

# Retrospective Analysis of the Risk Factors and Drug Resistance of Pathogenic Bacteria in Systemic Inflammatory Response Syndrome After Ureteroscopic Holmium Laser Lithotripsy for Impacted Ureteral Calculi

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**Objective:** To investigate the risk factors, pathogen distribution, and drug resistance of systemic inflammatory response syndrome (SIRS) after holmium laser ureteroscopic lithotripsy for impacted ureteral calculi (HLULIUC).

**Patients and Methods:** The clinical data of 293 patients with HLULIUC in our hospital from October 2017 to February 2021 were retrospectively collected, including age, BMI, stone size, operation time, urine routine, urine culture, basic illness, complete blood count, liver and kidney function, etc. Patients were divided into SIRS and non-SIRS groups according to whether they had SIRS or not. Then the differences in clinical data, blood and urine bacterial culture results, and drug resistance between the two groups were analyzed.

**Results:** The incidence of SIRS after HLULIUC was 17.75%. Logistic regression analysis showed that the risk factors of SIRS after HLULIUC include ureteral calculi  $\geq 1$ cm (OR=2.839, 95% CI=1.341–5.647, P=0.021), long operation time (OR=4.534, 95% CI=2.597–12.751, P=0.017), diabetes mellitus (OR=3.137, 95% CI=1.142–7.319, P=0.012), increased preoperative C-reactive protein (OR=1.864, 95% CI=1.05–4.347, P=0.032), and positive urine leukocytes (OR=3.514, 95% CI=1.7237–9.734, P=0.007) and culture (OR=6.034, 95% CI=3.097–15.751, P<0.001) before operation. The main pathogens causing SIRS after HLULIUC were *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa*. The pathogenic bacteria are sensitive to drugs including piperacillin/tazobactam, meropenem, tigecycline, teicoplanin, vancomycin, and imipenem. The resistance rates to quinolones (such as levofloxacin) and to the second- and third-generations of cephalosporins were as high as 52.94%–90.19%.

**Conclusion:** Ureteral calculi  $\geq 1$ cm, long operation time, diabetes, increased C-reactive protein, and preoperative positive urine leukocytes and culture are independent risk factors of SIRS after HLULIUC. *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa* are the main pathogenic bacteria for SIRS after HLULIUC. The pathogenic bacteria are sensitive to drugs, including piperacillin/tazobactam, meropenem, tigecycline, teicoplanin, vancomycin, and imipenem.

**Keywords:** impacted ureteral calculi, holmium laser ureteroscopic lithotripsy, systemic inflammatory response syndrome, risk factors, drug resistance, sensitivity

## Introduction

Ureteral calculi is a common disease in Urology. Common treatment options in the past include extracorporeal shock wave lithotripsy (ESWL) and open surgery.<sup>1–3</sup> However, these options are not safe and effective in treating impacted ureteral calculi

(IUC) with local chronic inflammation caused by stones lodged in the same position for a long time or encapsulated by edematous ureteral mucosa or polyps.<sup>1-3</sup> ESWL has a low stone removal rate, and open surgery is traumatic for the patient, which are not conducive to the recovery.<sup>4,5</sup> Patients with IUC are often associated with pathological changes such as hydronephrosis, infection, and ureteral stenosis, making clinical treatment difficult.<sup>6</sup> In recent years, with the continuous development of minimally invasive technology, holmium laser ureteroscopic lithotripsy (HLUL) has gained great development because of advantages such as minimal invasiveness, high efficiency of stone extraction, and quick postoperative patient recovery.<sup>7</sup>

Although HLUL can directly remove stones, promote stone excretion, and relieve ureteral obstruction, the procedure also brings various complications, such as infection, which is the most common one,<sup>8-10</sup> bleeding, and ureteral injury, etc.<sup>8,9</sup> Relevant studies show that the incidence of infection-related complications such as urinary tract infection, sepsis, and fever after HLUL is 4%-25%.<sup>11,12</sup> IUC often causes ureteral obstruction, and is usually accompanied by hydronephrosis and infection. In the HLUL, the release of bacteria and pyrogens will cause systemic inflammatory response syndrome (SIRS),<sup>13</sup> one of the most severe complications. If not controlled in time, it will further develop into urosepsis and multiple organ dysfunction syndrome (MODS), threatening the lives of patients.<sup>11-13</sup> At present, there are few reports on risk factors, pathogen distribution, and drug resistance for SIRS after holmium laser ureteroscopic lithotripsy for incarcerated ureteral stones (HLULIUC). Therefore, this paper aims to explore the risk factors, pathogen distribution, and drug resistance of SIRS after HLULIUC, so as to provide clinical reference for early prevention of SIRS.

## Method

### Patients Inclusion

A total of 293 patients with IUC who underwent HLUL in our hospital from October 2017 to February 2021 were included in this study. Their clinical data were collected retrospectively, including gender, age, BMI, stone size, operation time, urine routine, urine culture results, basic diseases, stone location, complete blood count, liver function and renal function. They were divided into SIRS group (n=52) and non-SIRS group (n=241) according to whether they had SIRS or not. Inclusion criteria: (1) Patients diagnosed as IUC by intravenous pyelography, urinary ultrasound, and urinary CT examination before the operation as previously reported<sup>13,14</sup> (2) Stones  $\leq 2$ cm; (3) Patients experiencing HLUL for the first time; (4) Patients and their families agreed with the study and signed informed consent. Exclusion criteria: (1) Patients with contraindications for Holmium laser lithotripsy; (2) Patients whose cardiopulmonary function could not tolerate the surgery; (3) Abnormal immune system; (4) Patients with hematological diseases; (5) Patients with severe liver or kidney dysfunction; (6) Patients with other ureteral obstruction diseases; (7) The presence of other organ infections or febrile diseases. All patients and their families signed informed consent, and the study was approved by the Chongqing HechuanHongren hospital ethics committee and was carried out in accordance with the Animal Welfare Guidelines and the Declaration of Helsinki.

### Surgical Approach

The same senior urologist performed the same operation as previously reported in the literature.<sup>15-17</sup> Patients with negative urine culture were treated with a single dose of prophylactic intravenous antibiotics (cefazolin, 2g) before operation. Patients with positive preoperative urine culture were treated with ceftriaxone 48 hours before surgical intervention and lasted until 1 day after operation. The Ureteroscopy was performed with F8/9.8 ureteroscopy (wolf medical devices, Mount Vernon, Illinois, USA). The holmium laser adopted the recomb laser system (Shanghai, China). The laser pulse energy was set to be 1.0–1.5 J, and the laser beam was 365  $\mu$ m with a frequency of 4–12 Hz. After the operation, all patients had a 30-day ureteral double-J tube retention period.

### Systemic Inflammatory Response Syndrome Criteria

The diagnostic criteria for SIRS were as reported in previous literatures,<sup>18,19</sup> including: (1) temperature  $> 38^{\circ}\text{C}$  or  $< 36^{\circ}\text{C}$ ; (2) Pulse  $> 90$  beats/min; (3) respiratory rate  $> 20$  breaths / min, or arterial carbon dioxide tension  $\text{PaCO}_2 < 32$  mmHg, and (4)  $\text{WBC} > 12 \times 10^9/\text{L}$  or  $\text{WBC} < 3 \times 10^9/\text{L}$ , any two of which can be diagnosed as SIRS.

## Bacterial Culture, Identification, Drug Sensitivity Test

Bacterial culture, identification, and drug susceptibility experiments are assisted in completing the experiment. The blood and clean mid-stage urine were collected and then sent to the laboratory for bacterial culture and identification. The bacterial culture and identification results were collected and then analyzed based on the patient's medical records.

## Statistical Analysis

SPSS 20.0 software was used for statistical analysis. K-S single sample test was used to evaluate whether the data conformed to the normal distribution. The measured data were expressed as mean±SD, with median (min, max) representing the data that do not conform to the normal distribution. Continuous variables with normal and non-normal distributions were analyzed by *t*-test and Mann Whitney *U*-test, respectively. The count data were expressed as percentages (%), and the count data were analyzed by the  $\chi^2$  test or Fisher's exact probability test. The risk factors of SIRS were analyzed by logistic regression, and the regression coefficient ( $\beta$ ), odds ratio (OR), and 95% confidence interval (95% CI) were calculated. The difference was statistically significant ( $P < 0.05$ ).

## Result

### Univariate Analysis of Risk Factors

A total of 293 patients with a mean age of 43.25±16.04 years were included in the study, of whom 129 were females (44.03%), and 164 were males (55.97%), with 52 cases in the infected group and 241 in the non-infected group. The incidence of SIRS after HLULIUC was about 17.75%. The univariate analysis results (see Table 1) showed that ureteral calculi  $\geq 1$ cm ( $P = 0.001$ ), long operation time ( $P < 0.001$ ), diabetes mellitus ( $P < 0.001$ ), increased C-reactive protein ( $P < 0.001$ ), and preoperative positive urine leukocytes ( $P < 0.001$ ) and culture ( $P < 0.001$ ) were risk factors for SIRS after HLULIUC. However, age, BMI, gender, stone location, hypertension, coronary heart disease, white blood cell count, red blood cell count, neutrophil count, hemoglobin, platelet count, lymphocyte count, liver function, and renal function were not risk factors ( $P > 0.05$ ).

### Multivariate Logistic Regression Analysis of Risk Factors

The logistic regression analysis results (see Table 2) showed that ureteral calculi  $\geq 1$ cm (OR=2.839, 95% CI=1.341–5.647,  $P=0.021$ ), long operation time (OR=4.534, 95% CI=2.597–12.751,  $P=0.017$ ), diabetes mellitus (OR=3.137, 95% CI=1.142–7.319,  $P=0.012$ ), increased preoperative C-reactive protein (OR=1.864, 95% CI=1.05–4.347,  $P=0.032$ ), and preoperative positive urine leukocytes (OR=3.514, 95% CI=1.7237–9.734,  $P=0.007$ ) and culture (OR=6.034, 95% CI=3.097–15.751,  $P<0.001$ ) were the risk factors of SIRS after HLULIUC. As shown in Figure 1 and Table 3, the area under the curve of operation time was 0.821, and the sensitivity and specificity were 86.53% and 67.63%, respectively, when the cut-off value was 24.5 min. The area under the curve of C-reactive protein was 0.733, and the sensitivity and specificity were 78.84% and 32.78%, respectively, when the cut-off value was 11.50mg/L.

### Bacterial Composition of Urine and Blood Samples

The results of blood and urine bacterial culture in 51 patients with SIRS were collected (Table 4). Among them, 23 blood samples were positive (45.09%), and 28 urine samples were positive (54.91%). The culture rates of Gram-positive and negative bacteria in urine samples were 32.14% (9/28) and 60.72% (17/28), respectively; and the fungal culture rate was 7.14% (2/28). The main bacteria in urine samples are *Escherichia coli* (39.28%), *Klebsiella pneumonia* (10.71%), *Staphylococcus aureus* (14.26%), *Enterococcus faecalis* (10.71%), and *Pseudomonas aeruginosa* (7.14%). In blood samples, the culture rates of gram-positive and negative bacteria were 30.43% (7/23) and 69.57% (16/23), respectively, and the fungal culture rate was 0%, with the main bacteria of *Escherichia coli* (43.49%), *Klebsiella pneumoniae* (17.39%), *Staphylococcus aureus* (8.69%), *Enterococcus faecalis* (13.05%) and *Pseudomonas aeruginosa* (8.69%).

**Table 1** Univariate Analysis of Risk Factors for SIRS After HLYLIUC

Parameter		SIRS Group (n=52)	Non-SIRS Group (n=241)	P value
Age	≥60	23 (44.23%)	85 (35.27%)	0.224
	<60	29 (55.78%)	156 (64.73%)	
BMI (kg/m <sup>2</sup> )		24.81±4.12	24.25±3.78	0.176
Sex	Male	27 (51.92%)	137 (56.85%)	0.517
	Female	25 (48.08%)	104 (43.15%)	
Stone size	<1cm	20 (38.46%)	151 (62.66%)	0.001
	≥1cm	32 (61.54%)	90 (37.34%)	
Stone location	Upper section	20 (38.46%)	62 (25.72%)	0.104
	Middle section	18 (34.62%)	106 (43.98%)	
	Lower segment	14 (26.92)	75 (31.12%)	
Operation time (min)		40.51±14.21	19.14±8.12	<0.001
Hypertension	Yes	13 (25.00%)	56 (23.24%)	0.786
	No	39 (75.00%)	185 (76.76%)	
Diabetes	Yes	34 (65.38%)	41 (17.01%)	<0.001
	No	18 (34.52%)	200 (82.99%)	
Coronary heart disease	Yes	6 (11.54%)	30 (12.45%)	0.856
	No	46 (88.46%)	211 (87.55%)	
Preoperative urine leukocytes	Positive	32 (61.54%)	53 (21.99%)	<0.001
	Negative	20 (38.46%)	188 (78.01%)	
Preoperative urine culture	Positive	28 (53.85%)	45 (18.67%)	<0.001
	Negative	24 (46.15%)	196 (81.33%)	
White blood cell count		8.02±3.14	6.45±3.54	0.127
Red blood cell count		3.62±0.53	3.78±0.41	0.324
C-reactive protein (mg/L)		21.01±7.12	9.85±8.05	<0.001
Neutrophil count		4.42±2.24	5.12±2.04	0.647
Hemoglobin		113.42±11.32	117±9.79	0.437
Platelet count		152.49±53.67	140.75±69.90	0.538
Lymphocyte count		3.02±0.78	3.22±0.58	0.267
Liver function	Normal	49 (94.24%)	219 (90.87%)	0.432
	Abnormal	3 (5.76%)	22 (9.13%)	
Kidney function	Normal	46 (88.46%)	216 (89.63%)	0.804
	Abnormal	6 (11.54%)	25 (10.37%)	

**Notes:** Preoperative positive urine leukocytes: Urine with more than 5 white blood cells under high power field is positive; Preoperative positive urine culture: Urine bacteria grow harmful bacteria. Kidney function abnormal: glomerular filtration rate 60–90mL / min.

**Abbreviations:** HLULIUC, holmium laser ureteroscopic lithotripsy for impacted ureteral calculi; SIRS, systemic inflammatory response syndrome, BMI: body mass index.

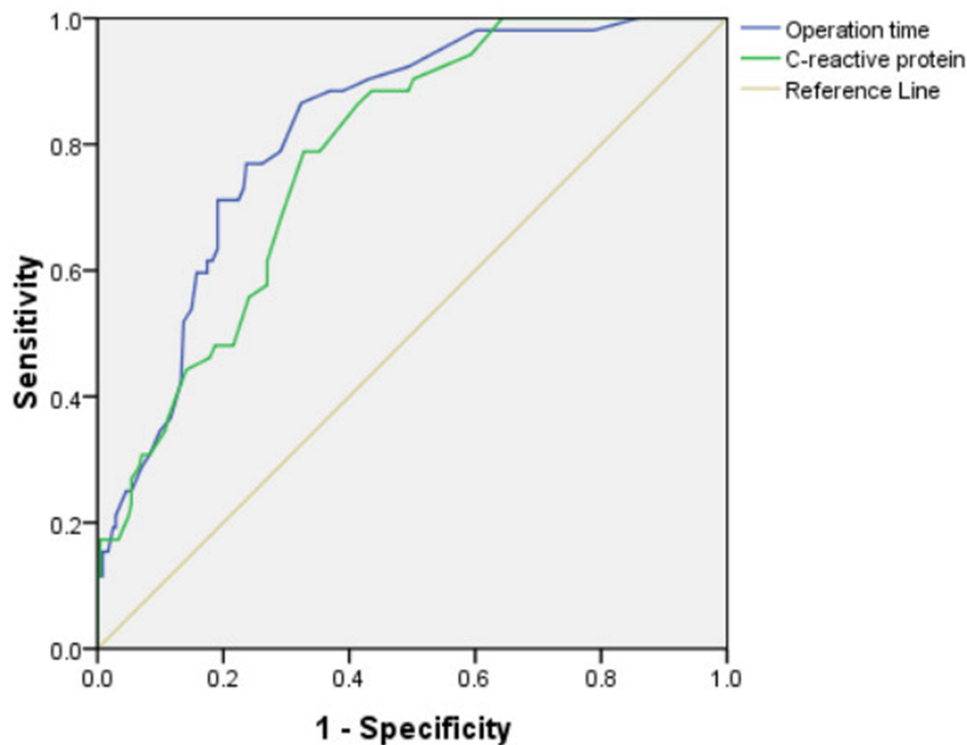
**Table 2** Multivariate Logistic Regression Analysis of Risk Factors for SIRS After HLYLIUC

Risk Factors	β	P value	OR value	95% CI
Stone size≥1cm	1.556	0.021	2.839	1.341–5.647
Operation time	1.927	0.017	4.534	2.597–12.751
Diabetes	1.234	0.012	3.137	1.142–7.319
Positive urine leukocytes before surgery	2.152	0.007	3.514	1.7237–9.734
Positive urine culture before surgery	3.478	<0.001	6.034	3.097–15.751
C-reactive protein	1.372	0.032	1.864	1.025–4.347

**Abbreviation:** HLULIUC, holmium laser ureteroscopic lithotripsy for impacted ureteral calculi.

## Analysis of Bacterial Drug Sensitivity and Drug Resistance

The analysis of bacterial drug sensitivity and drug resistance in patients with SIRS after HLULIUC is shown in Table 5. As can be seen, the main sensitive drugs for gram-positive pathogenic bacteria are vancomycin, linezolid, teicoplanin,



**Figure 1** ROC curve of clinical characteristics in predicting the development of systemic inflammatory response syndrome.

tigecycline, piperacillin/tazobactam, and cefoperazone/sulbactam. The main sensitive drugs for gram-negative pathogenic bacteria include vancomycin, imipenem, meropenem, ceftazidime, aztreonam, piperacillin/tazobactam, and cefoperazone/sulba. Gram-positive and negative pathogens showed strong resistance to penicillin G, ampicillin, compound sulfamethoxazole, levofloxacin, norfloxacin, and the first-third generation cephalosporins (resistance rate > 60%).

## Discussion

SIRS is a common and severe complication of ureteroscopic lithotripsy, with a risk of 5.7–9.7% after HLUL.<sup>20–22</sup> It not only prolongs the patient's hospital stay but also has the possibility of developing into multiple organ dysfunction, endangering the lives of patients.<sup>20–22</sup> Therefore, it is clinically important to clarify the risk factors for SIRS caused by ureteral lithotripsy. In this study, we found that the incidence of SIRS after HLULIUC is about 17.75%, significantly higher than that reported in previous studies.<sup>20–22</sup> This may be because patients with IUC often present with pathological changes of hydronephrosis, infection, and ureteral stricture, which increase the difficulty of the operation and the risk of infection.

Previous studies have shown that operation time and stone size are positively correlated with the occurrence of ureteroscopic lithotripsy complications. Operation time and stone size are risk factors for the complication of infection.<sup>23–26</sup> In this study, we also confirmed that operation time (OR=4.534, 95% CI = 2.597–12.751, P = 0.017) and stone size (OR=2.839, 95% CI=1.341–5.647, P=0.021) were independent risk factors for SIRS caused by HLULIUC. The possible reason for this result is that the larger the IUC, the more difficult the operation and the longer the operation time, gradually increasing the amount of bacteria and endotoxins absorbed into the blood through reflux or pelvic

**Table 3** ROC Curve, Cut-off Value, Sensitivity and Specificity Analysis of Operation Time and C-Reactive Protein

Parameter	Cut-off Value	Specificity	Sensitivity	AUC	95% CI
Operation time	24.5	67.63%	86.53%	0.821	0.765–0.877
C-reactive protein	11.50	32.78%	78.84%	0.733	0.667–0.799

**Table 4** Bacterial Composition of Urine and Blood Samples in Patients with SIRS After HLYLIUC

Urine Pathogens (n=28)	Composition Ratio (%)	Blood Pathogens (n=23)	Composition Ratio (%)
Gram-positive bacteria	9 (32.14%)	Gram-positive bacteria	7 (30.43%)
<i>Staphylococcus aureus</i>	4 (14.26%)	<i>Staphylococcus aureus</i>	2 (8.69%)
<i>Enterococcus faecalis</i>	3 (10.71%)	<i>Enterococcus faecalis</i>	3 (13.05%)
<i>Staphylococcus haemolyticus</i>	1 (3.57%)	<i>Staphylococcus haemolyticus</i>	0 (0%)
<i>Staphylococcus haemolyticus</i>	1 (3.57%)	<i>Staphylococcus haemolyticus</i>	2 (8.69%)
Gram-negative bacteria	17 (60.72%)	Gram-negative bacteria	16 (69.57%)
<i>Escherichia coli</i>	11 (39.28%)	<i>Escherichia coli</i>	10 (43.49%)
<i>Pseudomonas aeruginosa</i>	2 (7.14%)	<i>Pseudomonas aeruginosa</i>	2 (8.69%)
<i>Klebsiella pneumoniae</i>	3 (10.71%)	<i>Klebsiella pneumoniae</i>	4 (17.39%)
Proteus	1 (3.57%)	Proteus	0 (0%)
Fungus	2 (7.14%)	Fungus	0 (0%)
<i>Candida albicans</i>	1 (3.57%)	<i>Candida albicans</i>	0 (0%)
<i>Candida glabrata</i>	1 (3.57%)	<i>Candida glabrata</i>	0 (0%)

**Abbreviations:** HLYLIUC, holmium laser ureteroscopic lithotripsy for impacted ureteral calculi; SIRS, systemic inflammatory response syndrome.

**Table 5** Analysis of Bacterial Drug Sensitivity and Drug Resistance in Patients with SIRS After HLYLIUC

Drug	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>	<i>Enterococcus faecalis</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>
Penicillin G	–	100%	100%	–	–
Ampicillin	88.23%	90.19%	82.35%	84.31%	90.19%
Compound trimethoprim	67.12%	84.31%	90.19%	80.39%	92.16%
Cefazolin	74.31%	80.39%	84.31%	88.23%	88.23%
Ceftriaxone	68.63%	74.51%	66.67%	74.51%	76.47%
Cefepime	52.94%	54.59%	58.82%	56.86%	64.70%
Ciprofloxacin	–	35.29%	25.49%	–	–
Norfloxacin	–	68.62%	54.81%	–	–
Norfloxacin	68.63%	74.51%	60.78%	70.58%	76.47%
Amoxicillin-clavulanic acid	41.04%	56.87%	33.33%	35.29%	49.01%
Piperacillin/ Tazobactam	11.76%	7.84%	9.81%	13.72%	13.72%
Cefoperazone/Sulbactam	28.52%	27.45%	29.41%	17.65%	29.41%
Meropenem	3.92%	–	–	5.88%	9.81%
Imipenem	1.96%	–	–	0%	3.92%
Ceftazidime	9.81%	–	–	7.84%	13.72%
Nitrofurantoin	43.14%	37.25%	31.37%	–	–
Linezolid	–	0%	0%	–	–
Teicoplanin	–	0%	0%	–	–
Vancomycin	0%	0%	0%	0%	0%
Tigecycline	–	0%	0%	–	–
Aztreonam	23.53%	–	–	17.68%	29.41%

**Abbreviations:** HLYLIUC, holmium laser ureteroscopic lithotripsy for impacted ureteral calculi; SIRS, systemic inflammatory response syndrome.

mucosa. Ultimately, the bacteria and endotoxins entering the blood stimulate the body's immune system and cause SIRS. Diabetes, a chronic endocrine and metabolic disease, is a risk factor for various infectious diseases. Diabetic patients typically have weakened immune regulation and defense against external stimuli, which means their risk of postoperative infection is higher.<sup>27</sup> Studies have shown that diabetic patients are more likely to develop SIRS and urosepsis than non-diabetic ones after ureteral calculi.<sup>28,29</sup> In this study, we also confirmed that diabetes (OR=3.137, 95% CI=1.142–7.319, P=0.012) is an independent risk factor for systemic inflammatory response syndrome caused by HLYLIUC.

C-reactive protein (CRP), a special protein produced by the liver, is one of the more recognized reliable and accurate inflammatory response markers.<sup>30</sup> When there is acute and chronic inflammation in the body, the content of CRP increases significantly. At present, most studies suggest that CRP is a risk factor for various infectious diseases.<sup>31</sup> The study by Marco J Schnabel suggests that preoperative CRP helps predict SIRS after percutaneous nephrolithotomy and flexible ureteroscopy.<sup>32</sup> In this study, we also confirmed that preoperative elevated CRP (OR = 1.864, 95% CI = 1.05–4.347, P = 0.032) was an independent risk factor for SIRS after HLULIUC. Previous studies have shown that preoperative urine culture, intraoperative renal pelvic urine culture, and stone culture are risk factors for systemic inflammatory response syndrome caused by flexible ureteroscopy.<sup>33–35</sup> Mi et al suggest that although patients with urinary tract infection are treated with antibiotics before surgery, 9.7% of the patients still have SIRS. The author believes that the possible reason is that the biofilm formed by the bacteria in the stone makes it difficult for antibiotics to kill the bacteria.<sup>36</sup> In this study, we confirmed that both the preoperative urine leukocytes (OR=3.514, 95% CI=1.7237–9.734, P=0.007) and preoperative urine culture results were positive (OR=6.034, 95% CI=3.097–15.751, P <0.001), indicating that the patient's urinary system may be infected and that these two factors are independent risk factors for SIRS after HLULIUC. In ureteroscopic lithotripsy, bacteria and endotoxins in the stones will be released, causing SIRS. Therefore, adequate anti-infective treatment before surgery should be conducted for patients with impacted ureteral calculi as well as positive preoperative urine culture and urine white blood cell.

Current research suggests that the main bacteria causing infection after urinary tract surgery is *Escherichia coli*.<sup>37</sup> In this study, we found that the main pathogens causing SIRS after holmium laser ureteroscopic lithotripsy for impacted ureteral calculi were *Gram-negative bacteria* (blood: 69.57%, urine: 60.72%), and other pathogens were *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa*. In the past, quinolones, represented by levofloxacin, were widely used for preoperative prevention of urinary tract surgery due to their broad antibacterial spectrum, high concentration in urine, and significant antibacterial effect.<sup>38</sup> However, with the wide application of antibiotics in recent years, the drug resistance of urinary pathogens has increased significantly, bringing new challenges to the prevention and treatment of SIRS and sepsis after ureteroscopic surgery.<sup>39</sup> Studies have found that the resistance rate of *Escherichia coli* to quinolone antibacterial drugs is 40–80%, and the rate to second and third generation cephalosporins is as high as 39%–75%.<sup>40–42</sup> In this study, we found that the pathogens of SIRS after HLUL for impacted ureteral calculi showed strong resistance to ampicillin, levofloxacin, penicillin G, compound sulfamethoxazole, the second- and third- generations cephalosporins, and the resistance rate was as high as 52.94% - 90.19%. In addition, we found that these pathogens were sensitive to  $\beta$ -lactam combined with enzyme inhibitors (piperacillin/tazobactam), meropenem, imipenem, vancomycin, teicoplanin, and other antibiotics, and the drug resistance rate was 0%–13.72%. Therefore, we recommend using these antibiotics for anti-infection treatment for severe infection in the absence of drug sensitivity of pathogens.

This study has the following limitations: first, the current research is a retrospective study, meaning that the research design has inherent limitations and biases. Second, this is a small sample, single-center study, so its findings have limited. Third, there are inherent errors and biases in the current study results due to the differences in ethnicity, living environment, and medical conditions. Fourth, the surgical experience and skills of the surgical operators may have a certain impact on the research results. Fifth, this study is a single center study, multi center and large sample study, which needs to be further carried out.

## Conclusion

This study confirmed that ureteral calculi  $\geq 1$ cm, long operation time, diabetes, increased C-reactive protein, and preoperative positive urine leukocytes and culture are independent risk factors of SIRS after HLULIUC. *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa* are the main pathogenic bacteria for SIRS after HLULIUC. These pathogenic bacteria are sensitive to drugs including piperacillin/tazobactam, meropenem, tigecycline, teicoplanin, vancomycin, and imipenem. Most pathogens that cause SIRS are multidrug-resistant and require relevant precautions.

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## Disclosure

The authors declare no competing interests in this work.

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