



# Changes of renal function after retrograde intrarenal surgery using flexible ureteroscope in renal stone patients

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**Background:** Retrograde intrarenal surgery (RIRS) is widely performed for renal stones. Theoretically, removing renal stones could prevent the deterioration of renal function. However, two studies reported that not all patients would see an increase in renal function after RIRS. The aim of our study was to evaluate the change of renal function of the operative site, and to identify predictors of improvement or deterioration of renal function after RIRS.

**Methods:** We retrospectively reviewed renal stones patients who received RIRS and single-photon emission computed tomography (SPECT) before and after surgery. Improved renal function was defined as the change of glomerular filtration rate (GFR) >10% postoperatively, and that <-10% was regarded as deteriorated renal function. Logistic and least absolute shrinkage and selection operator regression analyses were used to identify predictors for the improvement or deterioration of renal function, and predictive nomogram models were built.

**Results:** A total of 120 renal stone patients were included. Twenty-one (17.5%), 79 (65.8%) and 20 (16.7%) patients had improved, stable and deteriorated renal function of operative site after surgery, respectively. Lower alkaline phosphatase, lower low-density lipoprotein, lower GFR of the operative site, thicker renal parenchyma, higher serum creatinine, and extracorporeal shock wave lithotripsy (SWL) history were associated with the improved renal function. The predictive accuracy of the model for the improved renal function was 0.800. Additionally, older age, longer flexible ureteroscopic time, thinner renal parenchyma and existence of ureteral stones were risk factors for deteriorated renal function. The predictive accuracy of the model for the deteriorated renal function was 0.725.

**Conclusions:** The renal function of most renal stone patients did not decrease after RIRS. For patients with potential deterioration of renal function postoperatively, urologists could shorten flexible ureteroscopic time to prevent the occurrence of this outcome.

**Keywords:** Renal stones; renal function; retrograde intrarenal surgery (RIRS); predictor; nomogram model

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## Introduction

The incidence of renal stones increased rapidly worldwide and its prevalence was about 1–19% across the world during the past twenty years (1,2). The cost of renal stones was about \$3.79 billion in 2007 in the USA, and it would increase to \$4.57 billion in 2030 (3). The recurrence of renal stones occurred in about half of patients five years after lithotripsy (2). Shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS) are commonly used for removing renal stones. RIRS using flexible ureteroscope was recommended as the first choice for patients with renal stones <2 cm (4,5). RIRS was safe that a minority of patients had complications, including postoperative fever (8.5%), ureteral perforation (3.5%) and urinary tract infection (2.4%) (6).

Theoretically, removing renal stones could prevent the deterioration of renal function. However, two studies, evaluating the change of renal function after RIRS, reported that not all patients would see an increase in renal function after RIRS (7,8), which may be associated with many factors, like preoperative renal function and flexible ureteroscopic time. In addition, both of them had some limitations. A study used estimated glomerular filtration rate (eGFR), which may not reflect the realistic change of renal function of operative site after RIRS (8). Based on this, another study used single-photon emission computed tomography (SPECT) to evaluating separate renal function and identified factors associated with improvement and deterioration of renal function (7). However, these predictors were inconvenient for clinical use. Besides, this study included renal stone patients receiving PCNL or RIRS, whose impacts on renal function were not the same. At present, there is limited knowledge about the effect of RIRS on renal function of operative site. If urologists could predict the change of renal function preoperatively, they could pay more attention on the related risk factors and prevent the deterioration of renal function as far as possible. The aim of this retrospective study was to evaluate the change of renal function after RIRS using SPECT in renal stone patients, identify predictors and develop nomogram model for predicting the improvement and deterioration of renal function. We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/tau-20-1521>).

## Methods

### *Study design and patients*

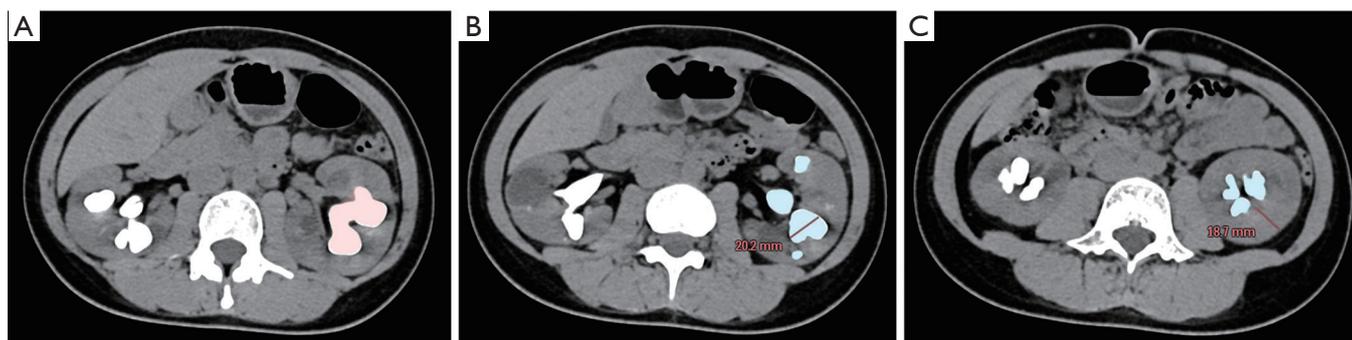
We retrospectively reviewed renal stone patients who underwent RIRS using flexible ureteroscope in West China Hospital, Sichuan University from July 2017 to June 2019. Renal stones were diagnosed by ultrasound of the urinary system or abdominal computed tomography. All these patients had unilateral stones. Patients who received SPECT before and after surgery were included in the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the West China Hospital of Sichuan University Medical Research Ethics Committee approved the study (2020508) and individual consent for this retrospective analysis was waived.

### *RIRS procedures*

All the surgeries were performed by one experienced surgeon. A 4.7 Fr double J ureteral catheter was placed two weeks before surgeries. With the patient in the lithotomic position, a 14/16 Fr ureteral access sheath was inserted into the ureter through a guidewire. Normal saline was irrigated at 160 cmH<sub>2</sub>O and 0.1 L/min by pressure pumps. Stones were fragmented using a 200 μm laser fiber with holmium laser. Pulse energy and frequency for fragmenting stones were 1.5 J and 20 Hz. Fragments >2 mm were extracted using a nitinol basket. The remaining fragments was dusted when laser was set as 0.8 J and 30 Hz. A 4.7 Fr double J ureteral catheter was again applied at the end of the surgery, and were removed 2–3 weeks later.

### *Data collection*

All patients received SPECT examination 12 months after surgeries. The primary outcome was the change of renal function of the operative site, which was evaluated by SPECT using <sup>99m</sup>Tc-DTPA or <sup>99m</sup>Tc-DMSA. To compare the results of this study with that reported by Piao *et al.* (7), we adopted the definition of the improvement and deterioration of renal function. Improved renal function was defined as glomerular filtration rate (GFR) [operative site-contralateral site (postoperative)] – [operative site-contralateral site (preoperative)] >10%, and that <-10%



**Figure 1** Segmentations of kidney on computed tomography in a renal stone patient. (A) Drawing an outline of renal stone in one segmentation and calculating its volume. (B) Calculating the maximal renal stone size of renal stone. (C) Calculating the renal parenchymal thickness.

was regarded as deteriorated renal function. The remaining patients were categorized into stable renal function group.

Preoperative factors associated with the change of renal function included demographic characteristics, disease history, operation data, laboratory data and imaging data. General characteristics were age, gender, body mass index (BMI) and history of smoking and drinking. Disease history mainly included diabetes mellitus, hypertension, hyperuricemia or gout and renal tubular acidosis. Operation data included the history of nephrolithotomy and flexible ureteroscopic time, which was defined as the time when endoscopy was inserted into the urethra. Apart from GFR, we also collected the following data, including renal parenchymal thickness, existence of hydronephrosis, ureteral stone and ureterostenosis, renal stone volume and maximal renal stone size. These data could be measures using IntelliSpace Discovery platform (Philips) (9). The schematic diagram of measuring renal stone volume, maximal renal stone size and renal parenchymal thickness were shown in *Figure 1*.

### Statistical analysis

Mean and standard deviation were calculated for quantitative factors when they were symmetrically distributed, they were presented as mean and standard deviation, and analyzed using analysis of variance (ANOVA). Otherwise, they were shown as median and interquartile range, and compared by Kruskal-Wallis test. Categorical factors were presented as quantity and percentage, and analyzed using Chi-square

test or Fisher's Exact test. We used logistic regression analysis and least absolute shrinkage and selection operator (LASSO) regression analysis to find factors associated with the improvement and deterioration of renal function, and two models for predicting the change of renal function after RIRS were also built. Nomograms of models were drawn. The sensitivity, specificity and predictive accuracy of the models were calculated. All the statistical analyses were conducted using R (version 3.6.3). P value <0.05 was considered as significantly different.

## Results

### Characteristics of patients and stones

A total of 120 patients were included in the study. About 21 (17.5%), 79 (65.8%) and 20 (16.7%) patients had improved, stable and deteriorated renal function of operative site postoperatively, respectively. The mean age was  $47.4 \pm 11.7$  years, and about two-thirds of patients were males. Half of the patients had received surgeries for removing renal stones, including SWL, RIRS, PCNL and open nephrolithotomy, with no significant difference between three groups ( $P=0.559$ ). Based on GFR of the operative site, 40.0% patients had mild renal impairment, followed by moderate renal impairment (28.3%), normal renal function (21.7%) and severe renal impairment (10.0%), and GFR grade was statistically different between three groups ( $P=0.046$ ). About half of the patients had ureteral stone or ureterostenosis. The median renal stone volume was  $1.80 \text{ cm}^3$  (*Table 1*).

**Table 1** Characteristics of patients and stones

Variable	Total (n=120)	Improved (n=21)	Stable (n=79)	Deteriorated (n=20)	P value
Demographic characteristics					
Age (year) <sup>†</sup>	47.4 (11.7)	46.9 (9.9)	46.4 (12.1)	51.5 (11.4)	0.219
Gender (male) <sup>§</sup>	81 (67.5%)	11 (52.4%)	57 (72.2%)	13 (65.0%)	0.22
BMI (kg/m <sup>2</sup> ) <sup>†</sup>	24.60 (3.73)	23.81 (3.22)	24.57 (4.08)	25.08 (2.86)	0.52
Smoking (yes) <sup>§</sup>	36 (30.0%)	4 (19.0%)	24 (30.4%)	8 (40.0%)	0.34
Drinking (yes) <sup>§</sup>	28 (23.3%)	3 (14.3%)	20 (25.3%)	5 (25.0%)	0.558
Disease history					
Diabetes mellitus (yes) <sup>§</sup>	9 (7.5%)	0 (0.0%)	7 (8.9%)	2 (10.0%)	0.351
Hypertension (yes) <sup>§</sup>	32 (26.7%)	8 (38.5%)	17 (21.5%)	7 (35.0%)	0.204
Hyperuricemia/Gout (yes) <sup>§</sup>	38 (31.7%)	6 (28.6%)	26 (32.9%)	6 (30.0%)	0.916
Renal tubular acidosis (yes) <sup>§</sup>	2 (1.7%)	1 (4.8%)	0 (0.0%)	1 (5.0%)	0.141
Operation data					
SWL history (yes) <sup>§</sup>	30 (25.0%)	9 (42.9%)	15 (19.0%)	6 (30.0%)	0.069
RIRS history (yes) <sup>§</sup>	20 (16.7%)	2 (9.5%)	13 (16.5%)	5 (25.0%)	0.412
PCNL history (yes) <sup>§</sup>	15 (12.5%)	2 (9.5%)	12 (15.2%)	1 (5.0%)	0.423
Open nephrolithotomy history (yes) <sup>§</sup>	12 (10.0%)	1 (4.8%)	9 (11.4%)	2 (10.0%)	0.667
nephrolithotomy history (yes) <sup>§</sup>	60 (50.0%)	11 (52.4%)	37 (46.8%)	12 (60.0%)	0.559
Flexible ureteroscopic time (min) <sup>†</sup>	26.80 (24.65)	26.10 (22.45)	24.30 (24.80)	34.05 (40.90)	0.214
Laboratory data					
RBC (10 <sup>12</sup> /L) <sup>†</sup>	4.63 (0.54)	4.40 (0.59)	4.72 (0.54)	4.53 (0.46)	0.037
Hemoglobin (g/L) <sup>†</sup>	136.80 (17.89)	132.67 (16.87)	137.96 (18.71)	136.55 (15.63)	0.487
ALP (IU/L) <sup>†</sup>	80.79 (22.10)	70.38 (17.93)	83.92 (23.44)	79.35 (17.41)	0.041
Serum uric acid (μmol/L) <sup>†</sup>	379.11 (88.94)	367.10 (96.43)	381.75 (87.82)	381.30 (88.86)	0.795
Serum creatinine (μmol/L) <sup>†</sup>	83.80 (30.75)	87.00 (37.50)	83.10 (26.60)	89.90 (35.25)	0.451
LDL (mmol/L) <sup>†</sup>	2.61 (0.75)	2.27 (0.66)	2.73 (0.72)	2.47 (0.82)	0.026
Triglyceride (mmol/L) <sup>†</sup>	1.66 (1.30)	1.52 (2.99)	1.59 (1.27)	1.93 (1.60)	0.145
Cholesterol (mmol/L) <sup>†</sup>	4.50 (0.88)	4.37 (0.71)	4.53 (0.91)	4.51 (0.91)	0.765
HDL (mmol/L) <sup>†</sup>	1.14 (0.37)	1.21 (0.43)	1.14 (0.35)	1.10 (0.55)	0.532
Imaging data					
GFR of operative site (mL/min) <sup>†</sup>	33.47 (14.60)	26.92 (9.96)	36.01 (14.80)	30.34 (15.71)	0.022
GFR of operative site <sup>§</sup>					0.046
Severe renal impairment (<15 mL/min)	12 (10.0%)	2 (9.5%)	6 (7.6%)	4 (20.0%)	
Moderate renal impairment (15–30 mL/min)	34 (28.3%)	10 (47.6%)	19 (24.1%)	5 (25.0%)	
Mild renal impairment (30–45 mL/min)	48 (40.0%)	9 (42.9%)	31 (39.2%)	8 (40.0%)	
Normal renal function (>45 mL/min)	26 (21.7%)	0 (0.0%)	23 (29.1%)	3 (15.0%)	

**Table 1** (continued)

Table 1 (continued)

Variable	Total (n=120)	Improved (n=21)	Stable (n=79)	Deteriorated (n=20)	P value
Renal parenchymal thickness (mm) <sup>†</sup>	21.60 (5.28)	23.63 (5.63)	21.66 (5.18)	19.25 (4.51)	0.027
Hydronephrosis (yes) <sup>§</sup>	91 (75.8%)	18 (85.7%)	59 (74.7%)	14 (70.0%)	0.461
Ureteral stone (yes) <sup>§</sup>	45 (37.5%)	8 (38.1%)	34 (43.0%)	3 (15.0%)	0.069
Ureterostenosis (yes) <sup>§</sup>	44 (36.7%)	7 (33.3%)	30 (38.0%)	7 (35.0%)	0.913
Ureteral stone or ureterostenosis (yes) <sup>§</sup>	62 (51.7%)	9 (42.9%)	46 (58.2%)	7 (35.0%)	0.120
Renal stone volume (cm <sup>3</sup> ) <sup>‡</sup>	1.80 (3.46)	2.02 (3.94)	1.75 (3.14)	2.46 (4.69)	0.188
Maximal renal stone size (mm) <sup>‡</sup>	13.7 (11.0)	10.8 (11.5)	12.8 (11.3)	15.7 (8.1)	0.162

<sup>†</sup>, data were presented as mean (standard deviation), and were analyzed with analysis of variance (ANOVA); <sup>‡</sup>, data were presented as median (interquartile range), and were analyzed with Kruskal-Wallis test; <sup>§</sup>, data were presented as quantity (percentage), and were analyzed with Chi-square test or Fisher's Exact test. BMI, body mass index; SWL, shock wave lithotripsy; RIRS, retrograde intrarenal surgery; PCNL, percutaneous nephrolithotomy; RBC, red blood cell; ALP, alkaline phosphatase; LDL, low density lipoprotein; HDL, high density lipoprotein; GFR, glomerular filtration rate.

#### ***Predictors for the improved renal function after RIRS and predictive model***

We firstly performed univariate logistic regression analysis and then selected factors with P value <0.100 for multivariate logistic regression analysis. It showed that lower alkaline phosphatase (ALP), lower low-density lipoprotein (LDL), lower GFR of the operative site, thicker renal parenchymal, higher serum creatinine and SWL history were predictors for the improved renal function of the operative site after RIRS (P<0.050) (Table 2). Apart from these factors, LASSO regression analysis also showed that BMI and HDL were associated with improvement of renal function (Figure 2A,B).

Due to the limitation of sample size, we only selected six factors both occurred in logistic and LASSO regression analyses to build a model for predicting the improvement of renal function, including SWL history, ALP, GFR of the operative site, LDL, renal parenchymal thickness and serum creatinine. The area under the curve (AUC) of receiver operating characteristic (ROC) was 0.798 (Figure 2C). We also performed an internal four-fold cross-validation for 1000 times, and the mean AUC of ROC was 0.730 (95% CI, 0.728–0.732). To decrease misprediction rate to supervise patients' follow-up, the cut-off value of probability of improved renal function was set as 0.256, and the sensitivity and specificity were 0.667 and 0.828 respectively, with the predictive accuracy of 0.800. To visualize the predictive model, a nomogram was drawn (Figure 2D). Hodges-Lehmann test showed that there was

no mismatch between predictive model and retrospective cohort ( $\chi^2=8.473$ , P=0.389).

#### ***Predictors for the deteriorated renal function after RIRS and predictive model***

Similarly, univariate logistic regression analysis showed that older age, larger renal stone size, longer flexible ureteroscopic time, thinner renal parenchyma and existence of ureteral stones were risk factors for deteriorated renal function after RIRS (P<0.100). The last three factors were still statistically different in multivariate logistic regression analysis (P<0.050) (Table 3). In addition, LASSO regression analysis screened out factors associated with the deterioration of renal function, including age, endoscopic time and renal parenchymal thickness (Figure 3A,B).

A predictive model for deteriorated renal function was developed based on four factors both occurred in logistic and LASSO regression analyses, including age, renal parenchymal thickness, endoscopic time and ureteral stone. The AUC of ROC was 0.807 (Figure 3C). After 1,000 times cross validation, it was 0.745 (95% CI, 0.743–0.748). When the cut-off value of probability of deteriorated renal function was 0.162, the sensitivity (0.800) and specificity (0.710) were high. The predictive accuracy was 0.725. The predictive nomogram was also demonstrated (Figure 3D). Hodges-Lehmann test indicated that indicated that the predictive accuracy of the nomogram model was good ( $\chi^2=3.977$ , P=0.859).

**Table 2** Factors associated with the improved renal function of operative site after retrograde intrarenal surgery

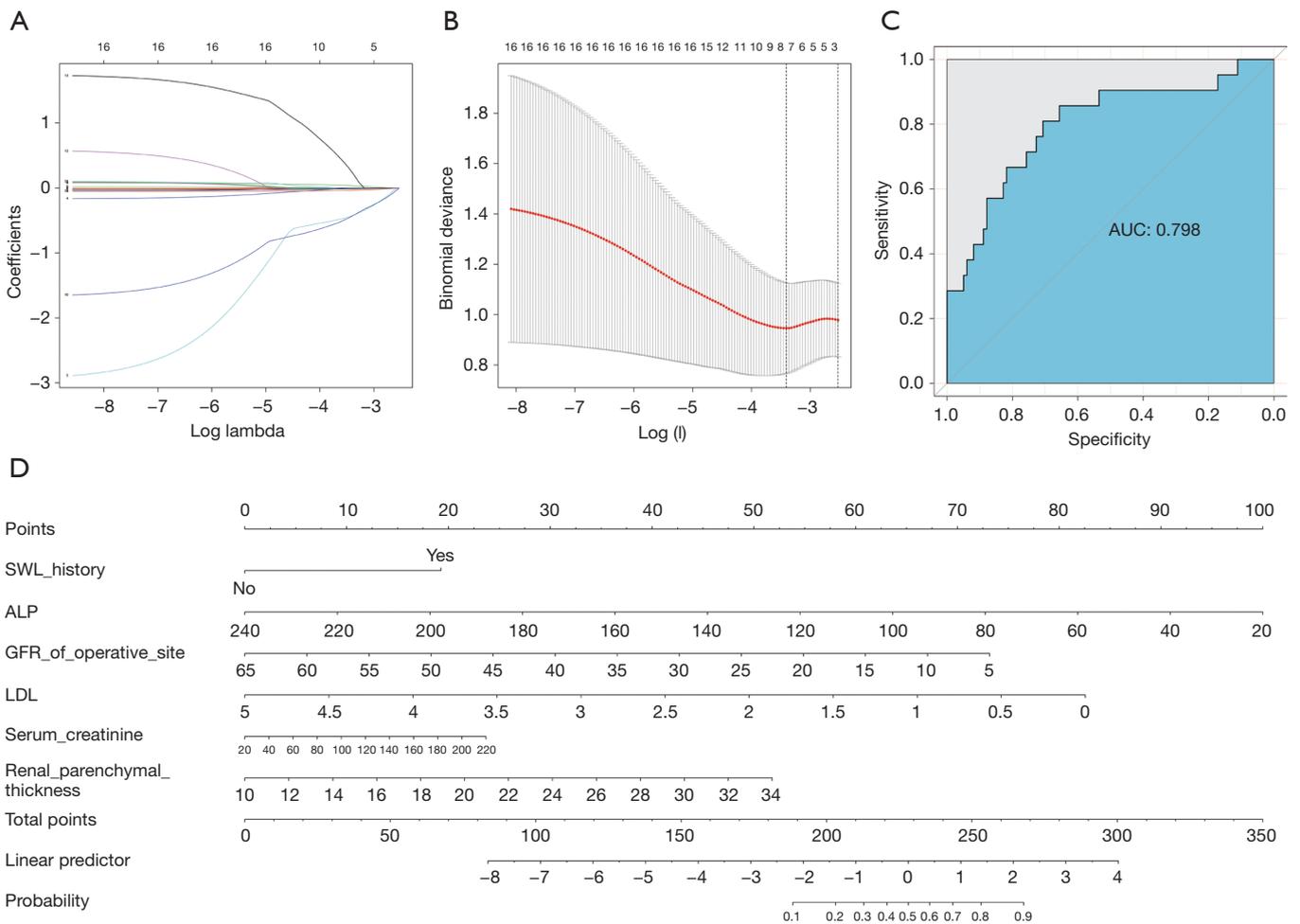
Variable	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Demographic characteristics				
Age (year)	1.004 (0.964–1.045)	0.857		
Gender (male)	0.456 (0.175–1.190)	0.108		
BMI (kg/m <sup>2</sup> )	1.118 (0.937–1.333)	0.216		
Smoking (yes)	2.030 (0.631–6.526)	0.235		
Drinking (yes)	2.027 (0.550–7.465)	0.288		
Disease history				
Diabetes mellitus (yes)	1.001 (0.376–2.665)	0.999		
Hypertension (yes)	0.520 (0.193–1.404)	0.197		
Hyperuricemia/Gout (yes)	1.194 (0.424–3.365)	0.737		
Renal tubular acidosis (yes)	0.204 (0.012–3.401)	0.268		
Operation data				
SWL history (yes)	0.359 (0.133–0.966)	0.042	0.321 (0.116–0.891)	0.029
RIRS history (yes)	2.111 (0.451–9.886)	0.343		
PCNL history (yes)	1.436 (0.299–6.899)	0.651		
Open nephrolithotomy history (yes)	2.500 (0.305–20.495)	0.393		
nephrolithotomy history (yes)	0.891 (0.347–2.287)	0.810		
Flexible ureteroscopic time (min)	1.002 (0.978–1.028)	0.848		
Laboratory data				
RBC (10 <sup>12</sup> /L)	2.602 (1.070–6.327)	0.035	2.381(0.800–7.086)	0.119
Hemoglobin (g/L)	1.015 (0.990–1.042)	0.246		
ALP (IU/L)	1.032 (1.005–1.059)	0.021	1.033 (1.005–1.062)	0.019
Serum uric acid (μmol/L)	1.002 (0.997–1.007)	0.495		
Serum creatinine (μmol/L)	0.985 (0.968–1.001)	0.071	0.975 (0.957–0.994)	0.011
LDL (mmol/L)	2.211 (1.103–4.429)	0.025	2.212 (1.082–4.522)	0.030
Triglyceride (mmol/L)	0.807 (0.603–1.080)	0.148		
Cholesterol (mmol/L)	1.225 (0.711–2.109)	0.465		
HDL (mmol/L)	0.507 (0.105–2.457)	0.399		
Imaging data				
GFR of operative site (mL/min)	1.042 (1.005–1.080)	0.026	1.043 (1.005–1.082)	0.026
Renal parenchymal thickness (mm)	0.909 (0.824–1.002)	0.056	0.903 (0.817–0.998)	0.049
Hydronephrosis (yes)	0.468 (0.127–1.720)	0.253		
Ureteral stone (yes)	0.970 (0.368–2.559)	0.951		
Ureterostenosis (yes)	1.194 (0.442–3.226)	0.727		

**Table 2** (continued)

Table 2 (continued)

Variable	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Ureteral stone or ureterostenosis (yes)	1.536 (0.594–3.973)	0.376		
Renal stone volume (cm <sup>3</sup> )	0.989 (0.902–1.084)	0.814		
Maximal renal stone size (mm)	1.022 (0.966–1.081)	0.444		

BMI, body mass index; SWL, shock wave lithotripsy; RIRS, retrograde intrarenal surgery; PCNL, percutaneous nephrolithotomy; RBC, red blood cell; ALP, alkaline phosphatase; LDL, low density lipoprotein; HDL, high density lipoprotein; GFR, glomerular filtration rate; OR, odds ratio; CI, confidence intervals.



**Figure 2** Predictive model for predicting the improved renal function after retrograde intrarenal surgery using flexible ureteroscope. (A) LASSO coefficient profiles of all the characteristics of patients and stones. (B) Identification of the optimal penalization coefficient Lambda in the LASSO model with 10-fold cross validation via minimum criteria. (C) Receiver operating characteristic curve of predictive model. (D) The nomogram of predictive model. LASSO, least absolute shrinkage and selection operator.

**Table 3** Factors associated with the deteriorated renal function of operative site after retrograde intrarenal surgery

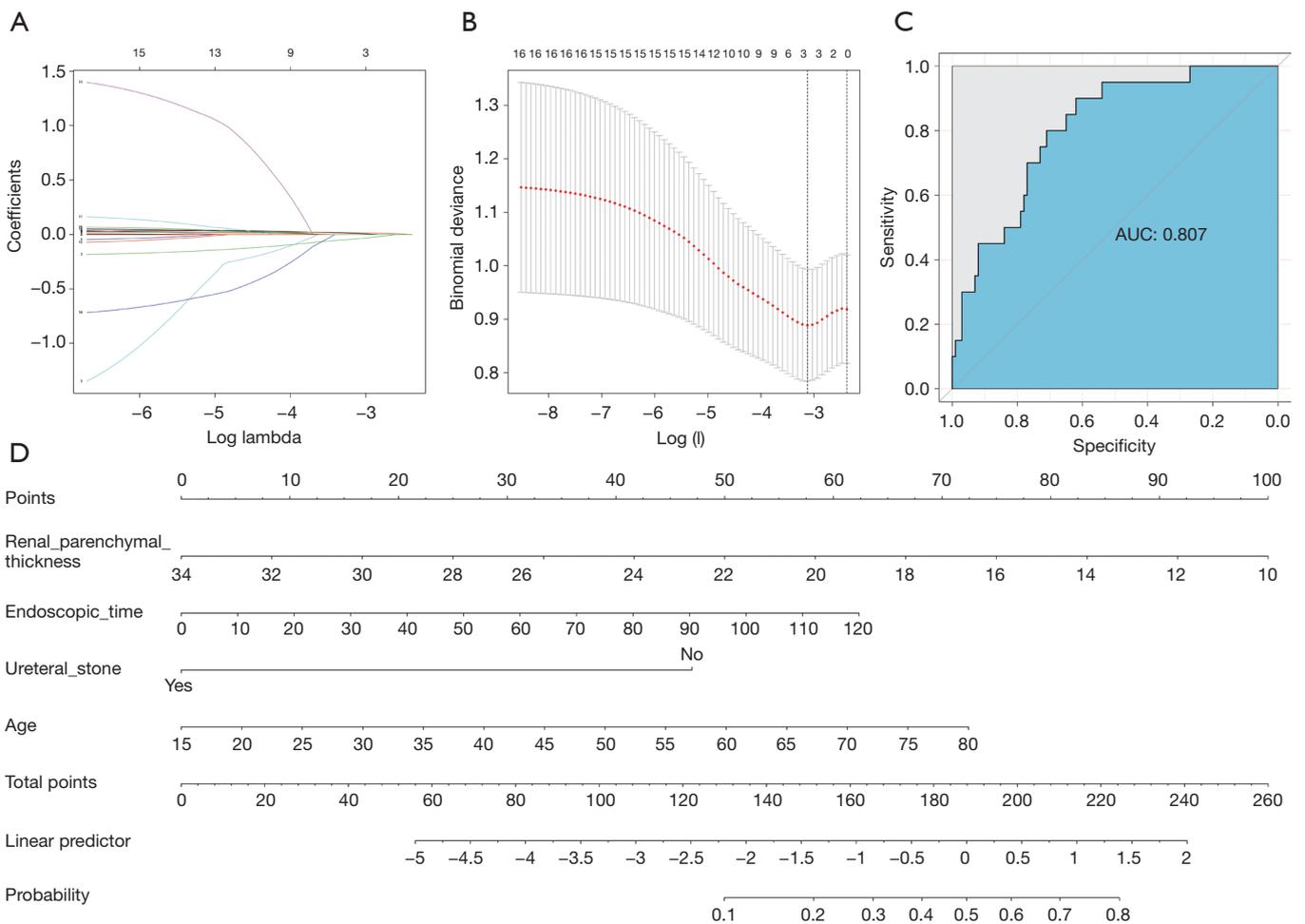
Variable	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Demographic characteristics				
Age (year)	1.041 (0.994–1.089)	0.086	1.041 (0.995–1.090)	0.082
Gender (male)	1.144 (0.417–3.143)	0.794		
BMI (kg/m <sup>2</sup> )	0.970 (0.816–1.152)	0.726		
Smoking (yes)	1.714 (0.634–4.639)	0.289		
Drinking (yes)	1.116 (0.366–3.400)	0.847		
Disease history				
Diabetes mellitus (yes)	1.476 (0.283–7.691)	0.644		
Hypertension (yes)	1.615 (0.580–4.499)	0.359		
Hyperuricemia/Gout (yes)	0.911 (0.320–2.588)	0.861		
Renal tubular acidosis (yes)	5.211 (0.312–86.975)	0.250		
Operation data				
SWL history (yes)	1.357 (0.470–3.920)	0.573		
RIRS history (yes)	1.889 (0.597–5.974)	0.279		
PCNL history (yes)	0.323 (0.040–2.611)	0.289		
Open nephrolithotomy history (yes)	1.000 (0.202–4.955)	1.000		
nephrolithotomy history (yes)	1.625 (0.612–4.316)	0.330		
Flexible ureteroscopic time (min)	1.031 (1.007–1.055)	0.012	1.033 (1.008–1.058)	0.008
Laboratory data				
RBC (10 <sup>12</sup> /L)	0.667 (0.277–1.064)	0.365		
Hemoglobin (g/L)	0.999 (0.973–1.026)	0.945		
ALP (IU/L)	0.996 (0.975–1.019)	0.749		
Serum uric acid (μmol/L)	1.000 (0.995–1.006)	0.904		
Serum creatinine (μmol/L)	1.007 (0.990–1.025)	0.412		
LDL (mmol/L)	0.738 (0.382–1.425)	0.365		
Triglyceride (mmol/L)	1.071 (0.814–1.409)	0.624		
Cholesterol (mmol/L)	1.011 (0.583–1.753)	0.969		
HDL (mmol/L)	1.747 (0.349–8.750)	0.497		
Imaging data				
GFR of operative site (mL/min)	0.982 (0.949–1.016)	0.293		
Renal parenchymal thickness (mm)	0.902 (0.820–0.991)	0.032	0.901 (0.817–0.992)	0.035
Hydronephrosis (yes)	0.697 (0.241–2.019)	0.506		
Ureteral stone (yes)	4.103 (1.130–14.907)	0.032	4.284 (1.165–15.749)	0.029
Ureterostenosis (yes)	0.917 (0.336–2.504)	0.865		

Table 3 (continued)

Table 3 (continued)

Variable	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Ureteral stone or ureterostenosis (yes)	0.441 (0.162–1.197)	0.108		
Renal stone volume (cm <sup>3</sup> )	1.038 (0.954–1.130)	0.384		
Maximal renal stone size (mm)	1.047 (0.992–1.105)	0.093	1.051 (0.994–1.111)	0.083

BMI, body mass index; SWL, shock wave lithotripsy; RIRS, retrograde intrarenal surgery; PCNL, percutaneous nephrolithotomy; RBC, red blood cell; ALP, alkaline phosphatase; LDL, low density lipoprotein; HDL, high density lipoprotein; GFR, glomerular filtration rate; OR, odds ratio; CI, confidence intervals.



**Figure 3** Predictive model for predicting the deteriorated renal function after retrograde intrarenal surgery using flexible ureteroscope. (A) LASSO coefficient profiles of all the characteristics of patients and stones. (B) Identification of the optimal penalization coefficient Lambda in the LASSO model with 10-fold cross validation via minimum criteria. (C) Receiver operating characteristic curve of predictive model. (D) The nomogram of predictive model. LASSO, least absolute shrinkage and selection operator.

## Discussion

In the study, we used SPECT to evaluate the change of renal function after RIRS and found that the improvement and deterioration of renal function of operative site occurred in 17.5% and 16.7% of patients, which were slightly different from the previous studies (7,8). Piao *et al.* reported that the increase and decrease of renal function of operative site were seen in 58.5% and 5.7% of renal stone patients after surgery respectively (7). The examination of separate renal function and definition of its change were the same in this study and ours. The reason for higher deteriorated rate and lower improved rate in our study may be that most renal stone patients in our study had already received nephrolithotomy previously, like SWL, PCNL and RIRS. Another study found that the deterioration of renal function only occurred in 4.9% patients after surgery, which was lower than that of our study (8). This study used eGFR to evaluate renal function. When the contralateral normal kidney still had compensatory potency, eGFR may not change significantly even though renal function of operative site decreased slightly postoperatively.

SWL history was positively correlated with the improvement of renal function. Fayad *et al.* reported that there was no statistically significant change in GFR six months after SWL using SPECT (10). Removing renal stones using SWL delayed the deterioration of renal function in patients with nephrolithiasis (11). All these evidences verified the benefits of SWL for renal function. In addition, we found that higher ALP may prevent the improvement of renal function. ALP, an enzyme hydrolyzing pyrophosphate (a vascular calcification inhibitor), could promote heterotopic calcification (12). Thus, elevated ALP may be associated with the recurrence of renal stones, leading to further renal deterioration. We also found that LDL was low in patients with improved renal function. Jiang *et al.* reported that high baseline LDL was associated with a more significant decrease in eGFR (13). The patients with LDL <2.6 mmol/L showed less progression of chronic renal disease than those with higher LDL (14). Interestingly, we found that thicker renal parenchyma promoted the improvement of renal function, while higher GFR of operative site and low serum creatinine may prevent this process. This result was not unexpectedly, because these kidneys with deteriorated function had space to improve, especially when the renal morphology was not affected. This phenomenon also occurred in the study of Piao *et al.* which reported that more than half of patients

with abnormal separate renal function before surgery had improved renal function postoperatively (7). Nordenström *et al.* found that low baseline renal function was a predictor of improvement of renal function in infants and children after surgery for ureteropelvic junction obstruction (15).

When it comes to deterioration of renal function after RIRS, we found that longer flexible ureteroscopy time, existence of ureteral stones and thinner renal parenchyma may be pivotal risk factors. Lane *et al.* also reported that prolonged ureteroscopy time was associated with increased complication rates (16). During flexible ureteroscopy, normal saline was continuously injected into the pelvis, which increased the intrarenal pressure. Existence of ureteral stones prevented the urine from flowing smoothly, and the urine collected in the renal pelvis, followed by increasing pressure. Excessive pressure leads to renal pelvis and tubular expansion and interstitial cellular infiltration, which induced production of inflammatory cytokines and oxidative stress, followed by tubular cell apoptosis, interstitial fibrosis, nephron loss, thinner renal parenchyma and final deteriorated renal function (17-19).

Compared with previous studies, we built models with high predictive accuracy for predicting the improvement and deterioration of renal function after RIRS. Using these models, urologists could screen out patients whose renal function are more likely to decrease postoperatively and gave some suggestions on how to prevent the recurrent renal stones, like sufficient drinking water (>2,500 mL/day), less salt and protein intake, more fruits intake rich in citrate and more exercise. Frequent urinary ultrasonography was also important during the follow-up to supervise renal stones and hydronephrosis as it was easy to perform without any radiation. Additionally, urologists could communicate with these patients about the renal function deterioration after surgery to reduce potential medical disputes and improve physician-patient relationships.

The study had several advantages and features. First, SPECT was used to precisely measure the renal function of operative site. Second, renal stone volume was accurately measured using IntelliSpace Discovery platform (Philips), which was firstly applied for studying renal stones. Third, we developed models for predicting the change of renal function after RIRS, which may support clinical decision-making.

However, there were also some limitations that could not be neglected. First, the sample size was relatively small. Some patients did not routinely receive urinary

ultrasonography postoperatively in our hospital, which resulted in the loss of follow-up of renal stone patients. Second, about a third of renal stone patients were accompanied with ureteral stones. Theoretically, ureteral stones would induce hydronephrosis, followed by the decrease of renal function. We should have evaluated the change of renal function of renal stone patients with or without ureteral stones separately. However, due to the small sample size, there may be biases when performing this subgroup analysis. More studies with large sample size are needed to tackle this problem.

## Conclusions

the renal function of most renal stone patients did not decrease after RIRS. For patients with potential deterioration of renal function postoperatively, urologists could shorten flexible ureteroscopic time to prevent the occurrence of this outcome.

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## Footnote

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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 approved by the West China Hospital of Sichuan University Medical Research Ethics Committee approved the study (2020508) and individual consent for this retrospective analysis was waived.

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