.O.N.E. score. Note: S.T.O.N.E., Stone size, Tract length, Obstruction, Number of involved calices, and Essence or stone density; ROC, receiver operating characteristic.

Comparing risk score and S.T.O.N.E. score for predicting SFR

We compared ROC curves for the risk score and S.T.O.N.E. score in predicting SFR. The AUC of S.T.O.N.E. score was 0.748 and the AUC of the risk score was 0.872. Delong's test demonstrated that the AUC of risk score was significantly greater (**Figure 4**; **Table 2**, P=0.006).

Predicting postoperative bleeding

Patients were divided into postoperative bleeding (n=38) and non-bleeding groups (n=66) based on transfusion requirements. Lasso regression on 17 factors identified that age, sex, bleeding volume, prior kidney surgery, affected side, stone type, burden, area, and number of tracts were correlated with postoperative bleeding (**Figure 5A**, **5B**). Using lambda.min, we constructed a risk score formula: -3.890032635 + Age × 0.027071507 + Sex × 0.045951461 + Bleeding Volume × 0.002977892 + Kidney Surgery History × 0.045192593 + Affected Side × 0.696569261 + Stone Type × -0.085806375 + Stone Burden × 0.000989632 + Stone Area × 0.001717812 + Number of Tracts × -0.304325453. The non-bleeding group had significantly lower risk scores ($P < 0.0001$, **Figure 6A**). The AUC was 0.779 for predicting bleeding (**Figure 6B**), with 71.05% specificity, 80.30% sensitivity, and 51.35% Youden's index.

Discussion

In the rapidly evolving landscape of minimally invasive surgery, Percutaneous nephrolithotomy (PCNL) has emerged as the preferred approach for treating large kidney stones [18]. Despite the potential complications associated with PCNL, such as bleeding and infection, its remarkable stone-free rate (SFR) has solidified its position as a primary treatment modality [19]. Nevertheless, the existing traditional scoring models used to assess the feasibility and potential outcomes of PCNL exhibit certain limitations that need to be addressed. These models often lack the precision to accurately predict postoperative outcomes, leaving both patients and medical practitioners with a degree of uncertainty regarding the potential success of the procedure.

The complexity of PCNL procedures, coupled with the inherent variability of patient factors, demands a more refined and tailored approach to outcome prediction. Traditional scoring models might not adequately capture the nuanced interplay of variables that contribute to the overall success of the surgery [20]. As a result, there is a pressing need for the development of new predictive models that can comprehensively incorporate a wider array of patient characteristics, stone attributes, and procedural details to provide a more accurate forecast of postoperative outcomes.

The CROES nomogram is a model generated by an algorithm utilizing multi-center patient data worldwide. This system accounts for several preoperative variables, calculating their relative weights via regression analysis to evaluate associations with stone-free rate (SFR) after PCNL [21]. However, limitations exist, for example, it excludes factors impacting outcomes such as hydronephrosis degree and stone den-

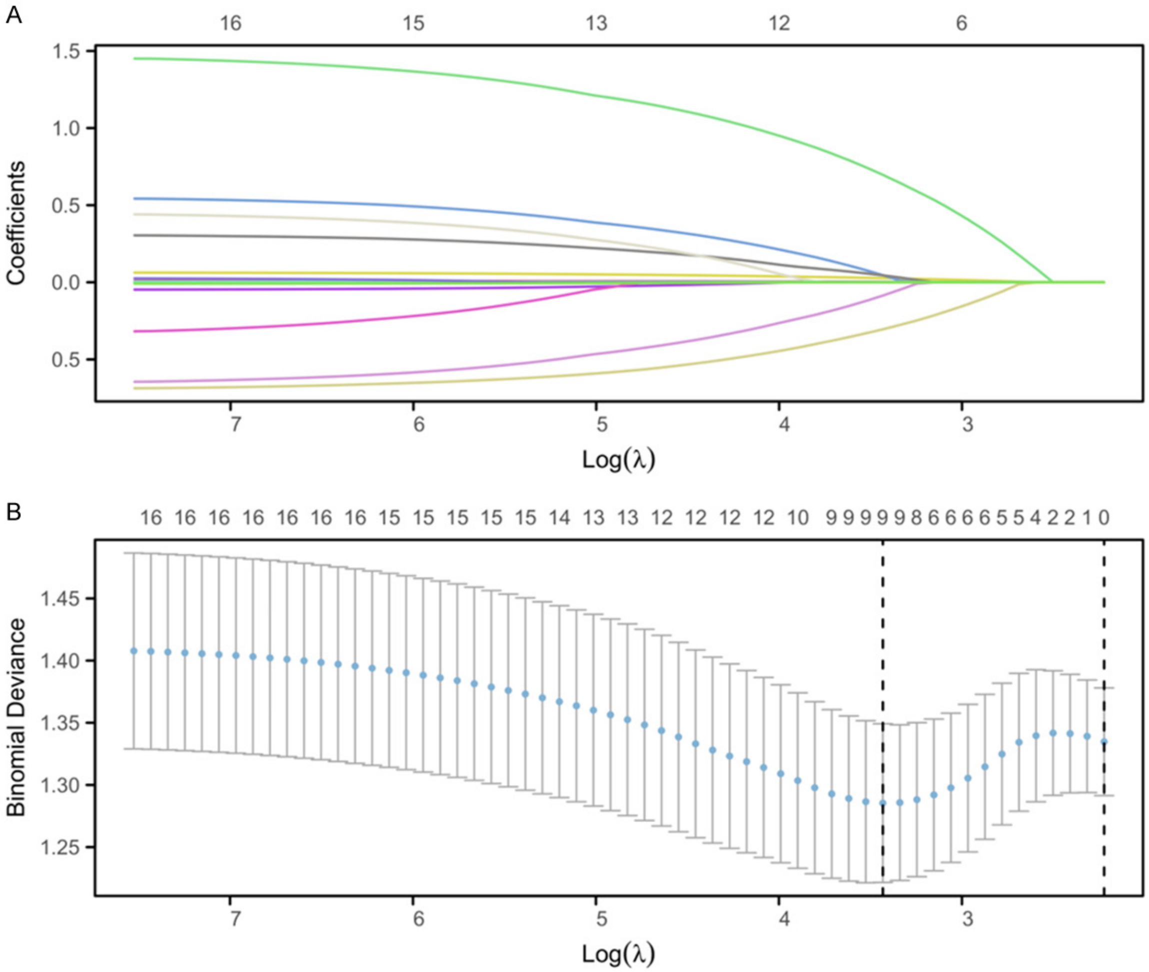


Figure 5. Risk model for the prediction of postoperative bleeding by the Lasso regression model. A, B. Coefficient distribution of LASSO regression analysis and parameter adjustment calculation (lambda) based on 10-fold cross-validation deviances.

sity. Complex calculations also hinder clinical application [22]. The S-ReSC score system is entirely based on stone distribution within the renal collecting system [20]. Similar to the Guy's stone score (GSS), the SReSC score relies on renal anatomy knowledge and stone location [23]. The CROES nomogram and S.T.O.N.E. avoid complex numerical calculations but decrease accuracy in assessing collecting system variations and complex stone morphology, neglecting other SFR-related factors [24]. While traditional regression models abide by the "one in ten rule" or EPV principle, which suggests that logistic regression models should be based on a minimum of about 10 events per explanatory variable to yield stable values, our study diverges by leveraging the Lasso regression approach. Lasso regression has distinct advantages that are particularly fitting for the challenges posed by our dataset. Specifically, it achieves variable screening by penalizing the absolute value of the regression coefficients. In contrast to ordinary logistic regression, Lasso regression does not necessitate a high sample size. It can produce robust results even when the number of events for each variable is limited. Furthermore, by employing cross-validation, Lasso regression prevents the creation of overly complex models. This makes it an ideal choice for scenarios like ours, characterized by limited sample size but numerous variables. Thus, in our context, the application of Lasso regression alleviates the need to strictly adhere to the traditional EPV rule.

Currently, research on the application of machine learning models in analyzing the postoperative outcome of kidney stones after PCNL is

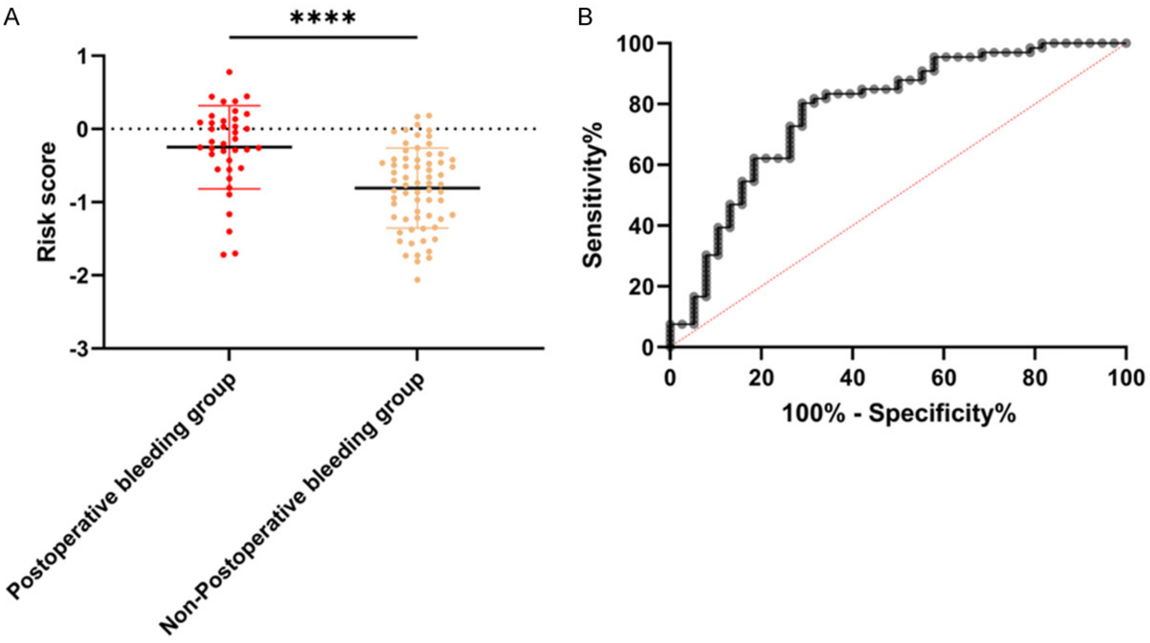


Figure 6. The level and area under the curve of risk score in predicting postoperative bleeding. A. Risk score in patients with or without postoperative bleeding. B. ROC curve of the risk score in predicting postoperative bleeding. Note: ROC, receiver operating characteristic; ****P < 0.0001.

still rare. In our study, we extracted clinical data from patients with staghorn stones, used Lasso regression to construct a risk model predicting postoperative SFR, and confirmed that the new Lasso model has stronger predictive performance than the S.T.O.N.E. score. Previous studies have applied the artificial neural network (ANN) model to predict postoperative SFR after extracorporeal shock wave lithography (ESWL) [25]. Postoperative renal injury after PCNL is mainly characterized by renal ischemia and renal injury. Postoperative renal ischemia is one of the common complications after PCNL [26]. The main mechanism is intraoperative stone extraction leading to renal parenchymal vascular embolization or compression, which may also be related to excessive intraoperative pulling of the renal hilum [27]. Severe renal ischemia can be manifested as hematuria and decreased renal function [28]. Therefore, monitoring and preventing postoperative renal ischemia is important to optimize the perioperative management of PCNL. Blood transfusion is the symptomatic treatment for postoperative bleeding, so clinicians pay great attention to the risk factors of postoperative bleeding. Traditional stone scoring systems can only predict postoperative SFR but not postoperative bleeding.

However, our developed Lasso model provides a high sensitivity of over 80% for predicting postoperative bleeding risk. As micro and ultra-micro percutaneous nephrolithotomy techniques continue to advance, more patients are opting for these less invasive surgical approaches [29, 30]. Increasing integration of machine learning models into clinical practice will enable physicians to select optimal PCNL methods based on patient factors, predict SFR using models, and adjust postoperative care accordingly [31]. Developing prediction systems that can forecast both postoperative complications and reoperation probability will play a vital role in future clinical treatment processes. In this era of medical informatics, AI technologies can integrate and analyze large-scale clinical data to select superior surgical techniques, effectively balancing surgical costs and outcomes. Big data analysis and simulation will greatly enhance the efficiency of the medical system. By combining previous results, appropriate patient treatment plans can be formulated, optimizing benefits and reducing costs. We believe our study has several key advantages: 1) Our developed software is generalizable for utilization by more clinical centers; 2) Predictive performance of the model will further improve as more data are accumulated; 3) The types of variables included can be adjusted as needed; 4) Postoperative complications can be predicted; 5) The model enables analyzing the effectiveness of different urinary stone treatments.

However, while we have established a new prediction model in this study, there are some limitations. For instance, when the Lasso algorithm analyzes a large amount of clinical data, it may find and report correlations between some clinical indicators, for example, we found in this study that a patient's history of hypertension is related to the postoperative stone clearance rate. However, these correlations may not have clinical significance. Therefore, we still need to use external databases repeatedly to verify these findings and further improve the performance of the model. Furthermore, the model derived from this study is related to the individual operation level of the surgeon performing the surgery. We can improve the wide applicability of the model by conducting multi-center studies and including more sample data. Finally, as the samples used in this study come from a single center and are limited, we need to further increase the sample size used by the Lasso model to improve the predictive effectiveness of the model.

In conclusion, we have successfully established a prediction model based on the lasso algorithm. This model can better predict the stone clearance rate and bleeding risk in patients with staghorn kidney stones after undergoing percutaneous nephrolithotomy.

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Disclosure of conflict of interest

None.

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