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Original Article

Predictive model of systemic inflammatory response syndrome after percutaneous nephrolithotomy for kidney calculi based on logistic regression

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Abstract: Objective: To establish a predictive model of systemic inflammatory response syndrome (SIRS) after percutaneous nephrolithotomy (PCNL) for kidney calculi based on logistic regression. Methods: The data of 148 patients with unilateral kidney calculi treated in Xi'an International Medical Center Hospital from October 2019 to September 2022 were analyzed retrospectively. According to development of SIRS after PCNL, the patients were divided into one group with SIRS after operation (occurrence group, n = 19) and another group without SIRS after operation (non-occurrence group, n = 129). The clinical data of patients were collected, and risk factors for SIRS after PCNL in patients with unilateral kidney calculi were analyzed by logistic regression. Results: Gender, body mass index (BMI), hypertension, diabetes mellitus (DM), calculi size ≥ 30 mm, renal insufficiency, and hydronephrosis were risk factors for postoperative SIRS ($P < 0.05$). According to multivariate logistic regression analysis, BMI, DM, hypertension, calculi size ≥ 30 mm, and hydronephrosis were independent risk factors for SIRS ($P < 0.05$). Based on the regression coefficient, a predictive model was established. The occurrence group had a higher risk score than the non-occurrence group ($P < 0.05$). According to receiver operating characteristic (ROC) curve-based analysis, the area under the curve of risk score for predicting SIRS in patients was 0.898. Conclusion: Patients with BMI ≥ 25 kg/m^2, DM, hypertension, calculi ≥ 30 mm, and/or hydronephrosis are more likely to suffer SIRS after PCNL. The risk score has high clinical value in the prediction of SIRS.

Keywords: Logistic regression, percutaneous nephroscope, kidney calculi, systemic inflammatory response syndrome, predictive model

Introduction

Urinary calculi can be classified into kidney calculi, ureteral calculi, bladder calculi and urethral calculi according to their anatomic location.Kidney calculi are the most common type in clinical practice [1]. Kidney calculi are deposits of hard minerals that form in the kidney and give rise to pain and discomfort when they pass through the urethra [2]. With various sizes and shapes, kidney calculi can be composed of different types of minerals, including calcium, uric acid, and cystine [3]. Moreover, people with a family history of kidney calculi and those with gout, obesity, or inflammatory bowel disease face a higher risk of kidney calculi [4, 5].

Various treatment methods are available for kidney calculi, and an appropriate treatment scheme can be adopted according to the location and size of calculi and the curative effect on previous calculi, among which surgery is an important means for clinical treatment [6, 7]. Percutaneous nephrolithotripsy (PCNL) is used to remove large or complex kidney calculi that cannot be treated by other non-invasive methods including shock wave lithotripsy or ureteroscopy [8]. PCNL possesses a series of advantages, such as percutaneous access to calices renales, large operation space, high calculi removal efficiency, relatively low cost, non-tendency of causing renal contusion and laceration, and convenience in secondary treatment

of calculi [9]. PCNL is generally considered a safe and effective option for the treatment of large/complex kidney calculi, but like any surgical procedure, it does have some risks, such as bleeding, infection or damage to surrounding organs [10].

PCNL is a surgical procedure to remove large or complicated kidney calculi [11]. Despite being a relatively safe and effective treatment, it also brings a risk for complications, including the development of systemic inflammatory response syndrome (SIRS) [12]. SIRS is a response of the body to a class of biologically active cytokines or inflammatory mediators (chemical factors) formed by immune cells (monocytes, T cells, B cells, macrophages) and specific non-immune cells (fibroblasts, endothelial cells) [13]. SIRS signs may be the result of the body's inflammatory response to surgery, which probably triggers extensive inflammation and tissue damage [14]. Patients with a history of infection or other diseases impacting the immune system face an increased risk of SIRS after PCNL [15].

In recent years, with the gradual increase in PCNL cases, the incidence of SIRS is also increasing year by year. In this study, we constructed a predictive model for SIRS after PCNL by logistic regression for the first time, which provides a new outcome measure for clinical SIRS prediction.

Materials and methods

Data sources and study subjects

The data of 281 patients with unilateral kidney calculi treated in Xi'an International Medical Center Hospital from October 2019 to September 2022 were analyzed retrospectively.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients with unilateral kidney calculi; (2) Patients who met the indications for PCNL and received surgery only with the standard single channel (F24); (3) Patients who had no obvious surgical contraindications after preoperative examination, or could tolerate medical treatment; (4) Patients who were operated by the same doctor; (5) Patients with complete clinical data; (6) Patients diagnosed with SIRS within 7 d after surgery.

Exclusion criteria: (1) Patients whose preoperative white blood cells (WBC) > 12 * 10^9 cells/L or < 4 * 10^9 cells/L; (2) Patients with preoperative basal body temperature > 38°C or < 36°C and basal heart rate > 90 beats/min; (3) Patients with long-term use of oral immunosuppressants, with hematologic diseases or a history of cancer; (4) Patients who had received phase II PCNL.

Diagnostic criteria for SIRS

(1) Heart rate (P) > 90 beats/min; (2) Body temperature (T) > 38°C or < 36°C; (3) Shortness of breath, respiratory rate > 20 beats/min, or hyperventilation, arterial blood gas $PaCO_2$ < 232 mm Hg; (4) WBC > 12 * 10^9 cells/L or < 4 * 10^9 cells/L, or immature granulocytes > 10%. A patient who meets any two or more of the above criteria is diagnosed with SIRS [16].

Sample screening

According to the inclusion and exclusion criteria, we selected a total of 148 patients with unilateral renal calculi. This study was carried out with the permission of the Medical Ethics Committee of Xi'an International Medical Center Hospital. We have drawn a flow chart (**Figure 1**) of the methods of this research.

Clinical data collection

The clinical data collected from the hospital information system in Xi'an International Medical Center Hospital included age, gender, past medical history, history of smoking, history of alcoholism, kidney calculi size, degree of hydronephrosis, and body mass index (BMI), operation time and postoperative blood transfusion.

Outcome measures

Primary outcome measures: Logistic regression was conducted to analyze the risk factors for SIRS after PCNL.

Secondary outcome measures: A risk model for predicting SIRS was constructed based on logistic regression coefficient. With the variables selected based on multivariate logistic regression (MLR) analysis, a nomogram risk model of SIRS after PCNL was constructed.

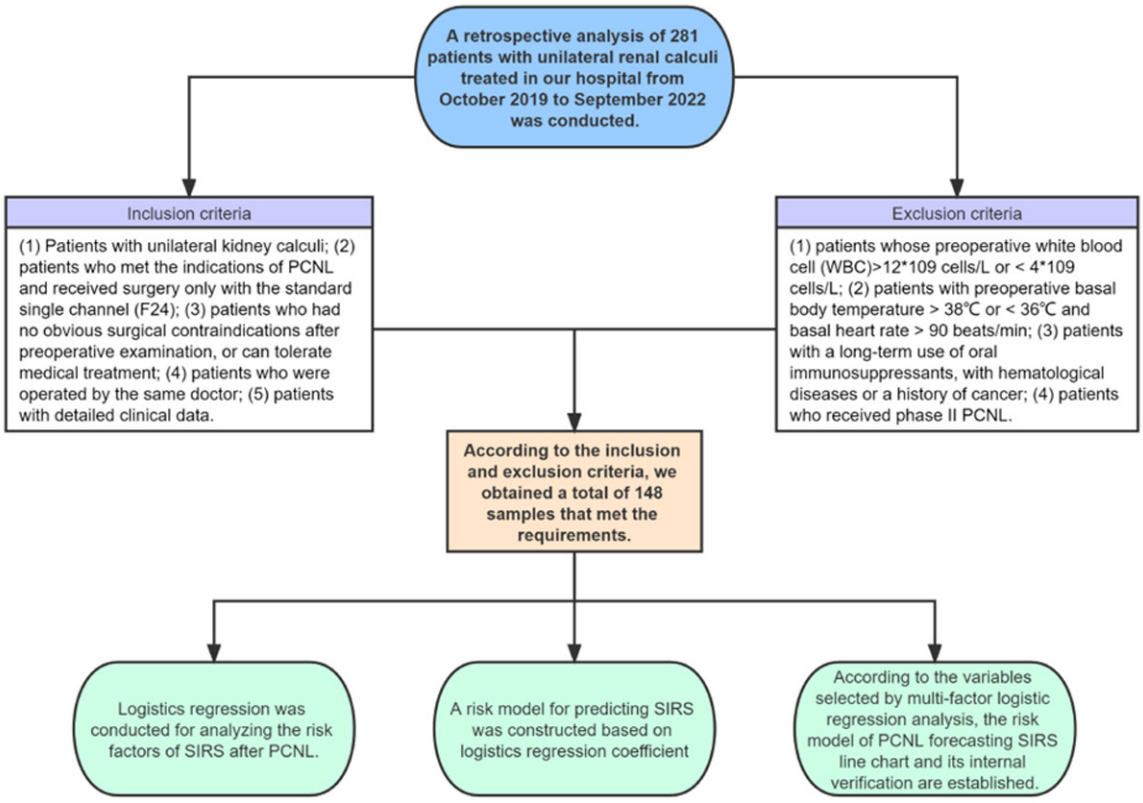

Figure 1. Research flow chart. Note: SIRS: Systemic inflammatory response syndrome; PCNL: Percutaneous nephrolithotomy.

Statistical analyses

The Chi-square test was adopted for inter-group comparison of the classified variables. Based on MLR analysis, the LR method was adopted for determining the clinicopathologic factors. This study adopted SPSS 20.00 (IBM Corp, Armonk, N.Y.) for analyses of data. With the R version 3.6.1 rms software package [17], a nomogram (https://www.r-project.org/) was constructed as mentioned above. Consistency index and a calibration curve were adopted to evaluate the accuracy of the validation model based on regression analysis. The efficacy of risk score for predicting SIRS after PCNL was analyzed by receiver's operator curve (ROC) curves. The Hosmer-Lemeshow test was adopted to evaluate the calibration of the model. $P < 0.05$ (2-sided) was considered a significant difference.

Results

Occurrence of SIRS after PCNL

The occurrence of SIRS in patients after PCNL was analyzed. According to the results, among the 148 patients, 19 patients suffered SIRS, showing an incidence of 12.83%. According to the development of SIRS after PCNL, the patients were divided into a group with SIRS after operation (occurrence group, n = 19) and another group without SIRS after operation (non-occurrence group, n = 129).

Univariate analysis of risk factors for SIRS after PCNL

The two groups were compared for clinical data. According to the comparison, the two groups were not significantly different in age, gender, history of smoking, history of alcoholism or fistula (all $P > 0.05$, **Table 1**), but there were notable differences in BMI, history of hypertension, history of diabetes mellitus (DM), renal insufficiency, calculi size and hydronephrosis (all $P < 0.05$, **Table 1**).

Multivariate analysis of risk factors for SIRS after PCNL

The indexes with statistical significance in univariate analysis were assigned (**Table 2**). Then

Table 1. Univariate analysis of factors impacting SIRS after PCNL

Factor	Non-occurrence group (n = 129)	Occurrence group (n = 19)	χ^2 value	*P* value
Age			4.059	0.043
≥ 60 years old	38	10		
< 60 years old	91	9		
Gender			0.859	0.353
Male	69	8		
Female	60	11		
BMI			7.511	0.006
≥ 25 kg/m^2	40	12		
< 25 kg/m^2	89	7		
History of smoking			0.248	0.617
Yes	60	10		
No	69	9		
History of alcoholism			0.426	0.513
Yes	38	7		
No	91	12		
History of hypertension			6.659	0.009
Yes	48	13		
No	81	6		
History of diabetes mellitus			11.909	0.001
Yes	42	14		
No	87	5		
Renal insufficiency			8.319	0.003
Yes	15	7		
No	114	12		
Calculi size			12.274	0.001
< 30 mm	93	6		
≥ 30 mm	36	13		
Degree of hydronephrosis			9.153	0.003
Mild and below	75	4		
Moderate and above	54	15		
Fistula			0.014	0.903
Yes	110	16		
No	19	3		
Operation time			3.336	0.055
≥ 2 h	45	10		
< 2 h	84	7		
Postoperative blood transfusion			2.861	0.090
Yes	4	2		
No	125	15		

Note: BMI: Body mass index; SIRS: Systemic inflammatory response syndrome.

logistic regression and LR were used to conduct regression analysis. According to the results, BMI, history of hypertension, history of DM, calculi size and degree of hydronephrosis were found to be independent risk factors for SIRS after PCNL (**Table 3**).

Construction of risk predictive model of SIRS after PCNL

Based on the logistic regression coefficient, the risk prediction equation was constructed as follows: logit(p) = -6.480 + (1.639 * BMI) + (1.464

Table 2. Assignment

Factor	Assignment
BMI	≥ 25 kg/m^2 = 1, < 25 kg/m^2 = 0
History of hypertension	Yes = 1, No = 0
History of diabetes mellitus	Yes = 1, No = 0
Renal insufficiency	Yes = 1, No = 0
Calculi size	≥ 30 mm = 1, < 30 mm = 0
Degree of hydronephrosis	Mild and below = 0, moderate and above = 1
SIRS	Yes = 1, no = 0

Note: BMI: Body mass index; SIRS: Systemic inflammatory response syndrome; PCNL: Percutaneous nephrolithotomy.

Table 3. Multivariate regression analysis of factors impacting SIRS after PCNL

Factor	Regression coefficient	Standard error	χ^2 value	*P* value	OR value	95% CI
BMI	1.639	0.663	6.109	0.013	5.151	1.404-18.894
History of hypertension	1.464	0.661	4.903	0.027	4.323	1.183-15.794
History of diabetes mellitus	2.067	0.69	8.962	0.003	7.897	2.041-30.554
Renal insufficiency	1.118	0.744	2.257	0.133	3.060	2.041-30.554
Calculi size	2.022	0.642	9.924	0.002	7.556	2.147-26.588
Degree of hydronephrosis	1.369	0.675	4.121	0.042	3.933	1.048-14.752

Note: BMI: Body mass index; SIRS: Systemic inflammatory response syndrome; PCNL: Percutaneous nephrolithotomy.

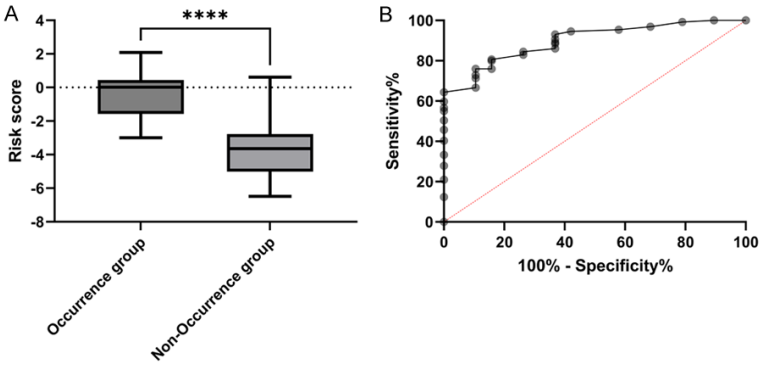

Figure 2. Risk score of SIRS after PCNL and its prediction curve. A. Risk score of patients with or without SIRS after PCNL. B. ROC curve of risk score in forecasting SIRS in patients after PCNL. Note: ROC: receiver operating characteristic curve; PCNL: Percutaneous nephrolithotomy; SIRS: Systemic inflammatory response syndrome. ****P < 0.0001.

* history of hypertension) + (2.067 * history of DM) + (2.022 * calculi size) + (1.369 * degree of hydronephrosis), and the Hosmer-Lemeshow test was adopted to test the goodness of fit of the regression equation (P = 0.822). The occurrence group had a higher risk score than the non-occurrence group. According to ROC curve-based analysis, the area under the curve of risk score for predicting SIRS after PCNL was 0.898 (**Figure 2**, 95% CI: 0.839-0.957, P < 0.001), implying that the score has good predictive performance. According to further comparison, patients with history of DM, BMI ≥ 25 kg/m^2, hypertension history, calculi size < 30 mm, or at least moderate hydronephrosis had a greatly higher risk score than the corresponding control groups (all P < 0.001, **Figure 3**).

Construction of nomogram model

According to the variables (BMI, history of hypertension, history of DM, calculi size, and degree of hydronephrosis) screened by MLR analysis and the risk score, a nomogram risk model for SIRS after PCNL was constructed, and the C-index of the model was 0.899 (0.839-0.958), which indicated that the nomogram was accurate (**Figure 4A**). The Bootstrap self-sampling method was adopted for internal verification. After 100 times of repeated self-sampling, the calibration curve (**Figure 4B**) was acquired, which was close to a diagonal, suggesting that the predicted risk was close to the actual risk, and the prediction ability of the model was good.

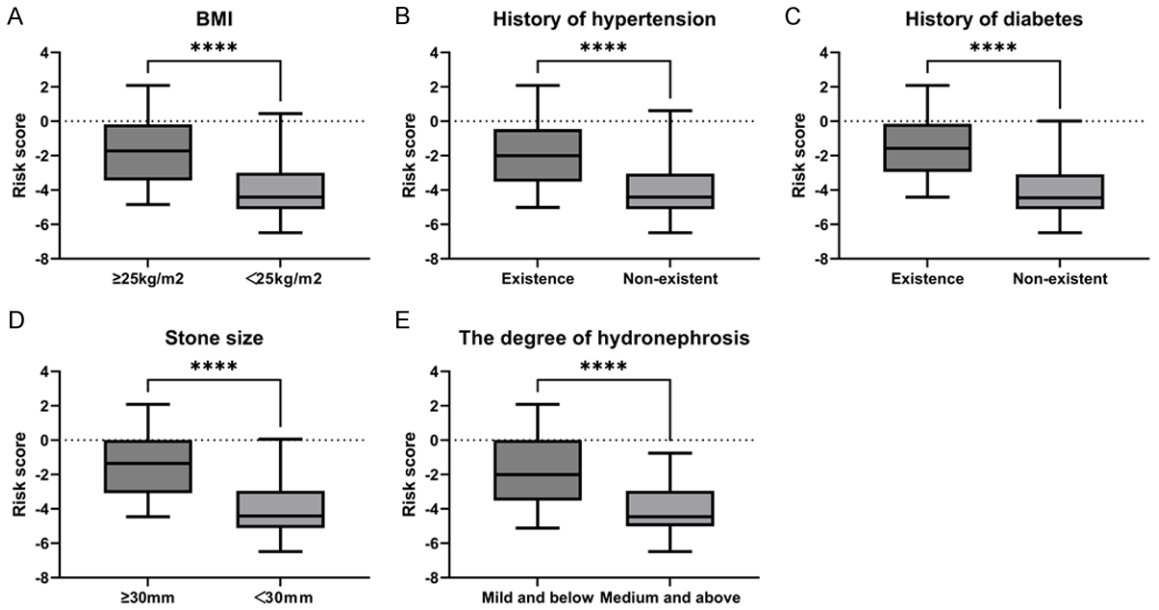

Figure 3. Risk score of patients with different clinical data. A. Comparison of the risk score between patients with different BMI; B. Comparison of risk score between patients with or without hypertension; C. Comparison of risk score between patients with or without DM; D. Comparison of risk scores between patients with different calculi sizes; E. Comparison of risk score between patients with different degrees of hydronephrosis. Note: BMI: body mass index. ****P < 0.0001.

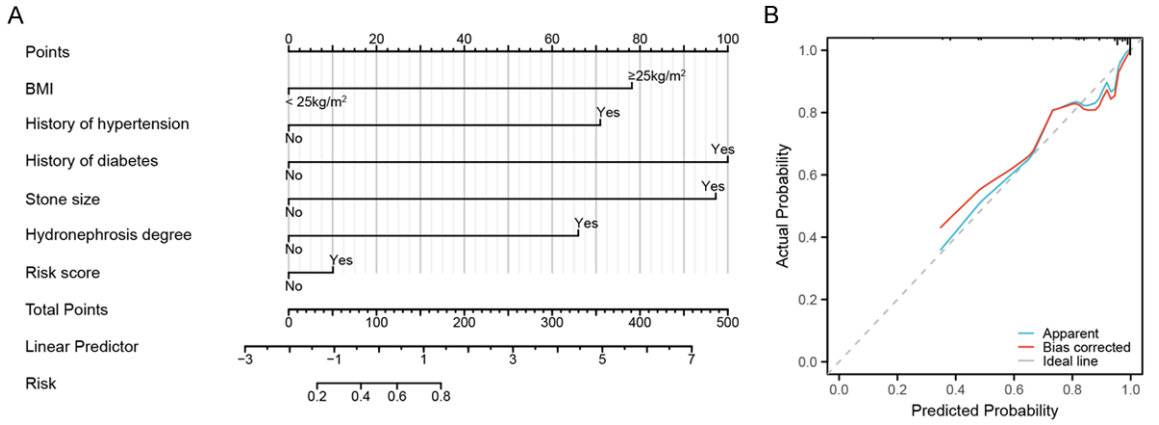

Figure 4. Nomogram model construction. A. Nomogram model of SIRS risk after PCNL; B. Calibration curve of nomogram risk model for predicting SIRS after PCNL. Notes: PCNL: Percutaneous nephrolithotomy; SIRS: Systemic inflammatory response syndrome.

Discussion

Kidney calculi alone will not severely damage the patient's body, but calculi incarceration may trigger intolerable pain and even cause urinary tract obstruction, which will cause poor urine discharge, hydronephrosis, urinary tract infection, or pain. Without timely and effective treatment, it may trigger disease including uremia and renal tumors [18]. PCNL has a series of unique advantages, including high calculi removal efficiency, less trauma, fewer complications, lower risk, and faster recovery in contrast to conventional surgical methods [19]. However, any surgical operation will inevitably trigger complications, among which SIRS is the most common after PCNL. Without effective control, SIRS will be a systemic inflammatory reaction in the early stage of systemic sepsis and septic shock [20].

Currently, the conclusions about SIRS after PCNL from the related clinical medical research and analysis are not completely consistent, and no unified and feasible standard of recognized authority has been developed. This study revealed that BMI, history of hypertension, history of DM, calculi size and degree of hydronephrosis were risk factors for SIRS after PCNL. BMI is a pivotal index to distinguish patients for obesity in clinical practice. Reportedly, people face an increased risk of cardiovascular disease as BMI increases, and with the increase of BMI or waist circumference, the prevalence of hypertension, DM, dyslipidemia, and an aggregation of risk factors show an upward trend [21, 22]. In this study, BMI ≥ 25 kg/m^2 was an independent risk factor for SIRS after PCNL. This may be due to the fact that excessive fat accumulation in overweight or obese patients leads to an increase in plasma osmotic pressure, a disturbance in the dynamic balance of the internal environment, and a decrease in immune cell function (such as WBC and macrophages), and thus patients with BMI ≥ 25 kg/m^2 have a higher susceptibility to inflammation [23].

Hypertension is a chronic disease that can give rise to a series of health problems [24]. Reportedly, inflammation may take a part in the development of hypertension [25]. With the increasing improvement of living standards, changes in diet and living habits, and the combined action and drive of genetic and other congenital factors, the number of people with DM worldwide is growing annually [26]. According to prior research [27, 28], patients with DM face a much higher incidence of urinary tract infections, especially complex urinary tract infections, than people without DM. In this study, DM and hypertension were independent prognostic factors for SIRS after PCNL. This is because to the partial immune deficiency of DM patients cannot be corrected by controlling blood glucose, which causes a weakened killing effect on bacteria [29]. The phagocytic activity of immune cells (such as neutrophils) in DM patients is decreased, which also results in the weakening of the killing effect on bacteria [30]. Hypertension itself will damage blood vessels and organs and cause tissue damage and inflammation, triggering an immune response, and promoting the development of SIRS [31]. Accordingly, for patients with DM or hypertension, the occurrence of SIRS should be a concern and reduction of operation time and strengthened use of antibiotics should be endured.

According to the results in this study, large renal calculi can easily trigger complications of SIRS after PCNL, because the risk for SIRS after PCNL may increase in the cases of large/complex kidney calculi (such as unilateral multiple calculi, staghorn calculi and cast calculi) with a diameter of ≥ 30 mm [32]. It may take longer to remove calculi during the operation. Ineffectively removed calculi may entail the establishment of additional channels. The surface of most kidney calculi may contain harmful substances (bacteria) that will enter the body during the operation [33]. Additionally, the use of booster pumps during lithotripsy releases toxins and bacteria that may enter the bloodstream and contribute to the development of SIRS after PCNL.

The most common cause of hydronephrosis is urinary tract obstruction, which can give rise to hydronephrosis associated with unilateral and localized renal or ureteral calculi [34]. In cases with comorbid infection, symptoms such as pyuria, chills, fever, headache and gastrointestinal dysfunction may occur, which may give rise to systemic poisoning [35]. This study revealed a correlation of the degree of hydronephrosis with SIRS after PCNL. This may be because of the increase in renal perfusion pressure and poor fluidity after calculi obstruction-caused hydronephrosis, which makes it easier for bacteria in the renal pelvis to grow and reproduce [36].

The risk predictive model was adopted to estimate the risk of an individual suffering from a specific disease or experiencing a specific result according to a variety of risk factors [36]. Logistic regression risk predictive model is a common risk predictive model, which adopts logistic regression to estimate the risk of a particular situation or a particular result based on various risk factors [37]. In the present study, a risk model to predict SIRS after PCNL was established based on logistic regression. According to the results, the ROC curve of risk score in predicting SIRS after PCNL was 0.898, and patients with a history of DM, BMI ≥ 25 kg/m^2, history of hypertension, and calculi size <

30 mm had greatly higher risk scores than the corresponding groups, suggesting a promising potential of risk score in providing an objective basis for individualized accurate treatment and prognosis of SIRS after PCNL.

Although this study has successfully established a post-PCNL SIRS predictive model, it has some limitations. First, because of limited time for sample collection, a small number of samples were collected. Additionally, in such a single-center study, verification cannot be conducted externally. Moreover, the model is universal, which requires verification with more data. We hope to carry out more experiments in the future to improve the results of this study.

To sum up, patients with BMI ≥ 25 kg/m^2, DM, hypertension, calculi ≥ 30 mm, and/or hydronephrosis are more likely to develop SIRS after PCNL. The constructed risk score has significant clinical value in the prediction of SIRS.

Disclosure of conflict of interest

None.

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