

Diagnostic Value of Intraoperative Stone and Pelvic Urine Culture Versus Preoperative Urine Culture in the Prediction of Postoperative Systemic Inflammatory Response Syndrome in Percutaneous Nephrolithotomy: A Prospective Study in a Tertiary Hospital

Marc Vincent T. Trinidad, MD and Joseph Michael Ursua, MD, FPUA

Department of Urology, East Avenue Medical Center

Objective: To compare the value of intraoperative stone culture (IOSC) and intraoperative pelvic urine culture (IOPUC) versus pre-operative urine culture (POBUC) in the early detection of systemic inflammatory response syndrome (SIRS) in patients undergoing percutaneous nephrolithotomy (PCNL).

Methods: This is a prospective clinical study which includes all adult patients undergoing PCNL. All patients who were operated on should have a negative preoperative urine culture (POBUC) results. Intraoperative pelvic urine culture (IOPUC) and stone culture (IOSC) were extracted and results were interpreted if they were contributory in acquiring SIRS post operatively.

Results: The demographics of each patient such as age, sex, having diabetes, laterality, location of calculi had no correlation to the development of SIRS. Patients with positive IOPUC and IOSC results yielded a significant value with odds of having SIRS 4.71 and 13.74, respectively.

Conclusion: In the study, all patients underwent PCNL with negative preoperative urine culture findings. Having intraoperative cultures, IOPUC and IOSC, can definitely help predict the occurrence of SIRS and ultimately be one step ahead in the management of these patients to decrease overall morbidity and mortality.

Keywords: percutaneous nephrolithotomy; post-operative systemic inflammatory response syndrome

Introduction

Percutaneous nephrolithotomy (PCNL) is the primary surgical intervention of choice in patients with large nephrolithiasis or staghorn calculi. Based on the 2019 European Association of Urology (EAU) guidelines, PCNL is the procedure of choice for patients with renal stones measuring >2 cm, multiple renal stones, failed extracorporeal shock wave lithotripsy, and <2 cm renal stones in lower calyx with narrow infundibulopelvic angle.¹ PCNL

is considered to be a safe procedure. However, complications may arise such as intraoperative bleeding, injury to other organs, pneumothorax, pneumoperitoneum, and infection.² Obstructions in the genito-urinary tract due to urolithiasis, tumor, strictures and stenosis, as well manipulation with urological instruments can result in urosepsis.^{3,4,5} In PCNL, there is manipulation of the genitourinary tract which can lead to the spread of the bacteria from the urine and urolithiasis which can ultimately lead to urosepsis. As a precautionary measure, urine

cultures and urinalysis are usually done prior to any urologic procedure. Giving prophylactic antibiotics is in accordance with the Infectious Disease Society of America and European Society of Clinical Microbiology and Infectious Disease Guidelines.^{6,7}

The authors hypothesized that having an intraoperative pelvic urine culture (IOPUC) and intraoperative stone culture (IOSC) will better predict the occurrence of systemic infection (SIRS) in patients who will undergo PCNL compared to a preoperative bladder urine culture (POBUC) alone - which is a more common practice.

This study aims to compare the value of IOSC and IOPUC versus POBUC alone in the early detection of SIRS in patients undergoing PCNL. This could potentially aid urologists in the early diagnosis and treatment of SIRS in patients undergoing PCNL to lower patient morbidity and mortality.

Methods

This was a prospective study that determined the value of performing IOPUC and IOSC in predicting postoperative systemic inflammatory response syndrome in patients scheduled for percutaneous nephrolithotomy (PCNL) in a tertiary center. Patients 18 years old and above who were admitted in East Avenue Medical Center and underwent PCNL from January to July 2019 were included in the study. Patients underwent PCNL only when they had negative POBUC results. Patients with positive POBUC were treated initially with intravenous antibiotics based on the results of the culture and sensitivity prior to PCNL. Patients with incomplete culture results were not included in the study.

All patients received general endotracheal anesthesia and proper asepsis/antisepsis techniques were done prior to operation. These patients underwent video cystoscopy and cannulation of ureterovesical opening using a 0.035-inch guidewire. A sterile French 6 open-ended catheter was placed through the use of the guidewire until the tip was at the collecting system.

Patients were put on prone position and strict asepsis and antisepsis technique was performed. Intraoperative urine culture was done by using a sterile aspirating needle to puncture the pelvocalyceal system under ultrasound and fluoroscopy guidance.

The urine specimen was sent straight to the laboratory for culture and sensitivity analysis.

Serial dilatations of the tract were done using sterile dilators up to French 30 size. An Amplatz sheath was placed under ultrasound or fluoroscopy guidance. Nephroscopy was then performed and lithotripsy of stones was done under low pressure irrigation using normal saline solution. Stone fragments were then collected for stone culture and sensitivity (IOSC).

All patients underwent double-J stent and nephrostomy tube insertion. Postoperatively patients were closely monitored for signs of SIRS, defined here to be the presence of two or more of the following: temperature $>38^{\circ}\text{C}$, $<36^{\circ}\text{C}$, heart rate >90 beats/min, respiratory rate >20 /minute or $\text{PaCO}_2 <32\text{mmHg}$, white blood cell count $>12000/\text{mm}^3$ or $<4000/\text{mm}^3$. Blood cultures were drawn in all patients who met SIRS criteria. Nephrostomy tubes were removed prior to discharge depending on the drainage, symptoms and when an antegrade nephrostogram revealed free drainage of urine from the collecting system down to the urinary bladder.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Independent Sample T-test, Mann-Whitney U test and Fisher's Exact/Chi-square test were used to determine the difference of mean, rank and frequency, respectively. Odds ratio and corresponding 95% confidence intervals from binary logistic regression were computed to determine which factors were related to SIRS. All statistical tests were two-tailed. Shapiro-Wilk test was used to test the normality of the continuous variables. Missing variables were neither replaced nor estimated. The null hypothesis was rejected at 0.05 α -level of significance. STATA 13.1 was used for data analysis.

Results

A total of 91 patients underwent PCNL from January 1 to July 31, 2019 and 83 patients were

included in the study. The mean age of these patients was 52.88, with the total of 37 male patients (44.58%) and 46 female patients (55.42%). There was no significant difference between the demographic data of the patients who developed SIRS compared to those who did not (Table 1). Twenty-four patients had positive pre-operative urine culture results and were treated prior to the procedure. Among these patients, 28 (41.18%) had positive IOPUC and 20 (32.26%) patients had positive IOSC results.

Twenty-five patients were diagnosed to have SIRS postoperatively, 14 of whom had positive IOPUC and 13 had positive IOSC results. The diagnostic accuracy of POBUC compared to SIRS was 69.88% with negative predictive value of 69.88% (Table 2). The diagnostic accuracy of IOPUC was 69.12% with a positive predictive value of 50% and negative predictive value of 82.50% (Table 3). Majority of patients who had positive IOPUC

were diagnosed with SIRS (66.67%) compared with patients who had positive IOPUC but did not develop SIRS (29.79%). IOSC had a diagnostic accuracy of 80.65% with a positive predictive value of 65% and negative predictive value of 88.1% (Table 4). Majority of patients who had positive IOSC had SIRS (72.22%) compared with patients who had positive IOSC but did not have SIRS (15.91%). The overall probability that the patient will be correctly classified was 80.65% for IOSC.

Majority of patients (55 total) were given pre-operative Ceftriaxone 1g intravenously. It was also shown that for every day increase in days post op, the odds of having SIRS increased by 14% (Table 5). Age, sex, having diabetes, laterality, location of calculi had no correlation to the development of SIRS. Patients with positive IOPUC and IOSC had significantly high odds of having SIRS (4.71 and 13.74, respectively).

Table 1. Demographic and clinical profile of the patients.

	Total (n=83)	With SIRS (n=25)	Without SIRS (n=58)	p-value
	Frequency (%); Mean + SD; Median (IQR)			
Age	52.88 ± 11.52	54.84 ± 10.46	52.03 ± 11.93	0.312
Sex				0.945
Male	37 (44.58)	11 (44)	26 (44.83)	
Female	46 (55.42)	14 (56)	32 (55.17)	
With Diabetes	16 (19.28)	7 (28)	9 (15.52)	0.186
Laterality				
Right	40 (48.19)	12 (48)	28 (48.28)	0.982
Left	45 (54.22)	14 (56)	31 (53.45)	0.830
Calculi				0.551
Nephrolithiasis	40 (48.19)	14 (56)	26 (44.83)	
Staghorn	42 (50.60)	11 (44)	31 (53.45)	
Ureterolithiasis	1 (1.20)	0	1 (1.72)	
Nephrostomy	83 (100)	25 (100)	58 (100)	-
Stent	70 (83.34)	21 (84)	49 (84.48)	0.956
Blood transfusion	5 (6.02)	2 (8)	3 (5.17)	0.619
Days post op	5 (4 to 8)	6 (4 to 13)	5 (4 to 7)	0.084
POBUC	0	0	0	-
IOPUC	28 (41.18)	14 (66.67)	14 (29.79)	0.007
IOSC	20 (32.26)	13 (72.22)	7 (15.91)	<0.001
On ceftriaxone	55 (66.27)	12 (48)	43 (74.14)	0.025

Table 2. Diagnostic accuracy of POBUC compared to SIRS result.

		SIRS		
		Positive Frequency (%)	Negative	Total
POBUC	Positive	0	0	0
	Negative	25 (100)	58 (100)	83 (100)
	Total	25 (100)	58 (100)	83 (100)
Sensitivity	0% (0% to 13.72%)		Positive LR	-
Specificity	100% (93.84% to 100%)		Negative LR	1.00
PPV	-		Prevalence	30.12% (20.53% to 41.18%)
NPV	69.88%		Accuracy	69.88%

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

Table 3. Diagnostic accuracy of IOPUC compared to SIRS result.

		SIRS		
		Positive Frequency (%)	Negative	Total
IOPUC	Positive	14 (66.67)	14 (29.79)	28 (41.18)
	Negative	7 (33.33)	33 (70.21)	40 (58.82)
	Total	21 (100)	47 (100)	68 (100)
Sensitivity	66.67% (43.03% - 85.41%)		Positive LR	2.24 (1.31 - 3.81)
Specificity	70.21% (55.11% - 82.66%)		Negative LR	0.47 (0.25 - 0.89)
PPV	50% (36.98% - 63.02%)		Prevalence	29.03% (18.2% - 41.95%)
NPV	82.50% (71.46% - 89.88%)		Accuracy	69.12%

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio

Table 4. Diagnostic accuracy of IOSC compared to SIRS result.

		SIRS		
		Positive Frequency (%)	Negative	Total
IOSC	Positive	13 (72.22)	7 (15.91)	20 (32.26)
	Negative	5 (27.78)	37 (84.09)	42 (67.74)
	Total	18 (100)	44 (100)	62 (100)
Sensitivity	72.22% (46.52% - 90.31%)		Positive LR	4.54 (2.17 - 9.49)
Specificity	84.09% (69.93% - 93.36%)		Negative LR	0.33 (0.16 - 0.70)
PPV	65% (47.05% - 79.52%)		Prevalence	29.03% (18.2% - 41.95%)
NPV	88.1% (77.65% - 94.03%)		Accuracy	80.65%

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

Table 5. Predictors of SIRS.

Parameter	Crude Odds ratio	95% CI	p-value
Age	1.02	0.98 - 1.06	0.308
Sex			
Male	(reference)	-	-
Female	1.03	0.40 - 2.66	0.945
With Diabetes	2.12	0.69 - 6.53	0.192
Laterality			
Right	0.99	0.39 - 2.53	0.982
Left	1.11	0.43 - 2.85	0.831
Calculi			
Nephrolithias	(reference)	-	-
Staghorn	0.66	0.26 - 1.70	0.388
Ureterolithiasis	-	-	-
Nephrostomy	-	-	-
Stent	0.96	0.27 - 3.48	0.956
Blood transfusion	1.59	0.25 - 10.18	0.622
Days post op	1.14	1.03 - 1.28	0.015
POBUC	-	-	-

Discussion

PCNL is a procedure that is performed only on patients with negative urine bladder culture preoperatively.⁸ Patients positive for any infection will be treated accordingly based on the results of the urine culture. However, there have been instances wherein preoperative urine cultures were negative but intraoperative pelvic urine and stone cultures were positive. Infected urine may develop into SIRS which could then lead to increase in hospital stay and longer antibiotics use. Even with proper treatment and preparation of patients, there will be risk for the development of post-operative urinary infections. The value of doing IOSC and IOPUC was validated in the current study with a diagnostic accuracy of 80.65% and 69.12% respectively.

According to Korets, et al. negative preoperative urine culture may be caused by extended antibiotic use. Therefore, his study recommends doing both IOPUC and IOSC to identify the specific causative organism and direct antimicrobial therapy.^{8,9} Compared to preoperative cultures, intraoperatively cultures are deemed more predictive of SIRS. In a report by Dogan, et al. postoperative SIRS developed

in 57.3% of patients with positive IOSC compared to only 26.6% who did not.¹⁰ Margel, et al. found that patients with positive IOSC had a 3.6% relative risk for the development of SIRS.¹¹ In the present study, patients with positive IOPUC had 4.71 odds of having SIRS while patients with positive IOSC culture had 13.74 odds of having SIRS.

Among those undergoing PCNL, populations who are at high risk of developing SIRS can be identified - patients with staghorn calculi, abnormal anatomy and diabetes, and immunocompromised patients. In the study of Mariappan, et al. large stones and dilated pelvocalyceal systems were seen as possible predictors of urosepsis.^{11,12} Although the results in the current study showed no significant correlation between patient demographics and location of stone and laterality, future studies with bigger population may yield better results.

Conclusion

The study showed that having an IOPUC and IOSC can predict SIRS in the post-operative period. The authors recommend routine IOPUC and IOSC for patients undergoing PCNL.

References

1. Turk C, Skolarikos A, et al. EAU Guidelines on Urolithiasis. EAU Guidelines 2019. 2019; 1-88.
2. Wein A, Kavoussi L, Partin A, Peters C. (editors). Campbell-Walsh Urology. Surgical Management of Upper Urinary Tract Calculi. 11th ed, Elsevier, Inc. 2016; 1276-82.
3. Singer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016; 315: 801.
4. Dellinger RP, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 2013; 39: 165.
5. Scotland K, Lange D. Prevention and management of urosepsis triggered by ureteroscopy. Res Rep Urol 2018; 10: 43–9.
6. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, Soper DE. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011; 52(5): e103–e120.
7. Liang C, et al. Systemic inflammatory response syndrome after percutaneous nephrolithotomy: An assessment of risk factors. Int J Urol 2008; 15: 1025-8.
8. Korets R, Graversen JA, Kates M, Mues AC, Gupta M. Post-percutaneous nephrolithotomy systemic inflammatory response: A prospective analysis of preoperative urine, renal pelvic urine and stone cultures. J Urol 2011; 186(5): 1899–903.
9. Margel D, Ehrlich Y, Brown N, Lask D, Livne PM, Lifshitz, DA. Clinical implication of routine stone culture in percutaneous nephrolithotomy—a prospective study. Urol 2006; 67(1): 26–9.
10. Dogan HS, Guliyev F, Cetinkaya YS, et al. Importance of microbiological evaluation in management of infectious complications following percutaneous nephrolithotomy. Int Urol Nephrol 2007; 39: 737.
11. Paonessa JE, Gnessin E, Bhojani N, Williams JC, Lingeman, JE. Preoperative bladder urine culture as a predictor of intraoperative stone culture results: Clinical implications and relationship to stone composition. J Urol 2016; 196(3): 769–74.
12. Mariappan P, Smith G, Bariol S, Moussa S, Tolley D. (2005). Stone and pelvic urine culture and sensitivity are better than bladder urine as predictors of urosepsis following percutaneous nephrolithotomy: A prospective clinical study. J Urol 2005; 173(5): 1610–4.