

## Research

# The Effect of the Duration between Preoperative Bladder Urine Culture and Semirigid Ureteroscopic Lithotripsy on the Rate of Systemic Inflammatory Response Syndrome Postoperatively

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Received: Apr 27<sup>th</sup>, 2021; Accepted: May 2<sup>nd</sup>, 2021; Published: May 5<sup>th</sup>, 2021

Citation: Akkas F, Sam E, Cinislioglu E, Karabulut I, Yilmazel FK, Sunger U, Atar FA. The effect of the duration between preoperative bladder urine culture and semirigid ureteroscopic lithotripsy on the rate of systemic inflammatory response syndrome postoperatively. *Urology Open A Open J*. 2021; 2(2): 65-69. doi: 10.33169/uro.UOAOJ-2-118

## ABSTRACT

### Purpose

The aim of this study is to analyze the preoperative and intraoperative factors that might induce systemic inflammatory response syndrome (SIRS) after semirigid ureteroscopic lithotripsy (SUL), and to evaluate the impact of duration between preoperative bladder urine culture (PBUC) and surgery on postoperative systemic inflammatory response syndrome (SIRS).

### Methods

A retrospective review was conducted including patients who underwent SUL in our center between June 2015 and June 2020. Prior to surgery, PBUC were obtained from all patients and postoperatively patients were observed for signs of SIRS. Univariable and multivariable binary logistic regression analysis were implemented to demonstrate the factors that predict SIRS postoperatively.

### Results

The entire study included a cohort of 572 patients. The rate of SIRS following SUL was 1.7%. Predictive factors for SIRS were listed as stone volume, surgical time, and history of recurrent urinary tract infection. No significant difference was detected in terms of the duration between PBUC and SUL when comparing the SIRS group with the other group.

### Conclusion

The duration between PBUC and SUL is not efficacious factor for SIRS. It may be useful to conduct prospective studies to enlighten this issue as endourologists deal with this duration dilemma often in daily practice.

**Keywords:** Semirigid ureteroscopic lithotripsy, Systemic inflammatory response syndrome, Preoperative bladder urine culture.

## INTRODUCTION

In the latest European Association of Urology (EAU), a considerable significance is given to methods of endourological treatments as they are more commonly practiced in recent years.<sup>1</sup> Semirigid ureteroscopic

lithotripsy (SUL) is successfully performed in clinical practice. Though urinary tract infections (UTI) ranging in clinical severity from fever to severe urosepsis are the most common complication after endourological stone surgery despite adequate perioperative antimicrobial prophylaxis.<sup>2,3</sup> As stated in EAU and American Urological Association (AUA)

guidelines, preoperative bladder urine culture (PBUC) or urine microscopy should be taken before endourological treatment procedures; yet the timing of PBUC prior to surgery was not specified.<sup>1,4</sup>

In countries with a high prevalence of urinary tract stones, long waiting times for elective stone surgeries are evident in tertiary health care facilities. This lengthens the duration between PBUC and surgical procedures.

In this study, we aim to demonstrate the preoperative and intraoperative factors that may lead to systemic inflammatory response syndrome (SIRS) in the early postoperative period and to determine the impact of the time between PBUC and SUL on the incidence of SIRS.

## MATERIAL AND METHOD

A retrospective evaluation of the data from patients who had SUL between June 2015 and January 2020 for ureteral stones was performed. Patients who underwent SUL following insertion of a double J stent (DJS) or nephrostomy for decompression in obstructive uropathy due to urolithiasis were excluded from the study. The patient cohorts with DJS prior to SUL were identified as those in whom DJSs were inserted for passive dilatation due to the inability to pass the ureteroscope into the target ureter in the first procedure. The clinical data from the second ureteroscopy (URS) was included. Furthermore, patients with positive preoperative PBUC results, patients who had SUL as an adjunctive treatment to simultaneous shock wave lithotripsy (SWL), and patients who underwent SUL as a diagnostic procedure were omitted from the review. Additionally, patients with conditions such as immune suppression, diabetes, preoperative fever and renal failure were excluded from the study as they had a higher risk of developing sepsis.

Preoperatively, PBUC and whole blood analysis were obtained from all patients. Intravenous prophylactic antibiotics (cefazolin or fluoroquinolone) were given during the induction of anesthesia in patients with negative PBUC results prior to surgery. All patients were investigated preoperatively with intravenous urography or non-contrast computed tomography (NCCT).

Patient monitoring was conducted in the urology ward on the day following surgery. Body temperatures of 38°C and above were documented. The presence of two or more of the following was described as SIRS: temperature >38°C or <36°C, heart rate >90 beats/minute, respiratory rate >20/minute, and white cell count >12,000/mm<sup>3</sup> or <4000/mm<sup>3</sup>. From patients with fever or SIRS, blood cultures (BC) and PBUC were collected. The study only included the patients who fulfilled the SIRS criteria in the first week following the surgical procedure.

The study group was separated into two cohorts as the normal group and the SIRS group. A comparison between the groups was made evaluating the demographic characteristics, stone characteristics [number, diameter (mm), volume (mm<sup>3</sup>), density (Hounsfield Unit)], surgical time, length of hospital stay (LOS), presence of previous DJS, history of ipsilateral stone surgery (ISS), preoperative PBUC positivity, history of recurrent urinary tract infection (UTI) and length of time between PBUC and SUL. The recurrent UTI definition provided in the EAU guidelines as at least three UTIs/year or two UTIs in the last six months was used in the study.<sup>5</sup>

All surgeries were performed in the lithotomy position. An 8.0/ 9.8F Karl Storz semirigid ureteroscope was advanced through the

ureter after the insertion of a 0.035-inch polytetrafluoroethylene-coated guidewire (Boston Scientific, Marlborough, Massachusetts). A 200 μm holmium-YAG laser (Lisa laser Sphinx, US) was used for performing laser lithotripsy. The stone fragmentation procedure was ceased when clinically insignificant residual fragments of less than 4 mm in diameter was achieved. In all cases of impacted stones, double J stent (DJS) (4F or 4.7F) was inserted. This decision was made by the urologist in charge of the surgery on the basis of the operation time and the severity of the adjacent ureteral wall edema.

Kidney-ureter-bladder (KUB) radiography was carried out to evaluate the presence of residual stones on the first day following surgery. On postoperative day one following SUL, patients whose DJS position was verified to be normal by KUB radiography with no complications were discharged. An assessment was made at the postoperative first month for DJS removal and at the third postoperative month for review of residual stones with KUB radiography and urinary ultrasound or NCCT scan. A procedure was described as successful if stone-free on the third postoperative month.

Categorical variables are presented by providing numbers and percentages. Descriptive statistics (mean, standard deviation, minimum, median, maximum) are used to define continuous variables. The Shapiro-Wilk test was applied in order to determine if the distribution of continuous variables was normal. A comparison of the mean values of two different groups was made using the independent sample t-test or the Mann-Whitney U test. By utilizing Fisher's exact test, the percentages of the categorical variables were compared. When p-values were <0.05, statistical significance was considered. In an attempt to identify predictors of SIRS, univariable and multivariable binary logistic regression analyses were executed.

## RESULTS

Five hundred and seventy-two patients were included in our study. The patients' demographics and characteristics are presented in (Table 1). The overall stone-free rate was 82.5%. There were 10 patients (1.7%) who met the criteria for SIRS; for the remainder of the patients, there were no infectious complications documented.

In SIRS group; mean stone volume, LOS, surgical time, and the rate of recurrent UTI history were significant. No statistical difference was observed in terms of the duration between PBUC and SUL between the normal groups and the SIRS groups (Table 2).

To evaluate the cut off duration of surgical time for SIRS, the ROC curve analysis was performed. The cut off value for operation time in predicting post-SUL SIRS was 47.5 minutes (The AUC: 0.877; sensitivity 100 %; specificity 78.1 %; 95 % CI: 0.835-0.920).

This study demonstrates the risk factors for SIRS postoperatively that were found significant in univariable analysis as presented in (Table 3). In univariable analysis; stone volume, surgical time, LOS, and the history of recurrent UTI were detected as determinants of SIRS.

As we avoided using stone diameter and volume simultaneously in multivariable analysis, considering these variables strongly correlated with each other, this may lead to multicollinearity issues. LOS was another factor that was not studied in the multivariable analysis. In multivariable analysis, stone volume, surgical time and the history of recurrent UTI were revealed as significant variables (Table 3).

**Table 1.** Demographic data, stone characteristics and clinical variables

Variables	
Number of patients, n(%)	572
Mean age± SD, year	45.5 ± 15.7
Mean BMI ± SD, kg/m2	26.9 ± 3.3
Sex, n(%)	
Male	390 (68.2)
Female	182 (31.8)
ASA, n(%)	
ASA 1	208 (36.4)
ASA 2	304 (53.2)
ASA 3	59 (10.3)
History of ipsilateral stone surgery, n(%)	186 (32.5)
Mean stone number ± SD	1.09 ± 0.37
Mean stone diameter ± SD, mm	11.2 ± 4.7
Mean stone volume ± SD, mm3	271 ± 40
Mean density ± SD, HU	1000 ± 324
Preop DJS, n(%)	63 (11.0)
Mean surgical time ± SD, min.	41.6 ± 10.3
Blood transfusion, n(%)	0 (0)
Mean LOS ± SD, day	1.14 ± 0.68
Preop recurrent UTI, n(%)	51 (8.9)
Stone free rate, n(%)	472 (82.5)
Mean duration between PBUC and SUL ± SD, day	10.3 ± 5.6
Postop SIRS, n(%)	10 (1.7)

SD, standart deviation; BMI, body massindex; ASA, American Society of Anaesthesia; ISS, ipsilateral stone surgery; SWL, shock wave lithotripsy; HU, hounsfield unit; DJS, double J stent; LOS, lenght of stay; UTI, urinary tract infection; PBUC, preoperative bladder urine culture; SUL, semirigid ureteroscopic lithotripsy

**Table 2.** Comparison of patients' characteristics according to SIRS

Variables	Normal group	SIRS group	P value
Number of patients	562	10	
Mean age± SD, year	45.5 ± 15.5	43.6 ± 24.5	0.925‡
Mean BMI ± SD, kg/m2	26.9 ± 3.33	26.8 ± 2.11	0.884†
Sex (female), n(%)	178 (31.7)	4 (40.0)	0.733§
ASA score, n(%)			
ASA1	205 (36.5)	3 (30.0)	0.452§
ASA2	299 (53.3)	5 (50.0)	
ASA3	57 (10.2)	2 (20)	
History of ISS, n(%)	182 (32.4)	4 (40.0)	0.735§
SWL history, n(%)	199 (35.4)	4 (40.0)	0.749§
Mean stone number ± SD	1.09 ± 0.36	1.20 ± 0.63	0.376†
Mean stone diameter ± SD, mm	11.2 ± 4.72	12.0 ± 1.54	0.705†
Mean stone volume ± SD, mm3	270 ± 38.5	356 ± 44.5	<0.001†
Mean HU ± SD	1000 ± 324	969 ± 334	0.760†
Preop DJS, n(%)	61 (10.9)	2 (20)	0.303§
Mean surgical time ± SD, min.	41.4 ± 10.2	54.2 ± 6.19	<0.001†
Mean LOS ± SD, day	1.09 ± 0.40	3.60 ± 3.50	<0.001‡
Postop DJS, n(%)	437 (77.8)	9 (90.0)	0.699§
Preop recurrent UTI, n(%)	47 (8.4)	4 (40.0)	0.008§
Duration between PBUC and SUL ±SD, day	10.2 ± 5.59	11.3 ± 6.3	0.574†

SSD, standart deviation; BMI, body massindex; ASA, American Society of Anaesthesia; ISS, ipsilateral stone surgery; SWL, shock wave lithotripsy; HU, hounsfield unit; DJS, double J stent; LOS, lenght of stay; UTI, urinary tract infection; PBUC, preoperative bladder urine culture; SUL, semirigid ureteroscopic lithotripsy  
† Independent Sample t test  
‡ Mann Whitney u test  
§Fisher Exact test

**Table 3.** To predict SIRS, univariable and multivariable analysis were applied

Variables	Univariable			Multivariable		
	OR	95% CI	P	OR	95% CI	p
Age	0.992	0.953-1.033	0.693			
BMI	0.986	0.814-1.193	0.883			
Sex (female)	1.438	0.401-5.160	0.577			
ASA3	0.477	0.090-2.517	0.383			
History of ISS	0.718	0.200-2.577	0.612			
History of SWL	1.216	0.339-4.360	0.764			
Stone number	1.672	0.520-5.378	0.389			
Stone diameter	1.032	0.879-1.211	0.705			
Stone volume	1.033	1.019-1.046	<0.001	1.046	1.026-1.065	<0.001
HU	1	0.998-1.002	0.759			
Preop DJS	0.499	0.127-1.963	0.32			
Surgical time	1.08	1.036-1.127	<0.001	1.172	1.086-1.265	<0.001
LOS	4.286	2.170-8.466	<0.001			
Postop DJS	2.574	0.323-20.514	0.372			
Preop recurrent UTI	7.305	1.991-26.802	0.003	0.029	0.003-0.263	0.002
Duration between PBUC and SUL	1.031	0.926-1.149	0.573			

SD, standart deviation; BMI, body massindex; ASA, American Society of Anaesthesia; ISS, ipsilateral stone surgery; SWL, shock wave lithotripsy; HU, hounsfield unit; DJS, double J stent; LOS, lenght of stay; UTI, urinary tract infection; PBUC, preoperative bladder urine culture; SUL, semirigid ureteroscopic lithotripsy

## DISCUSSION

SUL is an effective surgical method with high stone-free rate for treating ureteral stones, yet infectious complications are inevitable.<sup>6,7</sup> Infectious complications following URS may lead to an extended period of hospital stay with an impact on the prognosis of patients, increasing the potential risk for multiple organ dysfunction.<sup>7-9</sup> As a result, it is important to prevent infection-related complications in order to minimize morbidity rates. In this study, the incidence of SIRS was 1.7 % which is consistent with the rates stated in previous studies.<sup>10-12</sup>

There are several modifiable and non-modifiable factors mentioned in the literature that may be used as predictors of SIRS. Higher SIRS rates were correlated with larger stone burden, surgical time, infectious stone, irrigation with an increased flow rate, small-caliber UAS, URS preceding after obstructive pyelonephritis, a positive PBUC, and female sex.<sup>7,8,13</sup> Furthermore, history of urologic stone surgery, history of recurrent UTIs, preoperative pyuria, preoperative acute pyelonephritis, hydronephrosis, and the placement of a urethral catheter, DJS or percutaneous nephrostomy were recognized as factors increasing the risk for infectious complications in URS.<sup>14-17</sup> In both univariable and multivariable analysis conducted in our study; stone volume, surgical time, and the history of recurrent UTI were statistically significant predictors for SIRS.

Our research was not able to demonstrate the impact of factors in certain cases such as URS preceding obstructive pyelonephritis, acute pyelonephritis, and hydronephrosis due to the fact that all patients had stone surgery as elective cases. Compared with the non-SIRS group, the female sex rate in the SIRS group was higher, yet the difference was not statistically significant. The presence of DJS preoperatively was not identified as a predictive factor for SIRS in our study. We thought that the reason for this result might be that patients who were placed DJSs due to obstructive uropathy were not included in the study. The only reason for having a DJS preoperatively was passive dilatation in our study. Additionally, this outcome may have occurred as the mean time period for DJS insertion to achieve passive dilatation was less than 21 days.<sup>18</sup>

Stone cultures for prediction of infectious complications following PNL surgery and the management of postoperative antibiotic treatment were found to have an increased value in recent years.<sup>19-21</sup> The current researches revealed samples of preoperative bladder urine to be insufficient in identifying microorganisms surrounding the stone because the fragmented stone cultures were usually different from the stone surface or PBUC.<sup>22</sup>

In contrary to previous studies, no association was shown between renal pelvic urine culture (RPUC), stone culture (SC) and sepsis or SIRS in the study by Koras et al.<sup>23</sup> The common message of all the studies, however, is that intraoperative cultures may be crucial for guidance on antibiotic treatment postoperatively. In a study exploring the association of RPUC and SC with SIRS following URS, it was stated that PBUC was incompatible with RPUC and SC.<sup>9</sup> Reconsideration of the antibiotic therapy according to the results of the RPUC and SC was recommended in cases of postoperative infectious complications.<sup>9</sup> Nevertheless, in that study, 20 out of 23 patients with SIRS had PBUC, RPUC or SC growth, and PBUC, RPUC and SC were observed to be compatible in eight (40%) patients. Furthermore, no growth was observed in RPUC and SC in five (25%) patients, and only PBUC positivity was found; post-

operative antibiotic treatment was adjusted according to the PBUC results. Since RPUC and SC may be considered as time-consuming tests, it is clear that the value of PBUC may never be underestimated.

In countries with a high prevalence of urinary system stone disease in tertiary referral institutions such as our clinic, waiting times are extended in elective stone surgeries such as SUL. This leads to an increase in the duration between PBUC and SUL. The lengthening of this time interval raises questions in the minds of both patients and doctors. Surgeons may become suspicious that as time increases, re-infections may occur in those patients with a risk of UTI. It was shown in our research that the time period between PBUC and SUL was not a predictive factor for SIRS. The outcome revealed in our study may be a result of the fact that factors such as stone volume, surgical time and history of recurrent UTI, identified in the literature as risk factors for infectious complications postoperatively,<sup>8,14,24</sup> were observed more frequently in SIRS patients in comparison to patients with a normal postoperative period. The possible impact of the lengthening the waiting time in the study may have been obscured by these variables.

There are some limitations to our study. The operations were undertaken by urology specialists and residents. Thus, the parameters depending on the operator may be biased. The retrospective design was another limitation of our study.

## CONCLUSION

This study reviews the effect of the waiting time for SUL, taking the lead on the matter in the literature. In conclusion, the duration between PBUC and SUL was not identified to be a variable that could predict SIRS. Prospective studies may be useful for clarifying this issue, frequently encountered by endourologists in daily practice.

## FINANCIAL DISCLOSURE

The authors declared that this study received no financial support.

## CONFLICTS OF INTEREST

None.

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