

Original Article

Postoperative infection after ureterorenoscopic lithotripsy in Songkhla Hospital

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Keywords:

URSL, postoperative infection, urinary tract infection, risk factors

Abstract

Objective: Ureterorenoscopic lithotripsy (URSL) is the procedure of choice for treatment of ureteral stones. Postoperative acute pyelonephritis (APN) is a serious complication after URSL which may potentially progress to urosepsis and death. In this study we aimed to explore and record potential predictive factors associated with postoperative APN after URSL.

Materials and Methods: Ninety patients (2016-2022) with ureteral stone managed with URSL were identified. Postoperative APN was defined in patients with a body temperature $> 38^{\circ}\text{C}$ which persisted for at least 48 hours after URSL with clinical symptoms and/or urine culture was positive for organism growth. Multi-variable analysis with logistic regression was used to identify predictive factors for postoperative APN.

Results: Seven patients (7.8%) experienced postoperative APN and six patients (85.7%) developed systemic inflammatory response syndrome. All patients were managed conservatively with selective antibiotics, specifically treated with meropenem ($n = 3$), piperacillin/tazobactam ($n = 3$), and imipenem/cilastatin ($n = 1$). Most patients with postoperative APN were women (5/7 patients, 71.4%). The median age of the seven postoperative APN patients was 57.6 vs 54 years ($p = 0.48$) and the hospital stay was longer 5 vs 2 days, ($p < 0.01$). Preoperative APN was found in 12 patients (13.3%) and six patients (50%) developed perioperative APN. The multivariable analysis, showed that the only independent factor of postoperative APN was a history of preoperative APN

Conclusion: Postoperative infection is a serious condition after URSL that can increase the risk of morbidity and mortality. A single significant risk factor for postoperative infection was a history of preoperative APN. These patients should receive rigorous postoperative care to avoid serious complications.

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Introduction

Presence of urinary stones is one of the most common benign conditions in urology. The incidence of this condition varies by region and ethnicity. The lifetime incidence is approximately 10-15% and is increasing gradually year on year.¹ In Thailand the incidence of urinary stones was 94 cases per 100,000 population per year and 20% of these patients suffered from ureteric calculus.² Patients with ureteric stones frequently present with symptoms early in the course of the disease and can lead to serious conditions. The symptoms include pain, urinary tract infection (UTI), hematuria, and deterioration of kidney function.^{3,4} The management of ureteric stones has dramatically changed from open surgery to minimally invasive surgery over the past 20 years. The treatments of choice include expectant management, medical expulsive therapy, shockwave lithotripsy, laparoscopic ureterolithotomy, and ureterorenoscopic lithotripsy (URSL).^{5,6} Recently URSL has been accepted as the reference treatment and first-line treatment for ureteric stones. This procedure provides higher stone free rates, relatively fewer complications, and the reduced need for additional procedures.⁷ However, postoperative complications based on several series ranged from 2.5% to 6.7%.^{8,9} The most common postoperative complications were up-migration, perioperative infection, and damage to the ureter. The risk of postoperative infection is a particularly potentially serious complication because it may progress to severe sepsis and lead to death.⁸⁻¹¹

Recent studies revealed prolonged operation times,^{5,12-14} female,^{12,15,16} asymptomatic bacteriuria,^{12,14,15,17} history of pyelonephritis,^{13,16} and lower body mass index (BMI)¹⁸ as the potential risk factors for postoperative infection after URSL. Our objective was to investigate and report on postoperative infection after URSL and identify the potential risk factors for this condition.

Materials and Methods

After institutional review board approval (SKH IRB 2022-MD-IN3-1043) was received, we retrospectively reviewed the data of 90 patients with upper urinary tract stones who underwent URSL at Songkhla Hospital from January 2016 to December 2022. Patient characteristics including age, sex, BMI, mobility status, preoperative ureteral stent placement, stone diameter, number

of stones, stone location, preoperative pyuria, preoperative urine culture status, history of preoperative pyelonephritis, comorbidity, and operative time were collected. Patients all received prophylactic ceftriaxone 2 grams. In patients who had a history of allergy to penicillin, ciprofloxacin 400 mg was given. Acute pyelonephritis is defined as fever ($> 38^{\circ}\text{C}$), chills, flank pain, nausea, vomiting, or costovertebral angle tenderness with or without positive urinalysis and urine culture. A diagnosis of systemic inflammatory response syndrome (SIRS) was made based on presence of two or more of the following four criteria: white blood cell count $> 12,000/\text{mm}^3$ or $< 4,000/\text{mm}^3$; body temperature $< 36^{\circ}\text{C}$ or $> 38^{\circ}\text{C}$; heart rate $> 90/\text{min}$; respiratory rate $> 12/\text{min}$; or $\text{PaCO}_2 < 32 \text{ mmHg}$.

Procedure

For patients with preoperative ureteral stent placement, the stent placement was performed four weeks before surgery, and the ureteral stent was removed at the start of the URSL procedure. We used a 6/7.⁵ Fr rigid ureterorenoscope (Richard Wolf Medical Instruments Cooperation, Knittlingen, Germany). Stones were fragmented using a holmium: YAG laser (JenaSurgical MultiPulse Ho 35W, Jena, Germany) and a 400 μm laser fiber with an energy level of 0.5-1.5 J at a rate of 5-20 Hz. We picked out fragments using a nitinol stone retrieval basket (Zero Tip, Boston Scientific, Natick, MA, USA). A 16 Fr urethral catheter was inserted at the end of the procedure in all cases. A 6 Fr ureteral stent was placed if indicated and removed 2-4 weeks after the URSL.

Statistical analysis

Continuous variables are reported as mean \pm SD or median with interquartile range (IQR). Categorical variables are presented as number (percentage). Continuous variables were compared using T-test and Wilcoxon test as appropriate. Categorical variables were compared using Chi-square or Fisher exact tests. The risk factors for postoperative infection were determined using logistic regression to estimate the odds ratios with 95% confidence intervals. P-values < 0.05 were considered statistically significant. The analyses were performed using the R program version 4.1.1.

Results

The baseline characteristics of 90 patients managed with URSL are shown in Table 1. The median age was 54 years and 55 patients (61%) were male. Sixteen patients (18%) had hypertension and 36% were diabetic. The median hospital stay and BMI were 2 days and 25.3 kg/m², respectively. The mean operation time was 53 minutes and 28 patients (31%) underwent preoperative internal stenting. Twelve patients (13%)

had a history of APN before the operation and preoperative pyuria was observed in 37 patients (41%). Only 15 patients (17%) had asymptomatic bacteriuria. The median size of ureteric stone was 0.5 cm and 75 patients (83%) had one ureteric calculus. All patients received antibiotic prophylaxis. Eighty-eight patients (98%) received ceftriaxone, and patients with a history of allergy to penicillin received ciprofloxacin.

Table 1. Patient characteristics and preoperative findings

	Total (N=90)	Perioperative APN (n=7)	No perioperative APN (n=83)	P-value ^a
Sex				0.105
Male, n (%)	55 (61.1)	2 (28.6)	53 (63.9)	
Female, n (%)	35 (38.9)	5 (71.4)	30 (36.1)	
Age (years), mean (SD)	54.3 (12.8)	57.6 (13.7)	54 (12.7)	0.477
Hospital stays (days), median (IQR)	2 (1,2,8)	5 (5,6)	2 (1,2)	< 0.001
Weight (kg), median (IQR)	68 (61.2,78)	58 (46.5,79)	68 (62,78)	0.197
BMI (kg/m ²), median (IQR)	25.3	22.7 (18.9,27.1)	25.3 (23.9,28.9)	0.185
< 23, n (%)	(23.4,28.6)	4 (57.1)	14 (16.9)	0.025
≥ 23, n (%)	18 (20)	3 (42.9)	69 (83.1)	
	72 (80)			
Diabetes mellitus, n (%)	16 (17.8)	1 (14.3)	15 (18.1)	1
Hypertension, n (%)	32 (35.6)	4 (57.1)	28 (33.7)	0.241
Operative time (min), mean (SD)	53.1 (21)	59.3 (31.9)	52.5 (20)	0.417
Preoperative internal stent, n (%)	28 (31.1)	4 (57.1)	24 (28.9)	0.198
Mobility status, n (%)	89 (98.9)	7 (100)	82 (98.8)	1
Preoperative pyuria, n (%)	37 (41.1)	6 (85.7)	31 (37.3)	0.018
Preoperative APN, n (%)	12 (13.3)	6 (85.7)	6 (7.2)	< 0.001
Preoperative asymptomatic bacteriuria, n (%)	15 (16.7)	6 (85.7)	9 (10.8)	< 0.001
<i>Escherichia coli</i>	8 (53.3)	4 (66.7)	4 (44.4)	
<i>Escherichia coli</i> ESBL	1 (6.7)	1 (16.7)	0 (0)	
Group B <i>Streptococcus</i> spp.	1 (6.7)	0 (0)	1 (16.7)	
<i>Klebsiella pneumoniae</i>	3 (20)	1 (16.7)	2 (22.2)	
<i>Pseudomonas aeruginosa</i>	1 (6.7)	0 (0)	1 (11.1)	
Number of stone, median (IQR)	1 (1,1)	1 (1,1)	1 (1,1)	0.798
Size of stone				
Width (cm), median (IQR)	0.5 (0.5,0.8)	0.7 (0.6,0.8)	0.5 (0.5,0.8)	0.612
Length (cm), median (IQR)	0.9 (0.7,1)	1 (1,1)	0.9 (0.7,1)	0.248
ATB prophylaxis n(%)				1
Ceftriaxone	88 (97.8)	7 (100)	81 (97.6)	
Ciprofloxacin	2 (2.2)	0 (0)	2 (2.4)	

^ap-values were calculated using Chi-square test for categorical variables and T-test and Wilcoxon test for continuous variables. Fisher's exact test was used for comparison of categorical variables with low incidence. All comparisons assess the distribution of parameters across the type of postoperative events.

APN = acute pyelonephritis, SD = standard deviation, IQR = interquartile range, BMI = body mass index, ESBL = extended-spectrum beta-lactamase, ATB = antibiotic.



Seven patients (7.8%) experienced postoperative APN and six patients (85.7%) developed SIRS. The seven APN patients were treated with meropenem (n = 3), piperacillin/tazobactam (n = 3), and imipenem/cilastatin (n = 1) (Table 2). Most patients with postoperative APN were women (5/7 patients, 71.4%). The seven patients with postoperative APN had a higher median age compared to the overall age of the 90 patients but the results were not statistically significant (57.6 vs 54.3 years, p = 0.48). Hospital stay, however, was significantly longer (5 vs 2 days, p < 0.01). The average onset of clinical APN was 12.1 hours after the procedure. Twelve patients (13.3%) had a history of preoperative APN, and 6 (50%) of these patients developed postoperative APN. The size and number of ureteral stones were similar in both the preoperative and postoperative APN groups. Figure 1 illustrates the incidence of postoperative APN, which was observed in approximately 10% of each year. The multivariable analysis indicated that an independent factor for postoperative APN was a history of preoperative APN (Table 3).

Discussion

The majority of cases in urology are patients with presence of a urinary stone, which is a clinical challenge because most patients usually present with acute symptoms such as flank pain, hematuria, UTI, and a deterioration in kidney function.^{1,3,4} The management of ureteric stones varies depending on the clinical presentation and patient conditions.^{5,6} Acute management includes pain killer medication and/or insertion of an

Table 2. Patients with perioperative acute pyelonephritis

n = 7 patients	Data
Signs and symptoms	
Onset of fever, mean (SD)	12.1 hours post-op (8.4)
SIRS, n (%)	
No	1 patient (14.3)
Yes	6 patients (85.7)
Body temperature, mean (SD)	38.8 degree Celsius (0.5)
Heart rate, mean (SD)	104.3/min (22.1)
Respiratory rate, mean (SD)	20/min (1.2)
Laboratory results	
WBC count, mean (SD)	12425/mm ³ (4089)
WBC count in UA, n (%)	
0-1	2 patients (28.6)
5-10	2 patients (28.6)
50-100	2 patients (28.6)
> 100	1 patient (14.3)
Postoperative positive U/C, n (%)	2 patients (28.6)
Postoperative pathogen from U/C, n (%)	
<i>Escherichia coli</i>	1 patient (50)
<i>Escherichia coli</i> ESBL	1 patient (50)
Postoperative positive H/C, n (%)	0 patients (0)
Treatment	
ATB for APN, n (%)	
Meropenem	3 patients (42.9)
Piperacillin/tazobactam	3 patients (42.9)
Imipenem/cilastatin	1 patient (14.3)

SD = standard deviation, SIRS = systemic inflammatory response syndrome, WBC = white blood cells, U/A = urinalysis, U/C = urine culture, ESBL = extended-spectrum beta-lactamase, H/C = hemoculture, ATB = antibiotics, APN = acute pyelonephritis, min = minute.

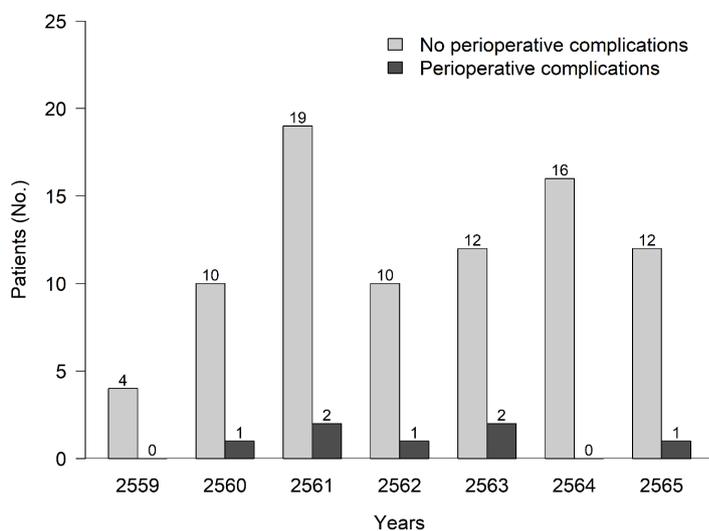


Figure 1. Distribution of ureterorenoscopic lithotripsy operations performed in Songkhla Hospital from 2016 to 2022. The incidence of perioperative acute pyelonephritis was between 5 and 10% each year.

Table 3. Analysis of risk factors of perioperative acute pyelonephritis after URSL^a

Factors	Univariate			Multivariable ^b		
	OR	95% CI	P-value	OR	95% CI	P-value
BMI < 23 kg/m ²	6.57	1.31-36.59	0.02	4.19	0.43-51.07	0.22
Preoperative pyuria	10.06	1.62-194.82	0.04	6.80	0.59-13.93	0.16
Female	4.42	0.89-32.18	0.09	1.17	0.95-13.94	0.89
History of APN	77.0	10.9-1589.29	< 0.001	33.31	3.66-803.45	0.006
Diabetes mellitus	0.75	0.04-4.89	0.80			
Hypertension	2.62	0.54-14.07	0.23			
Number of stone (s)	0.66	0.05-1.71	0.60			

^aAsymptomatic bacteriuria variable was removed from analysis; ^bFactors with $p < 0.10$ were moved forward for multivariable analysis.

URSL = ureterorenoscopy with lithotripsy, OR = odds ratio, CI = confidence interval, BMI = body mass index, APN = acute pyelonephritis.

internal urinary stent.¹⁷ URSL is the reference treatment for ureteric stones when the patient's condition is stable and/or the patient is free of infection.⁷ However, postoperative complications are relatively high (range 2.5-6.7%) in relation to other equivalent procedures.^{8,9} One of the most serious postoperative complications is infection. This complication can cause acute kidney injury and can progress to severe sepsis that may lead to death.⁸⁻¹¹ Recently published reports revealed that prolonged operative time^{5,12-14} and a history of preoperative pyelonephritis^{13,16} were potential predictive factors for perioperative infection. Our analysis focused on postoperative APN after URSL and management and outcomes after treatment for this condition. The primary endpoint was to provide the independent risk factors for postoperative APN.

Postoperative infection occurred in 8% of patients in our study. Six out of the seven patients (85.7%) with postoperative infection developed SIRS. No patient had clinical progression to severe sepsis and/or organ failure. Only two patients (29%) had postoperative positive urine cultures for organisms. Therefore, the clinical symptoms and/or initial laboratory outcomes may be more important than the results of urine cultures for physicians to initially manage these conditions. All patients with postoperative infection were managed conservatively with selective antibiotics. The incidence of postoperative infection was approximately 10% each year. The incidence of postoperative complications in this study seemed to be higher in comparison to recent similar studies. For patients with postoperative

APN, 6 out of 12 patients (50%) had a history of preoperative APN before intervention. A history of preoperative APN was the only independent factor associated with postoperative APN. The mean time to develop postoperative infection was 12 hours after the procedure. High risk patients, especially patients with a history of preoperative APN, should be closely observed for at least 12 hours after the procedure.

Our study showed a substantial association between preoperative and postoperative APN. The findings revealed that 6 out of 12 patients, 50%, with a history of preoperative infection experienced a postoperative infection. Our data were consistent with reports in the recent literature regarding the association between a history of preoperative APN and postoperative infection. Shreya et al. reported that a positive preoperative UTI or a prior history of UTI were the predisposing factors that increased the risk of postoperative infection.¹⁸ In our study, 7.8% of patients developed postoperative APN and 86% of these patients developed SIRS. Our data were consistent with recent studies. A urine culture is the most important tool for a diagnosis in such patients. Unfortunately, 29% of the patients in this current study had a positive postoperative urine culture and five patients (71%) had a significant number of WBCs in the postoperative urine. Mariappan et al. reported urine culture results that neither represented nor predicted infected stones or renal pelvic urine infection.¹⁹ The clinical symptoms and basic laboratory results are important tools for initial treatment and stone culture. However, a renal pelvic urine culture may be needed



to confirm a diagnosis and enable adjustment of the antibiotics.

Even though the American Urological Association and European Association of Urology guidelines recommend performing a urine culture and treat asymptomatic bacteria before the procedure, the guidelines were not followed due to health policies or patient limitations.^{20,21} Cole et al. reported that 20.9% of patients who developed postoperative infection did not have a preoperative urine culture²² but in our study urine samples were taken from all patients for preoperative urine culture and all patients received antibiotic prophylaxis before the procedure.

Antibiotic prophylaxis tends to reduce perioperative infection and septicemia and identification of organisms from preoperative urine culture is crucial information for choosing the prophylactic antibiotic and also to inform later treatment. However, intraoperative pathogens may differ from organisms identified preoperatively.²¹ In patients with a history of preoperative APN in particular, a preoperative urine culture provides essential evidence for selection of the prophylactic antibiotic.¹⁷ Recent studies reported that a ureteral access sheath and preoperative ureteral stent potentially offered reduced risk of postoperative complications and infection.^{17,20-23} A ureteral access sheath reduces collecting system pressure and decreases the rate of ureteral injury; therefore, the incidence of post-URS infections declined.¹⁷ Although preoperative stent placement facilitates the endoscopic procedure and improves stone free rate, the presence of preoperative ureteral stents for more than one month was associated with a higher risk of sepsis and was associated with occult bacterial colonization. In these reports, all patients with preoperative stent underwent URSL within four weeks and a preoperative stent was not an independent factor for postoperative APN.^{17,21-23}

Patients with urosepsis after URSL should be managed intensively and closely monitored. Appropriate antibiotics and supportive care are necessary in these patients. Urosepsis-related mortality was found to be 2.5 times higher in patients with urinary obstruction. If the clinical condition does not improve after treatment with broad-spectrum antibiotics, further investigations are required. Cross-sectional imaging and urgent decompression need to be considered.

There is no consensus on the optimal waiting time to observe the effects of antibiotics but if the clinical condition does not show improvement within 48 hours, drainage should be performed.¹⁸ In our report, all patients with postoperative infection were managed conservatively with selective antibiotics. None of the patients in this study required drainage or admission to the intensive care unit.

Our study has some limitations. The population was relatively small and was carried out at a single institute. An addition, since the nature of this study was retrospective, selection bias was potentially present along with missing data. However, our study has identified a potential risk factors for developing urosepsis after URSL. We believe this information can help urologists provide apposite postoperative care for urinary stone patients.

Conclusions

Postoperative infection is a common and serious complication after URSL. It may progress to urosepsis leading to death. All patients with this condition in this study were successfully treated with conservative management with antibiotics. The history of preoperative infection was the only predictive factor for postoperative infection.

Conflict of Interest

The authors declare no conflicts of interest.

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