



# Optimal duration of preoperative antibiotic treatment prior to ureteroscopic lithotripsy to prevent postoperative systemic inflammatory response syndrome in patients presenting with urolithiasis-induced obstructive acute pyelonephritis

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**Purpose:** There is no consensus on the optimal duration of preoperative antibiotic treatment prior to ureteroscopic lithotripsy in patients presenting with urolithiasis-induced obstructive acute pyelonephritis (APN). We aimed to identify surgeon-modifiable, preoperative risk factors associated with postoperative systemic inflammatory response syndrome (SIRS) in these patients.

**Materials and Methods:** This multicenter retrospective study evaluated 115 patients who presented with urolithiasis-induced obstructive APN between January 2008 and December 2019. All patients were administered intravenous third-generation cephalosporin until culture sensitivity confirmation or until ureteroscopic lithotripsy. Data were collected for age, sex, diabetes mellitus, performance status, stone features, hydronephrosis grade, preoperative renal collecting system drainage, laboratory data, operative time, and duration of preoperative antibiotic treatment. Sensitivity analysis using Youden's index and logistic regression analysis were used to assess risk factors of postoperative SIRS.

**Results:** Postoperative SIRS was identified in 32 (27.8%) patients. The incidence of postoperative SIRS was higher in patients who received preoperative antibiotic treatment for fewer than 14 days (38.8% vs. 12.5%;  $p=0.001$ ). Backward variable selection logistic regression analysis revealed maximal stone diameter  $\geq 15$  mm, duration of preoperative antibiotic treatment  $< 14$  days, and preoperative C-reactive protein (CRP) level  $\geq 6.0$  mg/L to be associated with higher risk of postoperative SIRS.

**Conclusions:** Patients with urolithiasis-induced obstructive APN planned for ureteroscopic lithotripsy should be administered at least 14 days of preoperative antibiotic administration and achieve a serum CRP level  $\leq 6.0$  mg/L to minimize the risk of postoperative SIRS.

**Keywords:** Antibiotics; Systemic inflammatory response syndrome; Urinary tract infections; Urolithiasis

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## INTRODUCTION

Urolithiasis-induced obstructive acute pyelonephritis (APN) is a common disease entity that can lead to systemic inflammatory response syndrome (SIRS) and septic shock when not managed within an appropriate time frame [1-3]. Treatment options for urolithiasis include medical expulsive therapy, chemolysis, extracorporeal shock wave lithotripsy (ESWL), and surgical intervention. Among these options, technological advancements in endoscopic instruments have led to increased use of ureteroscopic lithotripsy for treatment of ureteropelvic junction or ureter stones causing obstruction [4]. For patients with concurrent urinary tract infection (UTI), antibiotic treatment with or without drainage and ureteral stent placement or percutaneous nephrostomy (PCN) should be administered prior to ureteroscopic lithotripsy to minimize the risk of postoperative SIRS or sepsis subsequent to preexisting UTI.

Ureteroscopic lithotripsy should be cautiously considered for patients with urolithiasis concurrent with UTI. Increased intra-renal pressure resulting from pressurized intraoperative irrigation may induce bacterial or endotoxin intra-renal reflux and subsequent systemic infection [5-7]. Preoperative decompression with drainage catheters, including ureteral stents or PCNs, may reduce the bacterial toxin load within the renal collecting system and subsequent risk of postoperative SIRS or sepsis [8]. Despite these advantages, drainage catheters are commonly associated with undesirable urinary tract symptoms, namely, flank pain, frequency, urgency, and dysuria. Therefore, minimizing the duration of preoperative drainage is desirable. However, there are no definite guidelines clarifying the optimal durations of preoperative antibiotic administration and drainage in patients with urolithiasis-induced obstructive APN, leaving the appropriate timing of surgical intervention dependent on the urologist [1,9].

It is important to determine the risk factors of SIRS following ureteroscopic lithotripsy. Current evidence has suggested several indicators, including age, sex, diabetes mellitus (DM), performance status, stone size, stone multiplicity, serum C-reactive protein (CRP) level, preoperative culture confirmation, and operative time. In this study, we aimed to identify risk factors of postoperative SIRS in patients with urolithiasis-induced obstructive APN, focusing on surgeon-modifiable factors such as the duration of preoperative drainage and antibiotic treatment.

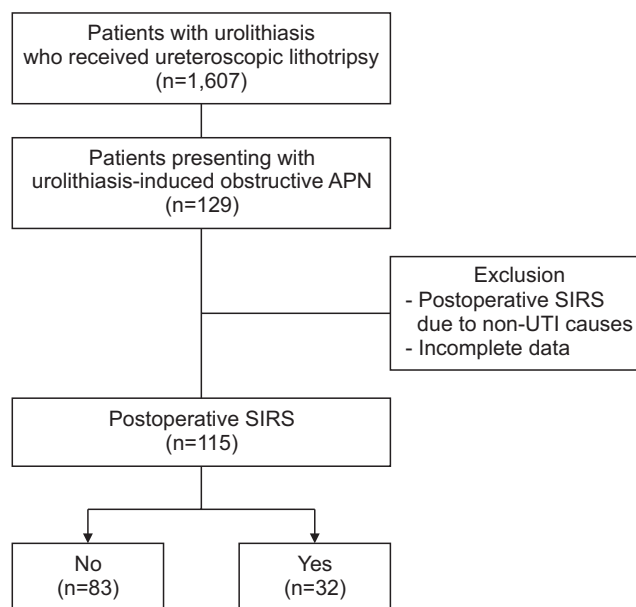


Fig. 1. Study cohort flow diagram. APN, acute pyelonephritis; SIRS, systemic inflammatory response syndrome; UTI, urinary tract infection.

## MATERIALS AND METHODS

### 1. Patient selection

This multicenter retrospective study evaluated data from 1,607 consecutive patients with urolithiasis who received ureteroscopic lithotripsy at Gangnam Severance Hospital (Seoul, Korea) or Dongguk University Gyeongju Hospital (Gyeongju, Korea) between January 2008 and December 2019. Patients with incomplete data and those who experienced postoperative SIRS due to non-UTI causes were excluded. Among these patients, 115 (7.2%) patients who presented with urolithiasis-induced obstructive APN were selected for analysis (Fig. 1). This study was approved by the Institutional Ethics Committee of the Yonsei University Health System, Seoul, Korea (approval number: 2019-0838-001) and all procedures were conducted in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments. The requirement for informed consent was waived for this study as it was based on retrospective, anonymous patient data and did not involve patient intervention or the use of human tissue samples.

### 2. Data collection and definitions

Patient data were collected for sex; age; body mass index; presence of DM; Eastern Cooperative Oncology Group (ECOG) performance status; stone features of maximal diameter, multiplicity, location, and laterality; degree of hydronephrosis; durations of preoperative antibiotic administration and drainage; preoperative laboratory values of hemoglobin,

white blood cell (WBC) count, neutrophil-to-lymphocyte (NLR) ratio, platelet count, creatinine, and CRP; preoperative blood and urine culture sensitivity confirmation; operative time; and incidence of postoperative SIRS or septic shock.

APN was defined based on the presence of related characteristic symptoms, fever higher than 37.8°C, and laboratory data (urine WBC count >5/high-power field). Laboratory tests were performed at initial presentation, the day before surgery, the first postoperative day, and whenever at the discretion of the treating urologist. Stone features were confirmed by computed tomography in all patients. The degree of hydronephrosis was categorized into low (grades 1 and 2) and high (grades 3 and 4) grades according to the system recommended by the Society for Fetal Urology [10]. SIRS was defined as more than two of the following conditions: heart rate >90 beats/min, respiratory rate >20 breaths/min, body temperature >38°C or <36°C, and WBC count >12,000/mm<sup>3</sup> or <4,000/mm<sup>3</sup> or proportion of immature neutrophils ≥10% [11,12].

### 3. Treatments

All patients were administered intravenous third-generation cephalosporin from diagnosis of UTI until urine and blood culture confirmation. Antibiotic susceptibility results were evaluated to consider antibiotic de-escalation or change of antibiotics until ureteroscopic lithotripsy. The decision for infected collecting system drainage at initial presentation was at the discretion of the attending urologist. Drainage was carried out by either retrograde ureteral stent placement or PCN. Hospitalization with intravenous antibiotics was continued until improvements in symptoms and performance status, stabilization of vital signs, and normalization of serum inflammatory values. Antibiotics were administered via intravenous injection during hospitalization, and they were changed to parenteral medication at discharge. Antibiotic treatment was continued during drainage placement and until surgery.

Ureteroscopic lithotripsy was performed using a flexible ureteroscope (Olympus, Tokyo, Japan), a semi-rigid ureteroscope (Richard Wolf GmbH, Knittlingen, Germany), or in combination. In both methods of ureteroscopic lithotripsy, the standard technique began with the placement of a hydrophilic safety guidewire (ZIPwire; Boston Scientific, Marlborough, MA, USA). Retrograde ureteropyelography was performed to exclude preexisting pathological lesions. In all flexible ureteroscopic lithotripsy, after placement of an Amplatz super stiff guidewire (Urowire XF; Boston Scientific), the 11/13-Fr or 12/14-Fr diameter ureteral access sheath (Navigator; Boston Scientific) was used, with a typi-

cal sheath length of 35 cm for female and 46 cm for male.

Stones were fragmented using a holmium yttrium aluminum garnet laser in all cases. Following the procedure, ureteral stents (Boston Scientific) were placed for all patients and removed after 1 to 2 weeks if there were no signs of infection. Operative time was recorded as the time from first endoscope insertion to Foley catheter placement after all procedures.

Postoperative intravenous antibiotics were routinely administered for 24 hours; however, treatments and hospitalization were prolonged when the patients' symptoms and inflammatory serum values suggested SIRS or sepsis. Patients were discharged with parenteral antibiotics at improved performance status, stabilized vital signs, and normalized serum inflammatory values.

### 4. Study endpoints

The primary study endpoint was to identify preoperative predictors of postoperative SIRS in patients initially presenting with urolithiasis-induced obstructive APN. Secondary endpoints were optimal durations of preoperative antibiotic administration and drainage to minimize risk of postoperative SIRS.

### 5. Statistical analysis

Comparisons between groups were assessed by Student's *t*-test for analysis of continuous variables and  $\chi^2$ -test for analysis of two or more variables. Logistic regression analyses were performed to investigate the prognostic significance of maximal stone diameter, duration of preoperative antibiotic treatment, NLR ratio, CRP, and operative time, which were dichotomized at 15 mm, 14 days, 3.0, 6.0 mg/L, and 60 minutes, respectively. These optimal cutoff values were based on sensitivity analyses using Youden's index. Multivariable analysis was performed to adjust for potential confounders. Backward variable selection logistic regression analysis was used to control the number of predictive variables for identifying predictors of postoperative SIRS. Statistical analyses were performed using SAS (version 9.2; SAS Institute, Cary, NC, USA) and R Statistical Package (ver. 3.1.3; Institute for Statistics and Mathematics, Vienna, Austria). All tests were two-tailed, with statistical significance set at a *p*-value <0.05.

## RESULTS

### 1. Baseline characteristics and postoperative systemic inflammatory response syndrome

Patient demographics and stone features of the overall

**Table 1.** Patient demographics and stone features according to postoperative SIRS

Variable	Overall	Postoperative SIRS		p-value
		No	Yes	
No. of patients	115	83 (72.2)	32 (27.8)	NS
Age (y)	65.0 (56.0–76.0)	69.0 (60.0–77.0)	58.5 (47.0–71.0)	0.003
Sex				0.027
Male	30 (26.1)	17 (20.5)	13 (40.6)	
Female	85 (73.9)	66 (79.5)	19 (59.4)	
Body mass index (kg/m <sup>2</sup> )	24.1 (21.8–26.7)	23.9 (21.6–26.7)	24.4 (22.3–27.3)	0.157
Diabetes mellitus	34 (29.6)	25 (30.1)	9 (28.1)	0.834
ECOG performance status (≥1)	22 (19.1)	12 (14.5)	10 (31.3)	0.047
Stone features				
Maximal diameter (mm)	8.2 (6.1–10.7)	7.9 (6.0–9.9)	9.8 (6.2–15.5)	0.043
Multiplicity (≥2)	14 (12.2)	5 (6.0)	9 (28.1)	0.001
Location				0.690
Ureter	96 (83.5)	70 (84.3)	26 (81.3)	
Renal pelvis	19 (16.5)	13 (15.7)	6 (18.8)	
Laterality				0.021
Unilateral	110 (95.7)	82 (98.8)	28 (87.5)	
Bilateral	5 (4.3)	1 (1.2)	4 (12.5)	
Hydronephrosis grade				0.586
≤II	48 (41.7)	32 (38.6)	16 (50.0)	
≥III	67 (58.3)	51 (61.4)	16 (50.0)	
Preoperative drainage type				0.135
PCN	32 (27.8)	27 (32.5)	5 (15.6)	
Ureteral stent	45 (39.1)	32 (38.6)	13 (40.6)	
Preoperative drainage	77 (67.0)	59 (71.1)	18 (56.3)	0.130
Period from APN to surgery (d)	12.0 (5.0–22.0)	15.0 (6.0–28.0)	7.0 (3.0–12.0)	0.027
Preoperative laboratory values				
Hb (g/dL)	12.4 (11.4–13.7)	12.5 (11.4–13.7)	12.2 (11.1–13.8)	0.751
WBC count (μ/L)	11,920 (8,580–16,450)	12,140 (8,643–16,093)	10,430 (7,820–16,840)	0.638
NLR	9.6 (5.0–15.9)	10.0 (5.2–17.0)	8.4 (4.5–14.2)	0.217
Platelet count (10 <sup>4</sup> /μL)	21.7 (15.2–26.5)	21.7 (14.3–24.6)	22.4 (15.8–32.4)	0.036
Cr (mg/dL)	1.1 (0.8–1.6)	1.0 (0.7–1.6)	1.2 (0.8–1.6)	0.686
CRP (mg/L)	98.2 (33.3–175.0)	108.6 (43.5–176.0)	45.5 (17.6–171.1)	0.070
Uropathogens on blood culture				0.504
<i>Escherichia coli</i>	22 (19.1)	18 (21.7)	4 (12.5)	
<i>Proteus mirabilis</i>	4 (3.5)	3 (3.6)	1 (3.1)	
<i>Klebsiella pneumoniae</i>	3 (2.6)	2 (2.4)	1 (3.1)	
Others	3 (2.6)	2 (2.4)	1 (3.1)	
Positive blood culture	32 (27.8)	25 (30.1)	7 (21.9)	0.748
Operative time (min)	45.0 (30.0–65.0)	40.0 (28.0–60.0)	58.5 (40.0–79.3)	0.059

Values are expressed as number only, median (interquartile range), or number (%).

SIRS, systemic inflammatory response syndrome; ECOG, Eastern Cooperative Oncology Group; PCN, percutaneous nephrostomy; APN, acute pyelonephritis; Hb, hemoglobin; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; Cr, creatinine; CRP, C-reactive protein.

cohort and according to postoperative SIRS are presented in Table 1. Among the 115 patients, 32 (27.8%) exhibited postoperative SIRS. Patients who exhibited postoperative SIRS were younger (58.5 y vs. 69.0 y;  $p=0.003$ ), had a higher proportion of ECOG performance status  $\geq 1$  (31.3% vs. 14.5%;  $p=0.047$ ), and had a short period from APN diagnosis to

surgery (7.0 days vs. 15.0 days;  $p=0.027$ ) compared to patients who did not exhibit postoperative SIRS. In both subgroups, the most common uropathogen identified on blood culture was *Escherichia coli*, followed by *Proteus mirabilis* and *Klebsiella pneumoniae*. The two subgroups were comparable in their distributions of classic prognosticators of postoperative

SIRS of DM, preoperative positive blood culture, NLR ratio, CRP levels, and operative time. There was no significant difference in the occurrence of postoperative SIRS according to the type of preoperative drainage ( $p=0.135$ ). There were no cases in which residual stones required secondary ureteroscopic lithotripsy or ESWL.

## 2. Predictors of postoperative systemic inflammatory response syndrome

Univariable and multivariable logistic regression models of predictors of postoperative SIRS are shown in Table 2. Univariable analysis revealed age, male sex, maximal stone diameter  $\geq 15$  mm, stone multiplicity  $\geq 2$ , duration of preoperative antibiotic treatment  $< 14$  days, preoperative NLR  $\geq 3.0$ , CRP  $\geq 6.0$  mg/L, blood or urine culture sensitivity resistance, operative time  $\geq 60$  minutes as independent predictors of postoperative SIRS. Backward variable selection logistic regression analysis revealed maximal stone diameter  $\geq 15$  mm, duration of preoperative antibiotic treatment  $< 14$  days, and preoperative CRP  $\geq 6.0$  mg/L to be independent predictors of postoperative SIRS.

## 3. Subgroup analysis on the rate of postoperative systemic inflammatory response syndrome according to the duration of antibiotic administration and serum C-reactive protein level

The rates of postoperative SIRS were investigated according to subgroups stratified according to the duration of antibiotic administration ( $\geq 14$  days vs.  $< 14$  days) and serum CRP level ( $\geq 6.0$  mg/L vs.  $< 6.0$  mg/L). The incidence of postoperative SIRS was higher in patients who received preoperative antibiotic treatment for fewer than 14 days (38.8% vs. 12.5%;  $p=0.001$ ). Among patients who had received preoperative antibiotic treatment  $\geq 14$  days, no difference was observed in the rate of postoperative SIRS according to CRP level ( $p=0.159$ ). However, among patients with elevated CRP level  $\geq 6$  mg/L, patients who received preoperative antibiotic treatment  $< 14$  days had a significantly higher rate of postoperative SIRS compared to patients who received preoperative antibiotic treatment  $\geq 14$  days (52.2% vs. 28.6%;  $p=0.01$ ). These findings suggest that the duration of preoperative antibiotic treatment may have a relatively higher impact on postoperative SIRS than that of serum CRP level.

## DISCUSSION

Current guidelines on urolithiasis do not clarify the optimal duration of preoperative antibiotic treatment in

patients with urolithiasis-induced obstructive APN who require surgical intervention. Postoperative SIRS has been reported in up to 21.5% of patients in this clinical scenario, warranting investigation of surgeon-modifiable risk factors that can be adjusted to prevent this clinical emergency [1]. In response to this unmet clinical need, we report that preoperative antibiotic treatment with or without drainage should be administered for at least 14 days and surgical intervention should be postponed until serum CRP level reaches 6.0 mg/L to minimize the risk of postoperative SIRS.

Preoperative UTI should be cleared with appropriate antibiotics prior to surgical intervention. Mitsuzuka et al. [13] investigated risk factors associated with postoperative febrile UTI following ureteroscopy for urinary stones, and reported that preoperative pyuria and APN were significant risk factors. The importance of UTI clearance with appropriate antibiotics prior to surgery in patients presenting with sepsis has been consistently highlighted in retrospective studies [14,15]. A matched-pair analysis was performed on patients who underwent ureteroscopic lithotripsy according to the presence of preoperative sepsis [14]. Patients with sepsis had significantly higher complication rates and longer hospital stay compared to those without sepsis, indicating the importance of preoperative UTI clearance. A randomized-controlled study evaluated the feasibility of immediate intervention versus delayed surgical intervention with antibiotic administration and decompression of the collecting system in patients with urolithiasis-induced obstructive sepsis [16]. Although immediate surgical intervention is feasible in terms of surgical results and complication rates, patients who received immediate intervention exhibited longer hospital stay and higher analgesic requirements. Our observation that preoperative antibiotic administration for fewer than 14 days is associated with higher risk of postoperative SIRS is consistent with previous recommendations of antibiotic treatment for 7 to 14 days for uncomplicated UTI and for up to 14 days for complicated UTI such as APN [17]. While contemporary guidelines do not suggest an optimal duration of preoperative antibiotics prior to surgical intervention in patients with obstructive APN, our results imply that 14 days is the minimal timeframe for safe and uncomplicated surgery.

Presence of UTI in an obstructed kidney is a urological emergency, and current guidelines recommend urgent decompression using a ureteral stent or a PCN, which are equally effective [18,19]. There is little evidence regarding the optimal duration of drainage in patients with obstructive APN. Kanno et al. [6] reported the safety of ureteroscopic lithotripsy following a median period of 13.4 days with a

**Table 2.** Association of preoperative risk factors with postoperative SIRS in patients with urolithiasis-induced obstructive APN

Variable	Univariable			Multivariable		
	Odds ratio	95% confidence interval	p-value	Odds ratio	95% confidence interval	p-value
Age	0.959	0.931–0.987	0.005			
Sex (male vs. female)	0.376	0.155–0.911	0.030			
Body mass index	1.078	0.971–1.198	0.160			
Diabetes mellitus (yes vs. no)	1.102	0.447–2.715	0.834			
ECOG performance status (≥1 vs. 0)	2.614	0.994–6.872	0.051			
Stone features						
Maximal diameter (≥15 mm vs. <15 mm)	3.524	1.157–10.740	0.027	32.500	2.434–434.000	0.008
Multiplicity (≥2 vs. 1)	6.104	1.861–20.030	0.003			
Location (ureter vs. renal pelvis)	0.779	0.539–1.126	0.184			
Laterality (bilateral vs. unilateral)	1.004	0.425–2.372	0.994			
Hydronephrosis grade (≥III vs. ≤II)	1.304	0.501–3.397	0.587			
Preoperative drainage (yes vs. no)	1.912	0.822–4.448	0.132			
Preoperative drainage type (PCN vs. ureteral stent)	0.522	0.161–1.692	0.279			
Duration of preoperative antibiotic treatment (<14 days vs. ≥14 days)	4.439	1.655–11.910	0.003	17.190	1.857–159.100	0.012
Preoperative laboratory values						
Hb (<12 g/dL vs. ≥12 g/dL)	1.111	0.443–2.786	0.822			
WBC count (<4,000 μ/L or ≥12,000 μ/L vs. 4,000–12,000 μ/L)	1.227	0.300–5.028	0.776			
NLR (≥3.0 vs. <3.0)	2.706	1.039–7.049	0.042			
Platelet count (<150,000 μ/L vs. ≥150,000 μ/L)	2.232	0.351–14.180	0.395			
Cr (≥1.2 mg/dL vs. <1.2 mg/dL)	2.588	0.914–7.333	0.073			
CRP (≥6.0 mg/L vs. <6.0 mg/L)	8.333	1.046–66.370	0.045	8.812	1.829–42.460	0.007
Positive blood culture (yes vs. no)	0.840	0.290–2.431	0.748			
Culture sensitivity confirmation before surgery (no vs. yes)	3.074	1.049–9.009	0.041			
Operative time (≥60 min vs. <60 min)	2.952	1.260–6.918	0.013			

SIRS, systemic inflammatory response syndrome; APN, acute pyelonephritis; ECOG, Eastern Cooperative Oncology Group; PCN, percutaneous nephrostomy; Hb, hemoglobin; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; Cr, creatinine; CRP, C-reactive protein. Backward variable selection logistic regression analysis was used to control the number of predictive variables for identifying predictors of postoperative SIRS.

ureteral stent or PCN drainage. Herein, postoperative fever or urosepsis was observed in 6% of patients, consistent with contemporary estimates in patients without obstructive APN. Youssef et al. [14] reported a matched-pair analysis to compare outcomes of ureteroscopic lithotripsy according to presence of previous sepsis. The incidence of overall complications was significantly higher in the 1.4% of patients who had sepsis, in which postoperative fever was observed in 7.2%. Herein, the mean duration of ureteral stent drainage in patients who had sepsis was 9.8 days, implying that this period may have been insufficient [14]. The importance of preoperative drainage was highlighted in an observational study in which patients with obstructive UTI sepsis underwent immediate ureteroscopic lithotripsy without drainage [20]. Uncontrollable postoperative sepsis was observed in 10.7% of patients, while success rate was low with 18.9% of patients requiring secondary ESWL. Taken together, these findings suggest preoperative drainage of at least 14 days in patients with obstructive APN for safe surgery.

Studies have highlighted the usefulness of preoperative CRP in prediction of postoperative infectious complications [21-23]. CRP, an inflammation marker, is an acute-phase protein of hepatic origin that increases subsequent to secretion of IL-6 by macrophages and T cells [24,25]. Ganesan et al. [22] reported that CRP was predictive of SIRS following percutaneous nephrolithotomy. In this study, the area under the receiver operating characteristic curves was utilized to set the optimal threshold level of CRP at 6.5 mg/L. This specific cutoff level was comparable to the level of 6.0 mg/L obtained using Youden's index sensitivity analysis in our study, which corroborates the clinical significance of CRP as a prognosticator of postoperative SIRS.

Operative time is generally considered a crucial factor associated with risk of postoperative febrile UTI [22,26]. During ureteroscopic lithotripsy, irrigation fluid increases intrarenal pelvic pressure, and systemic absorption of irrigation fluid containing bacteria or endotoxin through intra-renal reflux may lead to systemic propagation of UTI [26]. Theoretically, risk of postoperative UTI sepsis increases linearly with longer operative time. In our study, maximal stone diameter greater than 15 mm was an indicator of postoperative SIRS, while operative time was only significant in the univariable analysis. Considering that operative time was significantly longer in patients with stones larger than 15 mm, collinearity may have existed between these variables. Nonetheless, based on our results, we recommend that best effort should be made to complete surgery within 60 minutes, and when surpassed, irrigation fluid pressure should be minimized.

Generally accepted risk factors of postoperative SIRS that have not been aforementioned are old age, poor performance status, presence of DM, and stone multiplicity. Older patients are usually less immune-resistant than younger patients and are more likely to harbor multiple underlying diseases. We observed in our study that older male required a longer duration of preoperative antibiotics and drainage for UTI clearance compared to younger male. However, a noteworthy finding of our study was that younger age was associated with an increased risk of postoperative SIRS in the univariable analysis. We presume that this paradoxical observation may be due to a greater distribution of relatively younger patients who received preoperative antibiotics for fewer than 14 days. DM is a known predisposing factor of infection of all types. Notably, DM was not a prognosticator of postoperative SIRS in our study. We presume that strict DM management during preoperative infection control prior to anesthesia approval may have affected our results.

The strengths of this study were incorporation of comprehensive clinical data and the wide range of included potential risk factors. Of note, we focused on risk factors that are surgeon-modifiable, including duration of preoperative antibiotic treatment and preoperative laboratory values, which can be utilized in clinical decision-making. Moreover, the specific cutoff levels of laboratory values were determined by Youden's sensitivity analysis for ease of usability in clinical practice. At the same time, our study is not without limitations. First, data were collected over a long period of time, during which treatment modalities such as flexible ureteroscopes and antibiotics had considerably improved. Therefore, the results obtained from our study may not represent outcomes expected in the current era. Second, our database did not include information on concurrent inflammatory diseases, hematological disorders, or exposure to drugs, which may have affected postoperative SIRS. Third, our study was retrospective in nature, and the results are sensitive to selection bias. Lastly, we did not account for the association between the type of bacterial strains and postoperative SIRS, which may have affected the results. A well-controlled, prospective randomized trial with a larger number of patients is warranted to confirm our findings.

## CONCLUSIONS

Patients with urolithiasis-induced obstructive APN are prone to postoperative SIRS and are candidates for aggressive management. Our study implies that risk of postoperative SIRS can be reduced by performing ureteroscopic lithotripsy after at least 14 days of preoperative antibiotic

administration and when serum CRP level is less than 60 mg/L.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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## AUTHORS' CONTRIBUTIONS

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