Original Article

Factors associated with urosepsis following percutaneous nephrolithotomy

Krit Santanapipatkul

Division of Urology, Department of Surgery, Loei Hospital, Loei, Thailand

Keywords:
Factor, PCNL, urosepsis, staghorn stone, pelvic urine culture

Abstract

Objective: To evaluate factors associated with urosepsis after percutaneous nephrolithotomy (PCNL).

Materials and Methods: Seventy-six upper tract urinary calculi patients underwent PCNL at Loei Hospital between July 2014 to January 2019, all were enrolled onto the study. The following data were collected: demographics, type and size of stone, intraoperative data, pelvic urine culture and urosepsis complications after the procedure. Association of factors with urosepsis after PNCL were identified using a binary logistic regression model with a bootstrap estimation.

Results: Urosepsis complications occurred in 7 patients (9.2%). Mean (SD) of age was 54.4 (10.3) years. Of all patients, 2% with staghorn stone and 22% positive urine culture. Multivariable analysis indicated that staghorn stone (a OR =6.75; 95%CI: 1.59-28.63, p=0.01) and positive pelvic urine culture (a OR =7.51; 95%CI: 1.35-41.77, p=0.02) were associated with urosepsis after PCNL.

Conclusion: There was no mortality after PCNL in this study. Staghorn stone and positive pelvic urine culture may be associated with an increased risk of urosepsis complication.

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Corresponding author: Krit Santanapipatkul
Address: Division of Urology, Department of Surgery, Loei Hospital, Loei 42000, Thailand
E-mail: jozaeuro@yahoo.com
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Introduction

Urolithiasis is one of the most problematic health issues worldwide. Loei Hospital encounters many patients with urolithiasis. There are multiple modalities to treat stones, one of which is percutaneous nephrolithotomy (PCNL). PCNL is the treatment of choice for large upper urinary tract stones.

PCNL is a safe, minimally invasive procedure, in comparison to open surgery; however, some patients may develop complications including fever, hemorrhage, urosepsis or death after PCNL. Urosepsis occurred in only 1% of cases but mortality in these cases was high at 66-80%[1]. Rashid concluded that risk factors for sepsis after PCNL were number of stones, operative time, intraoperative bleeding and presence of residual stones[2]; these findings differed from those reported by Basal et al who found that stone size more than 2.5 cm and intraoperative hemorrhage requiring transfusion were the risk factors[3].

No conclusions about risk factors for sepsis after PCNL have been drawn to date. This study was conducted with the aim of identifying risk of post-PCNL sepsis in Loei Hospital.

Materials and Methods

This was a retrospective study of medical records of 76 urolithiasis patients who underwent PCNL in Loei hospital between July 2013 and January 2019. Exclusion criteria were patients with incomplete medical records and patients with conversion from PCNL to open surgery.

The operations were performed by one urologist. A single dose of prophylactic antibiotic was given 30 minutes to 1 hour prior to surgery. After intubation and induction of anesthesia, the patient would be turned into the lithotomy position and a ureteric catheter was inserted at the site where stones were present. In the prone position, renal access was achieved under fluoroscopic guidance. After successful access pelvic urine was aspirated and collected for bacterial culture, A guide wire was inserted into the collecting system, followed by tract dilatation with metal dilatation up to 30 Fr. An Amplatz sheath was used in all cases. A nephroscope was introduced and stones were disintegrated by pneumatic lithotripsy. After the procedure a JJ stent was inserted via the nephroscope and a decision was made whether to insert the nephrostomy tube again.

Urosepsis complication was defined by SIRS criteria plus evidence of urologic sources. SIRS criteria in this study were defined by two or more of the following: 1. Body temperature > 38 °C or < 38 °C; 2. heart rate > 90 bmp; 3. respiratory rate > 20 breaths/min; 4. white blood cell count > 12,000 cells/ml or < 4,000 cells/ml[4].

Data collected and recorded included demographic data (including sex, age, body mass index (BMI), underlying disease, history of urinary tract infection), stone data, intraoperative data and complication data. Categorical data are reported as number and percentage. Continuous data are reported as mean and standard deviation, normality distribution being ascertained by the Shaphiro-Wilk test. For inter-group comparison of Urosepsis a t-test was used for continuous data and Fisher's exact test for categorical variables. Factors affecting urosepsis were assessed using a binary logistic regression model. From the univariable analysis, variables which had a $p < 0.15$ were entered in the multivariable analysis by forward selection. The multivariable model only included significant factors with the forward selection method. Coefficients were estimated using the bootstrap method to improve the precision of estimation in a small sample size. A $p < 0.05$ was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows version 23.0 (IBM Corp, 2015).

Table 1. Clinical characteristics of study population.

Parameters	Number (%) (N=76)
Sex	
Male	54 (71.1)
Female	22 (28.9)
Age (year), mean ±SD	54.43 ± 10.27
BMI (kg/m^2), mean ± SD	22.89 ± 3.46
Underlying diseases	44 (57.9)
Diabetes mellitus	13 (17.1)
Hypertension	24 (31.6)
Dyslipidemia	6 (7.9)
Gout	3 (3.9)
Chronic kidney disease*	21 (27.6)
Past history UTI	21 (27.6)

*Chronic kidney disease is defined by a glomerular filtration rate less than 60 ml/min/1.73 m^2 for at least 3 months[5]

Results

Twenty-one patients (27.6%) had a history of urinary tract infection. Demographic data is shown in Table 1 and stone data is presented in Table 2. Staghorn stone was found to be the most common type of stone operated on by PCNL in this study and the median size of stone was 4.05 cm (IQR: 3.20-6.00). The univariate analysis found that the type of stone was a pre-operative risk factor for urosepsis, as shown in Table 3 and a positive renal pelvic culture was an intra-operative risk factor for urosepsis (Table 4). Multivariate analysis showed staghorn stone and renal pelvic culture positive were associated with urosepsis as shown in Table 5.

Table 2. Stone data.

Parameters	Number (%) (N=76)
RC	75 (98.7)
Renal pelvis stone	4 (5.3)
Multiple caliceal stone	2 (2.6)
Pelvic caliceal stone	14 (18.42)
Partial staghorn stone*	23 (30.3)
Staghorn stone**	32 (42.1)
Diverticulum stone	1 (1.3)
UC	3 (3.95)
Stone burden***, Median (IQR) (n=72)	4.05 (3.20-6.00)
Hydronephrosis	
Present	71(94.67)
Absent	4 (5.33)
Degree of hydronephrosis	
No hydronephrosis	4 (5.33)
Mild	9 (12.00)
Moderate	22 (29.33)
Severe	41 (54.67)

*Partial staghorn stone defined as a renal pelvic stone extending to only one calyx[6]

**Staghorn stone defined as a renal pelvic stone extending to at least two calices[6]

***Stone burden defined as the sum of the longest axial diameter of all stones[7]

Discussion

PCNL has become one of the preferred treatment options for upper urinary tract stones and PCNL is recommended as the first line treatment of larger stones > 2 cm. PCNL is a minimally invasive and safe procedure; however, it can be complicated by urosepsis which although is found infrequently it can prove lethal after PCNL. Several studies showed post-PCNL sepsis occurred in 0.3%-9.3% of cases[8,9]. In this study we found 9.2% of patients studied developed post-PCNL sepsis with no mortality.

Urosepsis after PCNL can be caused by bacterial growth in the renal pelvic urine or infected calculi. A biofilm can form which protects the bacteria from the antibiotic hence some bacteria remain active[10] during the manipulative actions and endotoxins will be released from stones[11]. The use of pressure irrigation during the process can result in bacteria and endotoxins from stones entering the bloodstream during stone manipulation through pyelovenous, pyelolymphatic and pyelotubular back flow and forniceal rupture[12].

Several studies have reported risk factors for post-PCNL sepsis including female gender, age, diabetes mellitus, history of UTI, white blood cells in the urine preoperatively, stone size, staghorn stone, degree of hydronephrosis, number of stones, amount of blood loss, operative time, and number of residual stones[2,13-15]. In this study, only pre-operative positive pelvic culture and staghorn morphology were found to be associated with urosepsis complications.

Many reports found that renal pelvis culture positive was a risk factor for fever, systemic inflammatory response syndrome (SIRS) and sepsis[13,16,17]. In this study we found that *E. Coli* (43.8%) was the most common organism in a positive renal pelvis culture. This was in line with previous reports[16-18] half of the organisms in urosepsis patients with a positive renal pelvis culture being *E. Coli*. In this study, patients with urosepsis were investigated by hemoculture. The findings were that out of the urosepsis patients one patient had an inconsistency in the organisms between the hemoculture and pelvic urine culture and 4 patients had negative hemocultures (Table 6).

Staghorn stone was associated with urinary tract infection with urease producing bacteria[19]. Several reports have reported the outcome of stone culture from staghorn stones and urease producing organisms were found in 44%-75.9% of cases[17,18,20]. It is difficult to conclude whether the UTI was caused by urea splitting bacteria as no examination of the culture stone was performed to confirm that urea splitting bacteria cause UTI in staghorn stone cases.

Selection of the antibiotic in post-PCNL urosepsis is important. This study found isolated

Table 3. Pre-operative factors related to urosepsis (N=76).

Characteristics	No (n=69)	Yes (n=7)	Total	P-value
Sex n (%)				0.40[b]
Male	50 (73)	4 (57)	54 (71)	
Female	19 (24)	3 (43)	22 (29)	
Age (years) mean ± SD	54.2 ± 10.6	57 ± 6.9	54.4 ± 10.3	0.49[a]
BMI (n=66)	2.2 ± 0.7	2.1 ± 0.7	2.2 ± 0.7	0.46[a]
Underlying disease n (%)				0.23[b]
No	31 (45)	1 (14)	32 (42)	
Yes	38 (55)	6 (86)	44 (58)	
Diabetes mellitus n (%)				1.0[b]
No	57 (83)	6 (68)	63 (83)	
Yes	12 (17)	1 (14)	13 (17)	
CKD n (%)				0.09[b]
No	52 (75)	3 (43)	55 (72)	
Yes	17 (25)	4 (57)	21 (28)	
Previous UTI n (%)				0.39[b]
No	51 (74)	4 (57)	55 (72)	
Yes	18 (26)	3 (43)	21 (28)	
Size of stone ≥ 4.2 cm n (%)				0.24[b]
No	39 (57)	2 (29)	41 (54)	
Yes	30 (44)	5 (71)	35 (46)	
Type of stone n (%)				0.04[b]
Non-staghorn stone	21 (30)	0 (0)	21 (28)	
Partial staghorn stone	22 (32)	1 (14)	23 (30)	
Staghorn stone	26 (38)	6 (86)	32 (42)	
Hydronephrosis (n=75) n (%)				1.0[b]
No	4 (6)	0 (0)	51 (68)	
Yes	64 (94)	7 (100)	71 (95)	

P-values were calculated from a Student t-test[a] and Fisher's exact test[b]. Data are expressed as mean (± SD) and number (%) depending on type of variable.

Table 4. Intra-operative factors related to urosepsis (N=76).

Characteristics	No (n=69) n (%)	Yes (n=7) n (%)	Total	P-value
Renal pelvic culture (n=72)				0.02[b]
Negative	54 (82)	2 (33)	56 (78)	
Positive	12 (18)	4 (67)	16 (22)	
Operative time (minutes)				1.0[b]
< 120	12 (17)	1 (14)	32 (17)	
≥ 120	57 (87)	6 (86)	63 (83)	
Number of access tracts				1.0[b]
1 tract	63 (91)	7 (100)	70 (92)	
> 1 tract	6 (8.7)	0 (0)	6 (8)	
Blood transfusion				0.06[b]
No	54 (78)	3 (43)	57 (75)	
Yes	15 (22)	4 (57)	19 (25)	
Residual stones (n=74)				0.58[b]
No	11 (16)	0 (0)	11 (15)	
Yes	56 (84)	7 (100)	63 (85)	

P-values were calculated from a Student t-test[a] and Fisher's exact test[b]. Data are expressed as mean ± SD and number (%) according to the types of variable.

Table 5. Univariable and multivariable analysis of post-PCNL urosepsis.

Variables	Univariable analysis		Multivariable analysis	
	OR (95%CI)	P-value	aOR (95%CI)	P-value
Underlying disease		0.02		
No	Ref			
Yes	4.89 (1.28 - 18.65)			
Blood transfusion		0.07		
No	Ref			
Yes	4.80 (0.89 - 25.76)			
Staghorn stone		<0.001		0.01
No	Ref		Ref	
Yes	9.92 (2.68 - 36.74)		6.75 (1.59 - 28.63)	
Hydronephrosis		0.12		
< Severe	Ref			
> Severe	0.33 (0.08 - 1.32)			
Size of stone (cm)		0.12		
< 4.2	Ref			
≥ 4.2	3.25 (0.73 - 14.54)			
Previous UTI		0.37		
No	Ref			
Yes	2.13 (0.41 - 11.06)			
Renal pelvic culture		0.01		0.02
Negative	Ref		Ref	
Positive	9.00 (1.63 - 49.77)		7.51 (1.35 - 41.77)	
CKD		0.10		
No	Ref			
Yes	4.08 (0.77 - 21.69)			
Diabetes mellitus	Ref	0.75		
No	0.79 (0.19 - 3.26)			
Yes				
Sex		0.42		
Male	Ref			
Female	1.97 (0.37 - 10.46)			
Operative time (minutes)		0.75		
< 120	Ref			
≥ 120	1.26 (0.30 - 5.40)			

aOR, adjusted odds ratio; The variables in univariable analysis were included by forward selection ($p < 0.15$). These consisted of underlying disease, blood transfusion, staghorn stone, hydronephrosis, size of stone, renal pelvic culture, and CKD. Those variables were excluded from the multivariable model due to their non-significance ($p > 0.05$) leaving only two variables which were significant ($p < 0.05$): staghorn stone and renal pelvic culture. The multivariable model was adjusted for staghorn stone and renal pelvic culture.

bacteria from urosepsis patients were more resistant to ampicillin, ceftriaxone, and ciprofloxacin while being relatively more sensitive to amoxycillin/clavulanate, ceftazidime, amikacin, gentamicin, and meropenam (Table 7). The drug of choice following PCNL needs to be from the following list amoxycillin/clavulanate, ceftazidime, amikacin, gentamicin, and meropenem.

This study does have some limitations, specifically that due to the retrospective nature of the study there were some incomplete data and also that the population studied was relatively small.

Table 6. Bacterial species detected in the cultures.

Variables	Urine culture non urosepsis n (%)	Urine culture urosepsis n (%)	Hemoculture non urosepsis n (%)	Hemoculture urosepsis n (%)
Not sent	5 (6.8%)	1 (1.3%)	69 (90.8%)	0 (0%)
Negative culture	52 (68.4%)	2 (2.6%)	7 (9.2%)	4 (57.1%)
Positive culture	12 (15.8%)	4 (5.3%)	0 (0%)	3 (42.9%)
Isolated organism				
Escherichia Coli	5 (31.3%)	2 (12.5%)	-	1 (33.3%)
Acinetobacter spp.	1 (6.3%)	1 (6.3%)	-	1 (33.3%)
Staphylococcus spp.	2 (12.5%)	-	-	-
Streptococcus spp.	2 (12.5%)	-	-	1 (33.3%)
Pseudomonas spp.	1 (6.3%)	-	-	-
Klebsiella spp.	-	1 (6.3%)	-	-
Mixed (Proteus+*E. coli*)	1 (6.3%)	-	-	-

Table 7. Intraoperative antibiogram-resistogram patterns of bacteria detected in the cultures.

Bacteria	Ampicilin	Amoxycillin/ clavulanate	Ceftriaxone	Ceftazidime	Meropenam	Ciprofloxacin	Amikacin	Gentamicin
E. coli								
1	R	I	R	R	S	R	S	S
2	R	S	R	R	S	R	S	S
*3	R	S	R	S	S	R	S	S
4	R	S	S	S	S	S	S	S
5	R	S	R	S	S	R	S	R
*6	R	S	R	S	S	R	S	S
7	ND	ND	ND	ND	ND	ND	ND	ND
Acinetobacter								
*1	ND	ND	R	R	R	R	S	S
2	ND	ND	R	R	S	R	I	S
Staphylococcus								
1	ND	ND	ND	ND	ND	S	ND	S
2	S	ND	ND	ND	ND	I	ND	S
Streptococcus								
1	ND	ND	R	ND	ND	ND	ND	ND
2	ND	ND	S	ND	ND	ND	ND	ND
Pseudomonas	ND	S	R	R	S	R	I	R
Klebsiella	ND	I	S	S	S	S	S	S
Mixed								
E. coli	R	I	S	S	S	R	S	S
Proteus	S	R	S	S	S	S	S	S

S = sensitivity, R = resistance, I=intermediate, ND = not done
*Urosepsis patients

Conclusion

PCNL is a safe operation for treatment of large upper urinary tract calculi; however, it can be complicated by urosepsis. This study found staghorn stone and a positive intraoperative pelvic culture to be risk factors for urosepsis complications. An intraoperative pelvic culture is important in caring patients with urosepsis particularly in UTI's which do not respond to previous antibiotics.

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Conflict of Interest

The author declares no conflict of interest.

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