Urolithiasis (2021) 49:451–456
https://doi.org/10.1007/s00240-021-01245-7

ORIGINAL PAPER

Does the duration between urine culture and percutaneous nephrolithotomy affect the rate of systemic inflammatory response syndrome postoperatively?

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Received: 6 November 2020 / Accepted: 15 January 2021 / Published online: 16 April 2021

Abstract
This study aimed to evaluate the preoperative and intraoperative factors that may cause systemic inflammatory response syndrome (SIRS) after percutaneous nephrolithotomy (PCNL) and to investigate the effect of the duration between urine culture (UC) and operation on postoperative SIRS. Three hundred and fifty-six patients who had PCNL between January 2015 and June 2019 were retrospectively included in the study. UC was obtained from all patients before the operation and during the puncture at the beginning of the operation. Postoperatively, patients were closely monitored for fever and other signs of SIRS. The post-PCNL SIRS incidence was 7%. In univariable and multivariable analyses, the rate of ipsilateral PCNL history, recurrent urinary tract infection (UTI) history, operation time and the length of hospital stay were significant predictive factors for SIRS. The duration between UC and PCNL was not a statistically significant variable in both univariable and multivariable analysis. Our study concluded that the duration between UC and PCNL is not an influential factor for post-PCNL SIRS. Clarifying this issue may be possible with prospective studies in which the effects of factors such as ipsilateral PCNL history and recurrent urinary tract infection history which has been proven to be risk factors for post-PCNL SIRS are restricted.

Keywords Percutaneous nephrolithotomy · Urine culture · Systemic inflammatory response syndrome

Introduction

Percutaneous nephrolithotomy (PCNL) has become the standard treatment for kidney stones larger than 2 cm. Advances in imaging and endourological instrumentation have made PCNL an effective and safe procedure. However, postoperative complications such as fever, systemic inflammatory response syndrome (SIRS) and sepsis may prolong hospital stays and even require intensive care unit support and auxiliary procedures.

The European Association of Urology (EAU) Urolithiasis Guidelines state that the kidney stone culture (SC) taken during surgery can help postoperative antibiotic selection [1]. Although the EAU guidelines state that SC taken during PCNL will help postoperative antibiotic treatment, the American Urological Association (AUA) Guidelines do not make any recommendations on this matter [2]. According to both EAU and AUA guidelines, urine culture (UC) or urine microscopy should be performed before operations for urinary system stones [1, 2]. However, it is not specified how long should be between the UC taken and the operation.

In countries with a high rate of urinary system stone disease, waiting times are prolonged in elective stone surgeries such as PCNL in the tertiary referral institutions. This causes prolongation of the duration between the UC taken before the operation and PCNL.

In this study, we aimed to evaluate the preoperative and intraoperative factors that may cause SIRS after PCNL and to investigate the effect of the duration between UC and operation on post-PCNL SIRS.

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Materials and methods

The ethical review committee of Health Sciences University, Dr. Sadi Konuk Training and Research Hospital approved this study (2019/504). Data of the patients who underwent PCNL for the treatment of renal stones larger than 2 cm between January 2015 and June 2019 at our center were retrospectively reviewed. Patients with factors predisposing to sepsis, such as immunosuppression, diabetes, preoperative fever and renal failure were excluded from the study. At the same time, patients with a history of open pyelolithotomy, a history of spinal cord injury and patients with urinary diversion were excluded from the study.

Preoperatively, all patients were evaluated by UC and whole blood analysis. Patients with positive UC results (100,000 cfu/mL) were treated with antibiotics at least 1 week before the surgery according to the culture antibiogram results and continued until the UC results were negative. Patients with negative preoperative UC results received prophylactic antibiotics (Cephalosporin group 2 or group 3) intravenously at induction of anesthesia and this continued until the nephrostomy tube was removed. Antibiotic choice and dosage were based on surgeon preference. All patients were evaluated preoperatively by intravenous urography or non-contrast spiral tomography to determine stone volume.

Three endourologists performed all surgical procedures. In our clinic, PCNL operations are performed in the supine or prone position depending on the surgeon's preference. Fluoroscopy-guided puncture was performed in both the positions. The peroperative urine sample taken during the puncture was sent for culture. If there was an evidence of infected urine at the time of surgery, a nephrostomy was left in place and antibiotics were given according to the result of UC taken by this puncture. PCNL was delayed until the urine color in nephrostomy becomes clear and the UC becomes steril. Amplatz-type renal dilator set was used for tract dilation and PCNL was performed through 24-Fr amplatz sheath and 19-Fr nepfroscope (Karl Storz GmbH & Co. KG, Tuttlingen, Germany). Lithotripsy was performed with ballistic lithotripter (Vibrolith®, Elmed, Ankara, Turkey). A nephrostomy tube was inserted at the end of all procedures. Decision regarding placement of a double-J stent (DJS) was given by the endourologist who performed the procedure by considering the duration of the intervention and complexity of the case. The DJS was removed 2 weeks after the procedure via a flexible cystoscope.

Patients with stable vital signs and clear urine, the nephrostomy catheter was clamped. The next day, nephrostomy catheters were removed from the patients who had no complaints such as fever or pain. The patients were discharged after 24 h of follow-up.

In the postoperative period, all patients were followed up in the urology service for fever, SIRS and sepsis. Body temperature of 38° C and above was recorded. SIRS was defined by the presence of two or more of the following: > 38 °C or < 36 °C, heart rate > 90 beats/min, respiratory rate > 20/min and white blood cell count > 12,000/mm^3 or < 4000/mm^3. Blood culture (BC) and UC were obtained from those with fever or SIRS. A chest X-ray was taken to exclude atelectasis, the nephrostomy continued to be drained and antibiotics shifted to a BC or UC pattern.

The study group was divided into two as those normal group and SIRS group and these groups are compared in terms of demographic characteristics, stone characteristics [volume (mm^3), density (Hounsfield Unit)] operation time, the presence of previous nephrostomy or DJS, the presence of postoperative DJS, history of ipsilateral PCNL history, history of urinary tract infection (UTI) and duration between UC and PCNL.

Categorical variables were presented by giving numbers and percentages. Mean and standard deviation of continuous variables are presented.The Shapiro–Wilk test was used to determine whether the distribution of continuous variables was normal. The means of two independent groups were compared using the independent sample *t* test or the Mann–Whitney *U* test. The percentages of the categorical variables were compared using the Pearson Chi-square or Fisher's exact test. Statistical significance was considered when p value was < 0.05. ROC curve analysis was performed to determine the cut-off operation time for post-PCNL SIRS. Spearman's correlation coefficient was used to evaluate the correlation between the duration of UC before PCNL and post-PCNL SIRS. Univariable and multivariable analyses were performed to determine predictors of post-PCNL SIRS. Statistical analysis was performed using Statistical Package of Social Sciences version 21 (IBM SPSS Statistics; IBM Corp., Armonk, NY, USA).

Results

This study included 356 patients; 59.3% were males ($n = 219$), while 40.7% were females ($n = 137$). Table 1 lists the patients' demographic and clinical characteristics. SIRS was observed in 25 patients (7%); the remaining patients' postoperative period in terms of infectious complications were normal. Chest radiography of 22 patients (6.1%) who needed intercostal access during PCNL and patients with fever in the postoperative period did not show any chest complications.

The rate of ipsilateral PCNL history, mean operation time, mean length of hospital stay and the rate of recurrent UTI history were statistically higher in SIRS group. The duration between UC and PCNL was not different

Table 1 Demographic and clinical characteristics

Number of patients	356
Mean age ± SD, years	44.3 ± 13.9
Mean BMI ± SD, kg/m^2	26.6 ± 3.1
Sex, *n* (%)	
Male	219 (59.3)
Female	137 (40.7)
ASA score, *n* (%)	
ASA1	123 (36.0)
ASA2	216 (55.2)
ASA3	17 (8.7)
Ipsilateral PCNL history, *n* (%)	45 (12.6)
SWL history, *n* (%)	69 (19.3)
Mean stone number ± SD	1.4 ± 0.8
Mean stone volume ± SD, mm^3	2535 ± 1056
Mean stone density ± SD, HU	1011 ± 321
Indwelling urethral catheter, *n* (%)	17 (4.7)
Preop nephrostomy, *n* (%)	19 (5.3)
Preop dj stent, *n* (%)	12 (3.3)
Mean access number ± SD	1.04 ± 0.19
Interkostal access, *n* (%)	21 (5.8)
Mean operation time ± SD, min	71.4 ± 17.2
Mean LOS ± SD, day	3.55 ± 1.55
Postop dj stent, *n* (%)	44 (12.3)
Stone free rate, *n* (%)	270 (75.8)
Blood transfusion, *n* (%)	11 (3.0)
Preop culture positive UTI, *n* (%)	54 (15.1)
Preop recurrent UTI, *n* (%)	50 (14.0)
Operation under antibiotic supression, *n* (%)	25 (7.0)
Mean duration between UC and PCNL ± SD, days	11.7 ± 4.8

SD standart deviation, *BMI* body mass index, *PCNL* percutaneous nephrolithotomy, *SWL* shock wave lithotripsy, *HU* Hounsfield unit, *LOS* length of stay, *UTI* urinary tract infection

between the normal group and SIRS group. In addition, we compared the groups in terms of the rate of short duration (≤ 10 days) and long duration (> 10 days). The rate of the long duration was observed to be higher in the SIRS group (68 vs %55), but the difference was not statistically significant (Table 2).

We did not observe any statistically significant correlation between the duration of UC before PCNL and post-PCNL SIRS (Table 3). The ROC curve analysis was performed to determine the cut-off duration of operation time for SIRS. The cut-off operation time for predicting post-PCNL SIRS was 83.5 min (The AUC: 0.710; sensitivity 56.0%; specifity 84.9%, 95% CI 0.602–0.818).

In univariable and multivariable analyses, ipsilateral PCNL history, mean operation time, mean length of hospital stay and the rate of preop recurrent UTI were statistically significant for post-PCNL SIRS (Table 4). On the other hand, in both univariable and multivariable analyses, the duration between UC and PCNL was not a predictive factor for post-PCNL SIRS.

Bacteriuria (0.105/mL) developed in three patients (*Escherichia coli* [2], *Proteus mirabilis*) as a result of urine cultures taken from patients with SIRS. In one patient, both urine and blood culture (*Klebsiella pneumoniae*) were positive. In 2 patients, only blood culture positivity (*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) was detected.

The association among the results of the UC before PCNL and the UC taken at the puncture is presented in Fig. 1. The rate of concordance was 55.5% (5/9 patients) in patients who were positive for both UC before PCNL and taken at the puncture in normal group. The consistency was 33.3% (1/3 patients) in the SIRS group.

During the study, four patients (1.1%) developed sepsis. The antibiotic regimen was changed in two patients according to the blood culture and sensitivity test findings, while in 2 patients, the antibiotic regimen was changed according to the UC taken during the puncture and sensitivity findings.

Discussion

Post-PCNL SIRS can be seen in the presence of preoperative sterile UC and the use of prophylactic antibiotics and has been reported to increase up to 20–30% in some series. It has the potential to progress to severe sepsis with 50–60% mortality rates (0–3%) [3–6]. Therefore, minimizing infection-related complications is priority to keep morbidity rates low. In the current study, the incidence of SIRS was 7%. The rate of SIRS in our study was lower than the rates given in the literature. The reason for this may be that patients with factors predisposing to sepsis, such as immunosuppression, diabetes, preoperative fever and renal failure were excluded from the study. However, Rivera et al. reported the rate of SIRS was as 9% in their prospective study [7].

Various modifiable and unchangeable factors have been described in the literature that may affect the rates of SIRS and sepsis after PCNL. Patient's age, diabetes, ipsilateral PCNL history, stone volume, operation time, number of tracts, amount of irrigation fluid, receipt of a blood transfusion, staghorn calculus, presence of nephrostomy, spinal cord injury and urinary diversion were associated with increased rates of sepsis [6–12]. Patients with comorbidities that suppress the immune system, a history of open pyelolithotomy, a history of spinal cord injury and patients with urinary diversion were excluded from our study. The amount of irrigation fluid was not evaluated because it was not included in the variables in our study. Stone volume, number of tracts, receipt of a blood transfusion and presence of nephrostomy did not differ between normal group and SIRS group in our study. The rate of ipsilateral PCNL

Table 2 Comparison of patients' characteristics between normal group and SIRS group

Variables	Normal group	SIRS group	*p* value
Number of patients	331	25	
Mean age ± SD, years	44.3 ± 14.1	44.7 ± 11.3	0.888*
Mean BMI ± SD, kg/m^2	26.7 ± 3.0	26.0 ± 2.5	0.295*
Sex, *n* (%)			
Male	200 (60.4)	19 (76.0)	0.123$^{\&}$
Female	131 (39.6)	6 (24.0)	
ASA score, *n* (%)			
ASA1	114 (34.4)	9 (36.0)	0.509$^{\&}$
ASA2	200 (60.4)	16 (64.00)	
ASA3	17 (5.1)	0 (0)	
Ipsilateral PCNL history, *n* (%)	38 (11.5)	7 (28.0)	0.026$^{¥}$
SWL history, *n* (%)	64 (19.3)	5 (20.0)	1.000$^{¥}$
Mean stone number ± SD	1.44 ± 0.85	1.32 ± 0.55	0.487*
Mean stone volume ± SD, mm^3	2514 ± 1053	2812 ± 1067	0.174*
Mean stone density ± SD, HU	1017 ± 323	936 ± 297	0.226*
Indwelling urethral catheter, *n* (%)	17 (5.1)	0 (0)	0.620$^{¥}$
Preop nephrostomy, *n* (%)	18 (5.4)	1 (4.0)	1.000$^{¥}$
Preop dj stent, *n* (%)	9 (2.7)	3 (12.0)	0.044$^{¥}$
Mean access number ± SD	1.03 ± 0.18	1.08 ± 0.27	0.290$^{\#}$
Interkostal access, *n* (%)	18 (5.4)	4 (16.0)	0.058$^{¥}$
Mean operation time ± SD, min	69.7 ± 16.4	94.4 ± 8.3	< 0.001$^{\#}$
Mean LOS ± SD, days	3.41 ± 1.46	5.16 ± 1.74	< 0.001*
Postop dj stent, *n* (%)	39 (11.8)	5 (20.0)	0.215$^{¥}$
Blood transfusion, *n* (%)	10 (3.2)	1 (4.0)	0.562$^{¥}$
Preop culture positive UTI, *n* (%)	49 (14.8)	5 (20.0)	0.560$^{¥}$
Preop recurrent UTI, *n* (%)	41 (12.4)	9 (36.0)	0.004$^{¥}$
Duration between UC and operation ± SD, days	11.9 ± 5.2	10.4 ± 5.6	0.169$^{\#}$
Groups according to duration, *n* (%)			
≤ 10 days	149 (45.0)	8 (32.0)	0.206$^{\&}$
> 10 days	182 (55.0)	17 (68.0)	

SD standard deviation, *BMI* body mass index, *ASA* American Society of Anaesthesia, *PCNL* percutaneous nephrolithotomy, *SWL* shock wave lithotripsy, *HU* Hounsfield unit, *LOS* length of stay, *UTI* urinary tract infection

*Independent sample *t* test, $^{\#}$Mann Whitney *U* test, $^{\&}$Pearson Chi-square, $^{¥}$Fisher exact test

Table 3 The association between the duration of UC between PCNL and post-PCNL SIRS

Sperman's rho*		Duration between UC and PCNL
Post-PCNL SIRS	CC	− 0.047
	Sig. (2-tailed)	0.373

CC correlation coefficient, *PCNL* percutaneous nephrolithotomy, *UC* urine culture

history, the rate of recurrent UTI history, the length of hospital stay and operation time were significantly higher in SIRS group in both univariable and multivariable analyses. Ipsilateral PCNL history, recurrent UTI history and operation time were factors that have been previously proven in the literature [11–14]. Aoran et all.'s study shows that PCNL operations exceeding 90 min increase the risk of infection [15]. In our study, we determined the cut-off value for post-PCNL SIRS as 83.5 min. This value is similar to the studies about this subject. Length of stay in hospital was determined as a predictive factor for SIRS after PCNL, but this prolongation may also be due to the development of postoperative infectious complications. It is known that infections developing after PCNL were related to increased postoperative morbidity and mortality, prolongation of hospital stay, decreased patient comfort and increased healthcare costs [12]. It is normal to attribute infections to surgery in the hospital after PCNL, as in all endourological surgeries. However, it should be kept in mind that urinary tract infection is among the

Table 4 To predict post-PCNL SIRS, univariable analysis and multivarible binary logistic resgression test were applied

	Univariable			Multivariable		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age (years)	1.002	0.973–1.032	0.888			
Gender (female)	0.482	0.188–1.239	0.130			
BMI (kg/m^2)	0.926	0.803–1.069	0.293			
ASA score	1.013	0.434–2.367	0.976			
History of PCNL	2.999	1.176–7.647	0.022	4.019	1.352–11.944	0.012
History of SWL	1.043	0.377–2.884	0.935			
Stone number	0.816	0.460–1.449	0.488			
Stone volume	1.000	1.000–1.001	0.176			
Hounsfield unite	0.999	0.998–1.000	0.227			
Urethral catheter	0.0	0.0 – NA	0.998			
Preop nephrostomy	0.725	0.093–5.662	0.759			
Preop dj stent	4.879	1.232–19.319	0.024			
Access number	2.268	0.479–10.747	0.302			
Interkostal access	3.312	1.028–10.672	0.045			
OT > 83.5 min	6.088	2.628–14.107	< 0.001	4.204	1.614–10.949	0.003
LOS	1.739	1.392–2.172	< 0.001	1.567	1.222–2.010	< 0.001
Postop dj stent	1.872	0.665–5.271	0.235			
Blood transfusion	0.759	0.093–6.192	0.797			
Preop culture positive UTI	1.439	0.516–4.016	0.487			
Preop recurrent UTI	3.979	1.651–9.589	0.002	3.239	1.147–9.150	0.027
Duration between UC and operation	0.946	0.874–1.024	0.172			

OR odds ratio, *CI* confidence interval, *BMI* body mass index, *ASA* American Society of Anaesthesia, *PCNL* percutaneous nephrolithotomy, *SWL* shock wave lithotripsy, *NA* not available, *HU* Hounsfield unit, *LOS* length of stay, *UTI* urinary tract infection

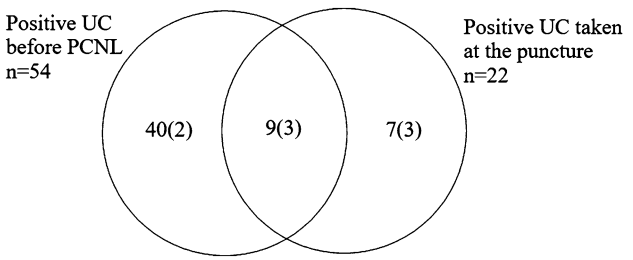

Fig. 1 The association between the positive results of the UC before PCNL and taken at the puncture

most common nosocomial infections and strongly associated with increased morbidity, length of stay and hospital costs [16, 17].

In addition to the variables mentioned in the literature, the duration between UC and PCNL were compared between SIRS group with others. After the investigation of the duration between UC and PCNL, which is a variable that has not been discussed in the literature until now, it was observed that infectious complications were not increased as the duration increased.

According to both EAU and AUA guidelines, it was stated that a sterile UC result should be seen before urinary system stone surgery, but how long should be between UC and operation was not explained. There is no study in the literature examining this issue. Our study shows the feature of being the first study on this subject. The prolongation of waiting time for PCNL may increase the probability of post-PCNL SIRS. The result determined in our study may be due to the fact that factors such as surgical time, history of recurrent urinary tract infection and operation history, which are known to be risk factors for infectious complications postoperatively in the literature [11–14], were observed more frequently in patients with SIRS compared to patients who had normal postoperative period. These factors may have masked the potential effect of the prolongation of waiting time in the study. We think that there is a need for prospective studies on this subject for PCNL and similar studies should be done for flexible ureteroscopy and semirigid ureteroscopy operations.

Our study has some limitations while evaluating its findings. The surgeries were performed by three endourologists. Thus, the operator-dependent parameters can be biased. However, it should be noted that all endourologists were at the same level of experience and all of them complied with

the study protocol. Another limitation of our study was the retrospective design. As an additional limitation, this study reflects the experience of a single center.

Conclusion

This study is the first study investigating the effect of waiting time for PCNL in the literature. Our study shows that increasing the duration between UC and PCNL did not influence the rate of post-PCNL SIRS. Apart from variables known to as risk factors for post-PCNL SIRS such as the history of ipsilateral PCNL history, recurrent UTI history and operation time, it should be kept in mind that increased hospital stay may be a risk factor.

Acknowledgements The investigators would like to thank all the patients who participated in this study. The authors have no direct or indirect commercial financial incentive associated with publishing the manuscript. All the co-authors participated equally in writing of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no confict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the insti tutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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