

# The Predictive Value of Preoperative Albumin–Globulin Ratio for Systemic Inflammatory Response Syndrome After Percutaneous Nephrolithotomy

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**Purpose:** This study aimed to assess the predictive value of preoperative albumin–globulin ratio (AGR) for systemic inflammatory response syndrome (SIRS) after percutaneous nephrolithotomy (PCNL).

**Methods:** Patients who underwent PCNL in Guizhou Provincial People's hospital between August 2017 and July 2019 were enrolled and retrospectively reviewed. The primary clinical outcome of the current study was the development of SIRS within 48h after PCNL. Univariable and multivariable logistic regression analyses were conducted to verify the predictive value of AGR for post-PCNL SIRS. In addition, receiver operating characteristic (ROC) curves were generated to compare the discriminatory ability of AGR with other inflammatory biomarkers.

**Results:** 354 patients who underwent PCNL were enrolled and 66 patients (18.64%) developed postoperative SIRS. None of the patients suffered postoperative sepsis in our study. Multivariate analysis demonstrated that female sex (odds ratio [OR]=2.939, 95% odds ratio [OR]: 1.368–6.315,  $p = 0.006$ ), CRP (OR = 1.008, 95% CI: 1.003–1.012,  $p = 0.001$ ), and AGR (OR = 0.048, 95% CI: 0.010–0.239,  $p < 0.001$ ) were all independent predictors for SIRS after PCNL. The optimal cut-off value of AGR for predicting postoperative SIRS was 1.145. In addition, AGR had a higher area under the curve (0.844) with sensitivity of 83.3% and specificity of 88.9% than C-reactive protein (0.808).

**Conclusion:** Preoperative AGR is a potential predictor for SIRS development after PCNL.

**Keywords:** albumin–globulin ratio, percutaneous nephrolithotomy, systemic inflammatory response syndrome

## Introduction

Urolithiasis is a worldwide disease with an increasing morbidity, which leads to heavy health and economic burdens.<sup>1</sup> The European Association of Urology guidelines have recommended percutaneous nephrolithotomy (PCNL) as the optimal treatment option for complex renal stones.<sup>2</sup> Systemic inflammatory response syndrome (SIRS) is a common complication after PCNL, which was reported with an incidence of 7% to 31% and might be lethal.<sup>3–7</sup> Therefore, it is important to identify some risk factors of post-PCNL SIRS in patients with renal stones. Several biochemical markers, such as neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR), have been previously reported to be potential in predicting post-PCNL SIRS.<sup>8–10</sup> However, it should be indicated that the sensitivity and specificity of these indicators need further improvement.

Albumin (ALB) and globulin (GLB) are two crucial components of serum proteins and play a potential role in systemic inflammation. Low serum ALB concentration not only reflects malnutrition but also can predict infectious

complications after cardiac surgery, oncologic surgery, and orthopedic surgery.<sup>11–13</sup> Globulin is an acute-phase protein during the host immune response, and its concentration increases shortly after the invasion of pathogen and toxin. High level of GLB indicates an inflammation status and the accumulation of various inflammatory cytokines.<sup>14</sup> Therefore, we suspected that the superposition effect of both ALB and GLB might serve as a potential predictor of SIRS after PCNL.

Although albumin–globulin ratio (AGR) has been reported to be effective in predicting outcomes in some urological tumors,<sup>15–17</sup> the relationship between the AGR and post-PCNL SIRS has not been reported. Hence, we conducted the current retrospective study to explore whether preoperative AGR can be used to predict post-PCNL SIRS in kidney stone patients.

## Materials and Methods

### Study Population

Patients who underwent PCNL in Guizhou Provincial People's Hospital between August 2017 and July 2019 were enrolled in our retrospective study. The inclusion criteria were listed as follows: (1) kidney stones identified with computed tomography, (2) treatment with PCNL (18F to 20F sheath), (3) no history of surgery for kidney stones, (4) no fever before PCNL that needed antibiotic treatment, and (5) available preoperative blood parameters and clinical data. The exclusion criteria were listed as follows: (1) urinary system malformations, (2) second-stage PCNL surgery, (3) severe complications occurred, such as bleeding requiring intervention and organ injury.

Computed tomography, blood tests (including complete blood count, liver function test, renal function test, C-reactive protein (CRP), Interleukin-6 (IL-6), and fasting blood sugar), and urine culture were routinely conducted for patients before operation. Patients with positive urine culture were given antibiotics for 7 days according to the drug sensitivity results, and PCNL was not performed until the urine culture turned negative. All patients received a single dose of antibiotic prophylaxis at 30 min before operation.

All procedures were conducted in accordance with the Declaration of Helsinki, and the Guizhou Provincial People's Hospital ethics committee approved the study (LSZ[2021]42).

### Data Collection

The perioperative clinical data of patients were retrospectively collected and analyzed. The primary outcome of the study was whether patients developed SIRS or sepsis after PCNL. AGR was defined as the ratio of the preoperative serum albumin level (g/L) to globulin level (g/L). The stone burden was calculated using the following formula: length (mm) × width (mm) ×  $\pi$  × 0.25. SIRS was defined as the development of two or more of the following conditions:<sup>18</sup> (1) core temperature of >38°C or <36°C, (2) heart rate of >90 beats/min, (3) respiratory rate of >20 breaths/min or partial PaCO<sub>2</sub> of <32 mmHg, (4) white blood cell count of >12,000 cells/mL or <4000 cells/mL. The presence of a confirmed infection and at least two SIRS criteria was defined as septic shock.<sup>19</sup>

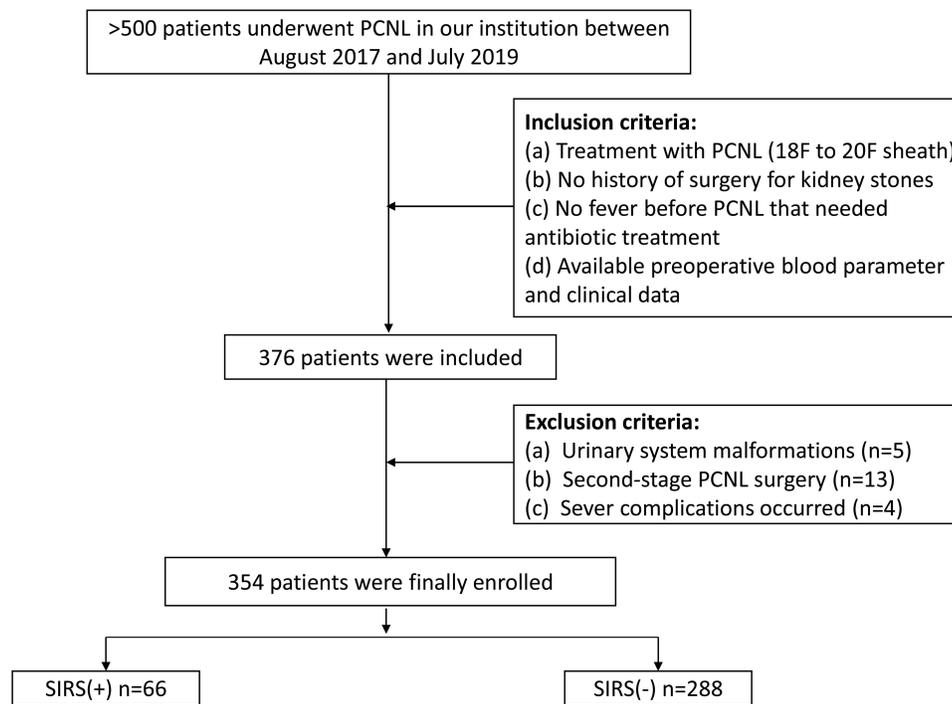
### Statistical Analysis

Statistical analysis was performed using SPSS 20.0 (IBM, USA). Continuous variables with normal distribution were compared using Student's *t*-test. The chi-square test or Fisher's exact test was applied to detect the difference between categorical variables. Univariate and multivariable logistic regression analyses were conducted to identify independent predictors of post-PCNL SIRS. Area under curve (AUC) was calculated from receiver operating characteristic (ROC) curves to evaluate the superiority of these independent predictive factors of SIRS. *p* < 0.05 was considered statistically significant.

## Results

### AGR Was Decreased in Patients with Post-PCNL SIRS

354 patients with renal stones who underwent PCNL in our hospital were enrolled. 66 (18.6%) patients developed SIRS after PCNL and none of the patients suffered sepsis. The patient selection flow diagram is shown in Figure 1. Statistically significant difference was found in terms of age, sex, the presence of multiple and staghorn nephrolithiasis, positive urine



**Figure 1** Selection flow diagram of the patients.

culture, white blood cell count, neutrophil count, serum creatinine, CRP, ALB, GLB, and AGR between patients with postoperative SIRS and those without postoperative SIRS (all  $p < 0.01$ ). In addition, patients with post-PCNL SIRS showed lower AGR (Table 1).

## Univariate and Multivariate Logistic Regression Analysis for Post-PCNL SIRS

Univariate logistic analysis showed that age, sex, the presence of multiple and staghorn nephrolithiasis, urine-white cell count, positive urine culture, white blood cell count, blood neutrophils count, serum creatinine, serum BUN, CRP, IL6, ALB, GLB, and AGR were all significantly associated with post-PCNL SIRS. Accordingly, we put age, sex, presence of staghorn nephrolithiasis, white blood cell count, serum BUN, CRP, and AGR into multivariate logistic regression analysis after excluding the multicollinearity. Results showed that female sex (odds ratio [OR] = 2.939, 95% odds ratio [OR]: 1.368–6.315,  $p = 0.006$ ), CRP (OR = 1.008, 95% CI: 1.003–1.012,  $p = 0.001$ ), and AGR (OR = 0.048, 95% CI: 0.010–0.239,  $p < 0.001$ ) were all significant predictors of post-PCNL SIRS (Table 2).

## Association Between AGR and Clinical Features

As shown in Figure 2, preoperative AGR showed higher AUC (0.844, 95% CI: 0.772–0.917) in predicting post-PCNL SIRS than CRP (0.808, 95% CI: 0.739–0.877). In addition, the AUC of ALB (0.762, CI: 0.701–0.823), GLB (0.701, 95% CI: 0.620–0.782), white blood cells (0.706, 95% CI: 0.623–0.789), and neutrophils (0.750, 95% CI: 0.6781–0.823) were also lower than AGR in predicting post-PCNL SIRS (Figure 3).

The sensitivity of preoperative AGR for predicting post-PCNL SIRS was 83.3%, and the specificity was 88.9%. The optimal cutoff value of AGR was 1.145 according to the ROC curve and Youden index (Youden index = sensitivity - (1-specificity)). A total of 267 patients with  $AGR \geq 1.145$  were categorized into the high AGR group and 87 patients with  $AGR < 1.145$  were categorized into the low AGR group (Table 3). We found that a lower AGR had a significant association with higher urine white cell count, positive nitrite, positive urine culture, higher white blood cell count, higher neutrophil count, higher CRP level, lower ALB level, and higher GLB level (Table 3).

**Table 1** Clinical Characteristics of Patients with or Without Post-PCNL SIRS

Variables	SIRS (+) n = 66	SIRS (-) n = 288	p value
Age (year)	54.00 (41.75, 61.25)	50.00 (42.00, 57.00)	<b>0.026</b>
Sex, female	37 (56.06%)	110 (38.19%)	<b>0.008</b>
BMI (kg/m <sup>2</sup> )	24.5 (22.2, 25.2)	24.3 (22.0, 25.5)	0.463
Hypertension (n, %)	10 (15.2%)	47 (16.3%)	0.816
Diabetes (n, %)	8 (12.1%)	41 (14.2%)	0.654
ASA 1 (n, %)	36 (54.5%)	149 (51.7%)	0.680
ASA 2 (n, %)	25 (37.9%)	121 (42.0%)	
ASA 3 (n, %)	5 (7.6%)	18 (6.3%)	
Stone burden (mm <sup>2</sup> )	162.58 (112.31, 374.83)	122.36 (84.82, 345.58)	0.082
Multiple nephrolith (n, %)	38 (57.6%)	122 (42.4%)	<b>0.025</b>
Staghorn nephrolith (n, %)	24 (36.4%)	85 (29.5%)	<b>0.009</b>
Hydronephrosis (n, %)	59 (88.8%)	267 (92.7%)	0.113
Urine-white cell (n/uL)	491.00 (79.00, 3156.00)	127.00 (27.75, 517.00)	<b>&lt;0.001</b>
Positive nitrite	31 (47.0%)	115 (39.9%)	0.295
Positive urine culture	25 (37.9%)	58 (20.1%)	<b>0.002</b>
White blood cells (10 <sup>9</sup> /L)	8.79 (6.39, 14.92)	6.63 (5.71, 7.81)	<b>&lt;0.001</b>
Neutrophils (10 <sup>9</sup> /L)	6.09 (4.31, 13.22)	3.96 (3.17, 5.48)	<b>&lt;0.001</b>
Hemoglobin (g/L)	101.00 (90.00, 123.25)	115.00 (98.00, 128.75)	0.092
Serum creatinine (umol/L)	129.4 (91.95, 197.93)	88.70 (71.00, 108.30)	<b>&lt;0.001</b>
BUN (mmol/L)	5.82 (3.53, 12.13)	5.52 (4.25, 7.66)	0.095
CRP (mg/L)	52.29 (20.92, 151.03)	3.68 (1.32, 14.38)	<b>&lt;0.001</b>
IL-6 (pg/mL)	32.4 (6.24, 56.00)	8.08 (3.30, 38.60)	0.325
ALB (g/L)	36.4 (29.1, 40.58)	41.7 (37.9, 45.2)	<b>&lt;0.001</b>
GLB (g/L)	34.1 (28.1, 36.6)	29.0 (25.6, 32.3)	<b>&lt;0.001</b>
AGR	1.13±0.36	1.46±0.26	<b>&lt;0.001</b>
Operative time (minutes)	75.00 (60.00, 90.00)	80.00 (60.00, 100.00)	0.156
LOS (days)	14.00 (12.00, 18.00)	9.00 (8.00, 13.00)	<b>&lt;0.001</b>

**Notes:** Data were presented in n (%) and median (interquartile range). Bold text in the p value column indicated that p < 0.05.

**Abbreviations:** BMI, body mass index; ASA, American Society of Anesthesiologists; LOS, length of hospital stay.

**Table 2** Univariate and Multivariate Analyses Regarding Post-PCNL SIRS

Variables	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p value	OR	95% CI	p value
Age (year)	1.023	1.003–1.044	<b>0.027</b>	0.990	0.963–1.018	0.473
Sex (female)	2.065	1.202–3.547	<b>0.009</b>	2.939	1.368–6.315	<b>0.006</b>
BMI (kg/m <sup>2</sup> )	0.965	0.878–1.061	0.462	/	/	/
Hypertension (n, %)	0.916	0.436–1.923	0.816	/	/	/
Diabetes (n, %)	0.831	0.370–1.867	0.654	/	/	/
ASA	0.770	0.510–1.162	0.214	/	/	/
Stone burden (mm <sup>2</sup> )	1.001	1.000–1.001	0.054	/	/	/
Multiple nephrolith (n, %)	1.847	1.075–3.173	<b>0.026</b>			
Staghorn nephrolith (n, %)	2.115	1.226–3.651	<b>0.007</b>	1.740	0.823–3.683	0.147
Hydronephrosis (n, %)	0.801	0.331–1.940	0.623	/	/	/
Urine-white cell (n/uL)	1.000	1.000–1.001	<b>0.000</b>	/	/	/
Positive nitrite	1.352	0.789–2.315	0.272	/	/	/
Positive urine culture	2.418	1.361–4.296	<b>0.003</b>	/	/	/
White blood cell (10 <sup>9</sup> /L)	1.393	1.261–1.539	<b>0.000</b>	/	/	/

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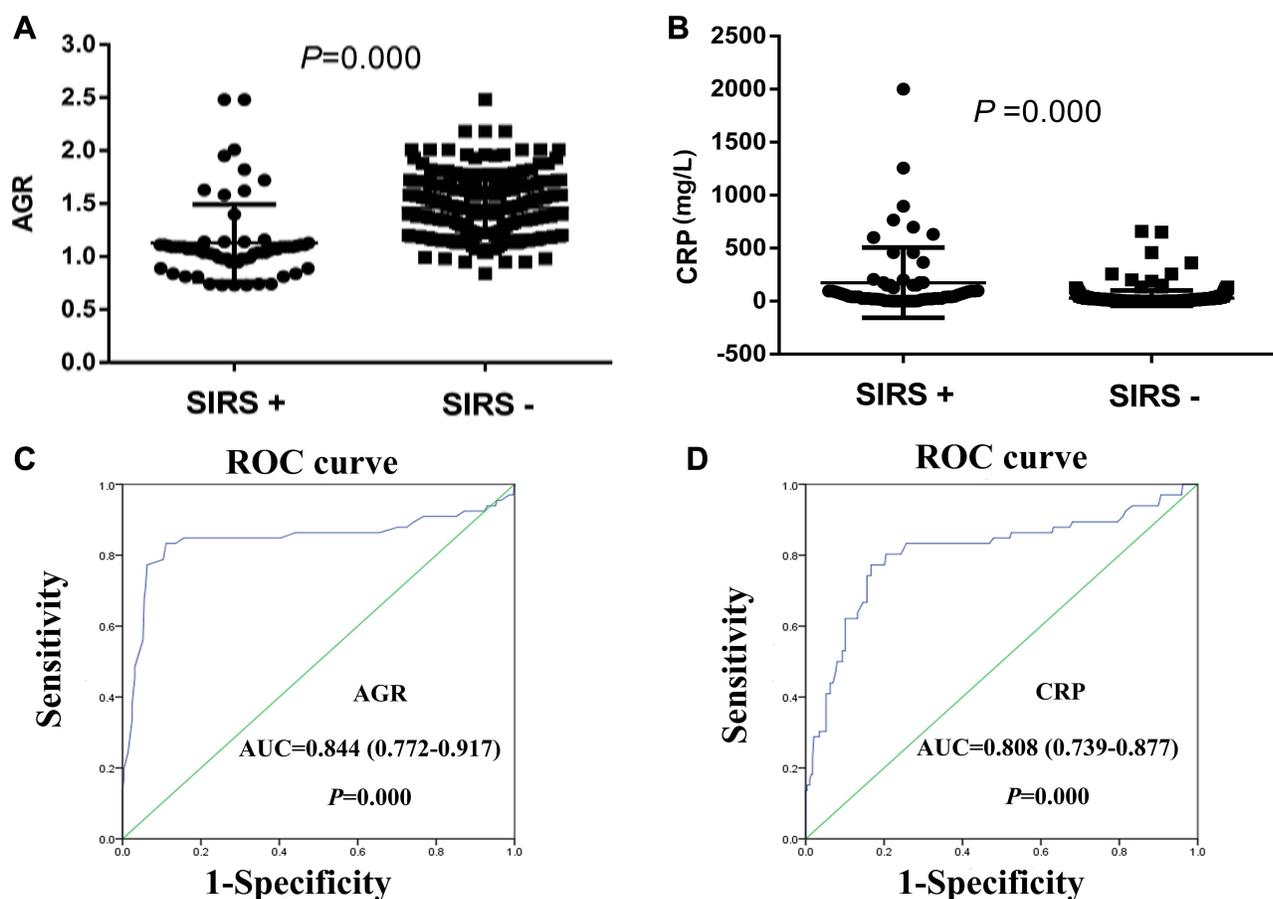
Table 2 (Continued).

Variables	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p value	OR	95% CI	p value
Neutrophils ( $10^9/L$ )	1.394	1.266–1.533	<b>0.000</b>	/	/	/
Hemoglobin (g/L)	0.990	0.978–1.002	0.093	/	/	/
Serum creatinine ( $\mu\text{mol/L}$ )	1.007	1.004–1.011	<b>0.000</b>	/	/	/
BUN (mmol/L)	1.084	1.008–1.165	<b>0.027</b>	0.991	0.895–1.097	0.858
CRP (mg/L)	1.013	1.008–1.018	<b>0.000</b>	1.008	1.003–1.012	<b>0.001</b>
IL-6 (pg/mL)	1.000	1.000–1.001	0.201	/	/	/
Albumin (g/L)	0.853	0.813–0.895	<b>0.000</b>	/	/	/
Globulin (g/L)	1.152	1.090–1.217	<b>0.000</b>	/	/	/
AGR	0.007	0.002–0.030	<b>0.000</b>	0.048	0.010–0.239	<b>0.000</b>
Operative time (minutes)	0.994	0.986–1.002	0.156	/	/	/

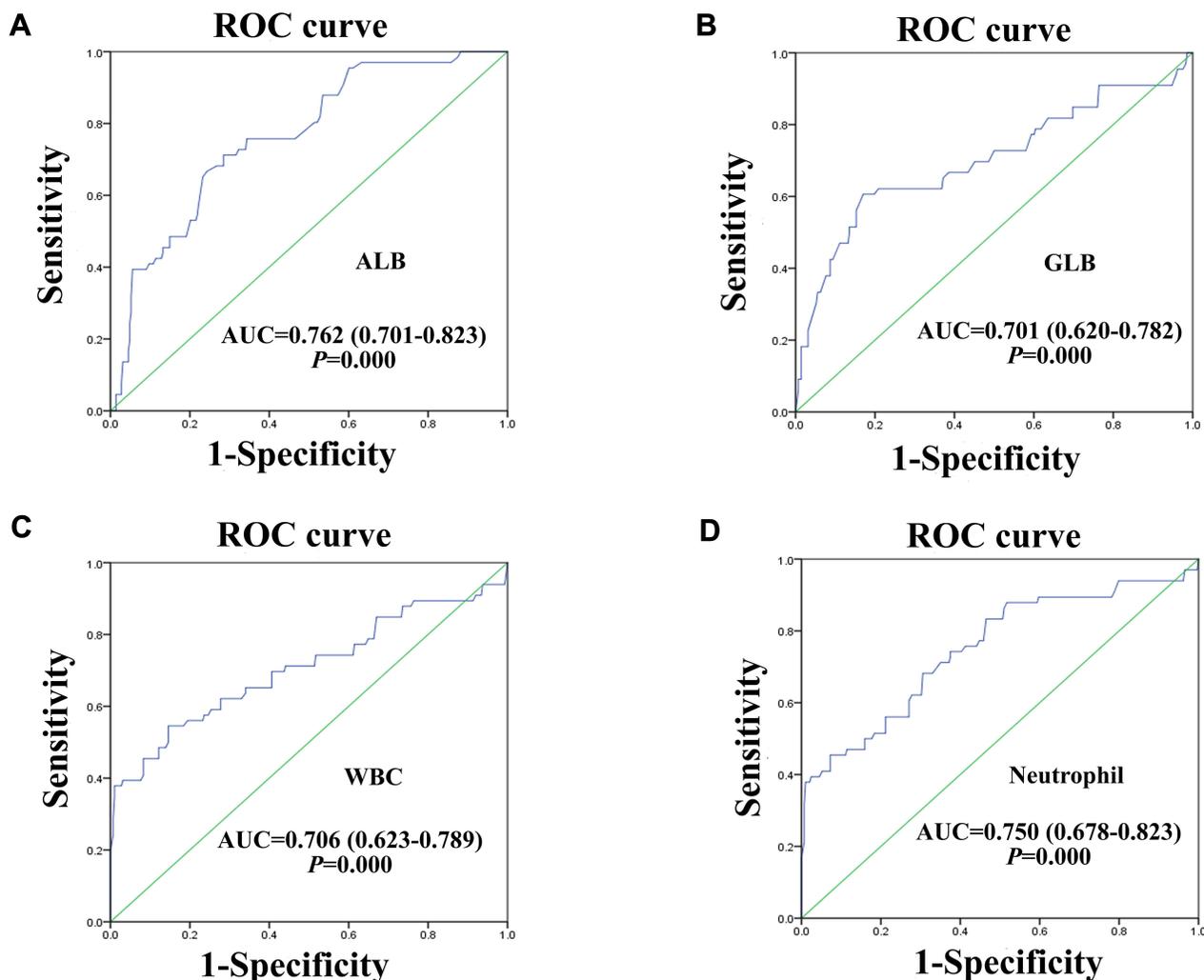
**Notes:** Bold text in the p value column indicated that  $p < 0.05$ . / indicated the analysis was not applicable for the corresponding item.  
**Abbreviations:** BMI, body mass index; ASA, American Society of Anesthesiologists; LOS, length of hospital stay.

## Discussion

Infectious complications are common in patients undergoing PCNL. SIRS after PCNL is reported with an incidence of 7% to 35% and about 0.5% of the patients may progress to fatal septic shock.<sup>2</sup> Similarly, the incidence of post-PCNL



**Figure 2** AGR and CRP levels of patients with and without post-PCNL SIRS and their ROC curves for the predicting post-PCNL SIRS. (A and B) AGR and CRP levels of patients with or without post-PCNL SIRS; (C and D) ROC curves of AGR and CRP for the predicting post-PCNL SIRS in patients with renal stones.



**Figure 3** ROC curves of other markers for predicting post-PCNL SIRS in patients with renal stones. (A) ROC of ALB; (B) ROC of GLB; (C) ROC of WBC; (D) ROC of neutrophil.

SIRS was found to be 18.6% in our current study. Identifying risk factors of post-PCNL SIRS to prevent its occurrence has attracted much attention of the urologists in recent years. Although findings in different studies are not consistent, older age, preoperative positive urine culture, larger stone, female sex, and longer operative time are frequently identified as potential risk factors for SIRS after PCNL.<sup>20–23</sup> Other metrics, such as systemic immune-inflammation, NLR, LMR, PLR, procalcitonin and CRP, have also been reported to be associated with post-PCNL SIRS.<sup>8–10,24,25</sup> Despite all the efforts which have been made, a new effective and reliable indicator is still worth of further exploration to help improve the sensitivity and specificity of prediction.

As two important serum proteins, ALB can reflect the nutritional status and lack of albumin may lead to insufficient synthesis of immunoglobulin, which then weakens the immune system and increases the risk of postoperative infection.<sup>26</sup> GLB often reflects a status of acute systemic immune response. They have been proved to play a potential role in inflammation. In the current study, we found that both ALB and GLB were independent predictors for SIRS after PCNL. Serum ALB level was significantly lower, while GLB was higher in patients with post-PCNL SIRS. However, the AUC was only 0.762 and 0.701 for ALB and GLB in predicting post-PCNL SIRS, respectively, which was relatively low.

As a combination of albumin and globulin, AGR was previously mainly used as a predictor of cancer progression and cancer-related mortality.<sup>15–17</sup> Few studies have explored the relationship between AGR and postoperative infectious complications. Lu et al reported that in patients with unilateral, solitary, and proximal ureteral stones, AGR <1.2 was an

**Table 3** Clinical Characteristics of Patients Stratified by AGR Level

Terms	Low AGR Group AGR <1.145 (n = 87)	High AGR Group AGR ≥1.145 (n = 267)	p value
Age (year)	54 (49, 62)	49 (40, 56)	<b>0.000</b>
Sex, female	41 (47.13%)	106 (39.70%)	0.222
BMI (kg/m <sup>2</sup> )	24.5 (22.3, 25.2)	24.3 (21.8, 25.5)	0.970
Hypertension (n, %)	12 (13.8%)	45 (16.9%)	0.500
Diabetes (n, %)	16 (18.4%)	33 (12.4%)	0.157
ASA I (n, %)	34 (39.1%)	134 (50.2%)	0.072
ASA 2 (n, %)	48 (55.2%)	112 (41.9%)	
ASA 3 (n, %)	5 (5.7%)	21 (7.9%)	
Stone burden (mm <sup>2</sup> )	150.8 (112.3, 343.2)	126.9 (87.1, 351.9)	0.084
Multiple nephrolith (n, %)	45 (51.7%)	115 (43.1%)	0.159
Staghorn nephrolith (n, %)	33 (37.9%)	76 (28.5%)	0.097
Hydronephrosis (n, %)	77(88.5%)	245 (91.8%)	0.358
Urine-white cell (n/uL)	383.0 (161.0, 3052.0)	104 (24, 477)	<b>0.000</b>
Positive nitrite	51 (58.6%)	94 (35.2%)	<b>0.000</b>
Positive urine culture	46 (17.2%)	83 (23.4%)	<b>0.000</b>
White blood cell (10 <sup>9</sup> /L)	7.43 (6.17, 13.12)	6.63 (5.71, 7.88)	<b>0.000</b>
Neutrophils (10 <sup>9</sup> /L)	5.23 (4.12, 11.05)	3.91 (3.17, 5.48)	<b>0.000</b>
Hemoglobin (g/L)	114.0 (87.0, 123)	114.0 (98.0, 135.0)	<b>0.042</b>
Serum creatinine (umol/L)	105.2 (93.5, 155.2)	87.4 (71.0, 108.3)	<b>0.000</b>
BUN (mmol/L)	5.82 (4.17, 7.87)	5.41 (4.25, 7.82)	0.200
CRP (mg/L)	59.27 (18.26, 134.12)	3.43 (1.19, 11.56)	<b>0.000</b>
IL-6 (pg/mL)	35.1 (7.28, 56.0)	7.44 (2.6, 33.5)	0.526
ALB (g/L)	35.3 (28.7, 40.2)	42.7 (38.1, 45.6)	<b>0.000</b>
GLB (g/L)	35.2 (29.5, 36.6)	28.7 (25.6, 31.7)	<b>0.000</b>
Operative time (minutes)	75.0 (60.0, 90.0)	80.0 (60.0, 100.0)	0.143
LOS (days)	15.0 (13.0, 19.0)	9.0 (8.0, 12.0)	<b>0.000</b>
SIRS	55 (62.5%)	11 (4.1%)	<b>0.000</b>

**Notes:** Data were presented in n (%) and median (interquartile range). Bold text in the p value column indicated that  $p < 0.05$ .

**Abbreviations:** BMI, body mass index; ASA, American Society of Anesthesiologists; LOS, length of hospital stay.

independent predictor of sepsis after flexible ureteroscopy and the AUC was 0.685.<sup>27</sup> In addition, Xun et al also identified AGR <1.5 as an independent predictor of post-PCNL sepsis and the AUC was 0.65 in their study.<sup>28</sup> Actually, the AUC was unsatisfactory in both two studies and the authors recommended that combining AGR with other risk factors would be better in predicting sepsis after endourological surgeries. In our current study, the optimal cut-off value of preoperative AGR for predicating SIRS after PCNL was found to be 1.145 with 83% sensitivity and 88.9% specificity and the AUC was 0.844, which showed a good diagnostic performance. Moreover, the AUC of AGR for predicting post-PCNL SIRS was also higher than many other previous indicators, such as NLR (reported with 0.596–0.831),<sup>4,8,9</sup> LMR (reported with 0.649–0.734),<sup>8–10</sup> PLR (reported with 0.617–0.685),<sup>8–10</sup> preoperative positive midstream urine culture (reported with 0.65)<sup>29</sup> and so on. Patients whose AGR <1.145 were found to be with lower serum ALB level, higher serum GLB level, higher urine white cell count, positive urine nitrite, positive urine culture, higher white blood cell count, higher neutrophil count and higher serum CRP level, so these patients are suggested to be carefully evaluated and treated before performing PCNL in the future.

There are several limitations in our study. First, it was a retrospective study with small sample size in a single clinical center. Second, the current study lacked the measurement of some specific inflammatory markers such as procalcitonin. Third, different cutoff values of AGR in different cohorts may lead to various results, and lack of consensus for a common value may limit the application of the marker in clinical practice. Hence, multicenter studies with larger sample size were needed to verify our findings, and an optimal AGR value for predicting post-PCNL SIRS was needed to be further determined in the future.

## Conclusions

Preoperative AGR is a potential predictor for SIRS development after PCNL. Patients with AGR <1.145 are suggested to be carefully evaluated and treated before performing PCNL.

## Abbreviations

AGR, albumin–globulin ratio; ALB, Albumin; AUC, Area under curve; ASA, American Society of Anesthesiologists; BMI, Body Mass Index; CI, confidence interval; CRP, C-reactive protein; GLB, globulin; LMR, lymphocyte-to-monocyte ratio; LOS, Length of hospital stay; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio; PCNL, percutaneous nephrolithotomy; PLR, platelet -to-lymphocyte ratio; ROC, receiver operating characteristic; SIRS, systemic inflammatory response syndrome.

## Data Sharing Statement

Records and data of this study are saved in the patients' secure medical records of Guizhou Provincial People's Hospital. The records and data could be accessed from Fa Sun.

## Ethics Approval and Informed Consent

This study belonged to a retrospective study, so patient consent to check their medical records was waived. And all patient information collection and processing were strictly confidential, and our procedures were carried out according to the Declaration of Helsinki. The Guizhou Provincial People's Hospital ethics committee approved the study (ID: LSZ [2021]42).

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## Disclosure

The authors report no conflicts of interest in this work.

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