Original Article

Clinical outcomes and complications of percutaneous nephrolithotomy (PCNL) in multidrug resistant (MDR) bacteriuria

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Abstract

Objective: To evaluate the outcomes and complications of percutaneous nephrolithotomy (PCNL) in patients with multidrug resistant (MDR) urine cultures in comparison with those with normal urine cultures.

Materials and Methods: A retrospective cohort study was completed in patients who underwent PCNL at Maharaj Nakorn Chiang Mai Hospital between January, 2019 and August, 2021. The medical record charts of patients were reviewed and divided into 2 groups: those with a preoperative positive multidrug resistant culture (MDR, n=37) and those with a negative urine culture (No MDR, n=73). The following data were collected: demographics, size of stones, intraoperative data, preoperative urine cultures and postoperative complications. Association between factors and postoperative complications after PNCL were identified using a binary logistic regression model.

Results: Sepsis complications occurred in 8.2% of the patients (No MDR, n=2, MDR, n=7). The results of the multivariate analysis demonstrated a significant association between a positive preoperative MDR urine culture and postoperative sepsis complications (odds ratio (OR) = 15.21, 95%CI 1.59-145.35, p = 0.018). Conversely, female patients exhibited a decreased risk in comparison to male patients (OR 0.03, 95%CI 0.001-0.75, p = 0.003).

Conclusion: The prevalence of positive MDR bacteriuria in patients who underwent PCNL in Maharaj Nakorn Chiang Mai Hospital was relatively high. The female gender exhibited a prophylactic effect, while a positive MDR urine culture emerged as a significant risk factor for postoperative complications associated with sepsis, even in the presence of appropriately administered preoperative prophylactic antibiotics.

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Introduction

Kidney stone disease is a common problem in urology that affects patients in terms of pain, quality of life and daily life function. There are several treatment methods including both minimally invasive and open surgery. According to the 2016 American Urological Association (AUA) and 2021 European Association of Urology (EAU) guidelines on the management of the condition, percutaneous nephrolithotomy (PCNL) is a minimal invasive procedure and a preferred treatment for large upper tract stones as the first-line treatment, especially those that are more than two centimeters in diameter.[1,2] Renal calculi may be accompanied by urinary tract infection which must be treated with antibiotics before surgery. Complications of PCNL include fever, bleeding, and sepsis or septic shock which can lead to significant morbidity and even death.

Infection complications have been reported in 32% of patients undergoing PCNL, which include fever, and sepsis. Several previous studies have shown that preoperative positive urine or stone cultures, number of access points, and the need for blood transfusion are associated with postoperative infection.[3,4] Some of the preoperative urine cultures, perioperative urines and stone cultures have been recorded as having differentiated organisms.[5] This variety can mean that antibiotic treatment may not be able to sterilize the urine, especially in the case of bacterial resistant organisms. Bacterial resistance also increases the complexity of treatment as well as the medical costs and the length of the hospital stay. Patients who exhibit preoperative multidrug resistance are more likely to have postoperative complications.[6] Some studies have reported that positive preoperative cultures controlled with antibiotics for at least 72 hours are sufficient to control the infections in these cases.[7]

Resistant bacteria are usually resistant to more than one antibiotic and are considered multidrug resistant (MDR) bacteria if they are resistant to at least one agent in three or more antimicrobial categories.[8] Our observations have indicated an increase in the incidence of bacterial resistant organisms in our clinical practice. Therefore, there is an urgency to investigate the prevalence of MDR pathogens and their association with postoperative infectious complications. The findings can be used to determine the risk factors for postoperative complications for pertinent preoperative counselling, as well as determining the role of antibiotic prophylaxis. The research objective is to evaluate the outcomes and complications of PCNL in patients with MDR urine cultures compared with those with normal urine cultures.

Materials and Methods

After approval from the Research Ethics Committee of Chiang Mai University (Study Number SUR 2563-07824), a retrospective cohort study was completed on all PCNL patients at Maharaj Nakorn Chiang Mai Hospital between January 2019 - August 2021 with patients who were 18 years or older. Urine samples were collected via midstream clean void one month prior to the operation and were then cultured. The exclusion criteria were patients in whom urine cultures were not carried out, were on antiplatelet or anticoagulant medications, had undergone prior urinary diversions e.g. PCN or DJ stent, had undergone secondary nephoscopy or failed PCNL.

Patients with MDR urine cultures were treated with culture-specific antibiotics for approximately one week and received prophylactic antibiotics just before surgery.

In a study by Patel et al. which investigated the presence of multidrug resistant bacteriuria before PCNL postoperative infection complications were able to be predicted. In this study the estimated required sample size was 115 patients to enable effective calculation of the postoperative sepsis outcome.

Multidrug bacterial resistance is defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories

Sepsis was defined as two or more criteria of the quick sepsis-related organ failure assessment (qSOFA) being met, specifically: respiratory rate of ≥ 22 breaths/min, altered consciousness (Glasgow Coma Scale score of < 13), and systolic blood pressure of ≤ 100 mmHg.[9] Data was collected from post-procedure until discharge to home.

Results

We analyzed the data of 110 patients, who were divided into 2 groups, preoperative culture with multidrug resistance (37 patients) and negative urine culture (73 patients). Patient characteristics are shown in Table 1. There were no statistically significant differences in sex, body

Table 1. Baseline characteristics between MDR and no MDR

Parameters	No MDR n=73	MDR n=37	P-value
Age, years mean (SD)	57.86 (10.82)	53.38 (8.99)	0.032
Sex			0.838
Male n (%)	44 (60.27)	21 (56.76)	
Female n (%)	29 (39.73)	16 (43.24)	
BMI, kg/m^2 mean (SD)	22.51 (4.47)	21.78 (3.50)	0.383
Preop creatinine, mg/dl mean (SD)	1.26 (0.73)	1.56 (1.45)	0.149
Stone number mean (SD)	3.76 (3.26)	3.25 (2.66)	0.415
Stone size, cm mean (SD)	3.04 (1.53)	3.22 (2.26)	0.628
Staghorn stone n (%)			1.000
No	35 (48.61)	18 (48.65)	
Yes	37 (51.39)	19 (51.35)	
Diabetes mellitus n (%)			0.792
NO	61 (83.56)	30 (81.08)	
Yes	12 (16.44)	7 (18.92)	
Antibiotics given 30 days prior n (%)			0.015
No	11 (15.07)	0 (0.00)	
Yes	62 (84.93)	37 (100.00)	
Positive urine culture n (%)			<0.001
No	68 (93.15)	0 (0.00)	
Yes	5 (6.85)	37 (100.00)	
Number of access points n (%)			0.481
1	68 (93.15)	33 (89.19)	
>1	5 (6.85)	4 (10.81)	
Access tract n (%)			0.442
Upper pole	46 (63.01)	27 (72.97)	
Middle pole	9 (12.33)	5 (13.51)	
Lower pole	18 (24.66)	5 (13.51)	
Point access n (%)			0.015
Supracostal	11 (15.07)	14 (37.84)	
Subcostal	62 (84.93)	23 (62.16)	
History of previous procedure n (%)			0.081
No history of surgery	57 (78.08)	23 (62.16)	
History of PCNL	4 (5.48)	1 (2.70)	
History of NL	12 (16.44)	13 (35.14)	
Blood loss (ml) mean (SD)	199.73 (151.22)	206.76 (125.37)	0.808
Transfusion n (%)			0.299
No	68 (93.15)	32 (86.49)	
Yes	5 (6.85)	5 (13.51)	
Sepsis n (%)			0.006
No	71 (97.26)	30 (81.08)	
Yes	2 (2.74)	7 (18.92)	
Postoperative fever n (%)			0.004
No	35 (47.95)	7 (18.92)	
Yes	38 (52.05)	30 (81.08)	
Stone free n (%)			0.225
Stone free	38 (52.05)	14 (37.84)	
Retain stone	35 (47.95)	23 (62.16)	
Length of stay (days) mean (SD)	10.37 (2.48)	11.73 (4.74)	0.050

MDR = multidrug resistant, PCNL = percutaneous nephrostomy, NL = nephrolithotomy, SD = standard deviation

mass index (BMI), preoperative creatinine, or diabetes mellitus. Patients who had MDR and positive urine cultures received antibiotics prior to the procedure for at least 7 days or until negative urine cultures were achieved. All patients were given prophylactic antibiotics, specifically third-generation cephalosporin or specific to urine culture results. The majority of the patients underwent subcostal access: 84.9% with negative culture, 62.2% with MDR culture. The proportion of patients undergoing an upper pole calyceal approach were 63% with negative culture and 73% with MDR culture. Patients in the MDR urine culture group were more likely to develop postoperative fever.

Out of all MDR organisms, *Escherichia coli* was the most prevalent MDR organism at 43.2% (Fig. 1) with Enterococcus faecalis (16.2%) and Staphylococcus saprophyticus (8.1%). Seven out of 37 patients with positive MDR urine cultures developed postoperative sepsis, compared with 2 of 73 patients with non-MDR cultures (p = 0.006).

Table 2 shows the univariate analysis of factors associated with postoperative sepsis. There was an association between patients with underlying diabetes mellitus and postoperative sepsis (OR = 4.59, p = 0.036), and also with a positive urine culture (OR = 16.48, p = 0.010). There was an increased risk of postoperative sepsis with a positive MDR urine culture (OR = 8.28, p = 0.011). Patients with postoperative sepsis had relatively longer hospital stays and required more blood transfusions (OR = 1.22, p = 0.037 and OR = 6.71, p = 0.018) respectively. Multivariate analysis showed the female sex was associated with a decreased risk of post operative sepsis, whereas positive MDR culture was associated with postoperative sepsis. All these results are shown in Table 3.

Discussion

Current evidence suggests that most renal stones can be cleared with retrograde intrarenal surgery (RIRS) or minimally invasive surgery, with PCNL still being the first-line treatment for stones more than 2 cm. However, the procedures can be complicated by sepsis which can lead to significant morbidity and even death. Several studies have shown that sepsis complications after PCNL occurred in 0.3-9.3% of cases.[10-12] In this study, we found 8.2% of patients studied developed postoperative sepsis with no mortality.

This study included a total of 45 female patients, among whom only 1 patient developed postoperative sepsis. Multivariate analysis indicated that female gender was a prophylactic factor for post-PCNL sepsis. This finding could be attributed to several factors. One possible explanation is anatomical differences between males and females with regard to the urinary tract. In the female anatomy the urethra is generally shorter, which may reduce the likelihood of bacteria ascending to the kidneys when compared to the longer male urethra. Additionally, differences in hormonal and immune responses between males and females may also play a role in influencing susceptibility to infection and the development of sepsis. However, it's important to note that individual patient characteristics and medical histories can also impact the likelihood of complications.[13,14]

The prevalence of MDR bacteria in preoperative urine cultures before PCNL was 34% and increased the risk of development of postoperative complications associated with sepsis fifteen-fold. This finding is concerning because MDR bacteriuria is a challenge in the treatment of patients with stones increasing the complexity and results with regard to greater prevalence of patient morbidity, longer length of stay, and higher hospital costs. Our study found that *E. coli* was the most common MDR organism and the second most common was *E. faecalis*, the same findings reported in previous studies.[6,14] AUA 2016 and EAU 2021 guidelines recommend that the physician should always treat urinary tract infections before stone removal. In patients with clinically significant infections and obstructions, the patient should undergo drainage for several days before PCNL.[1] However, there are no evidence-based guidelines for antibiotic prophylaxis in patients with stones that have a positive MDR urine culture. In real life clinical situations, we treat infections with empirical antibiotics in accordance with the urine culture sensitivity.

The results from this study, indicate that the presence of MDR bacteria in the urine culture increases the potential for postoperative sepsis. However, if we attempt to eradicate the colonization and treat until the urine culture is negative, the renal function will continue to decrease due to the obstruction. We also know that the stone

Table 2. Univariate analysis for postoperative sepsis

Parameters	Odds ratio	95 % C.I. for odds		P-value
		Lower	Upper	
Age	1.01	0.95	1.08	0.742
Sex				
Male	Reference			
Female	0.16	0.02	1.34	0.092
BMI	0.93	0.77	1.13	0.480
Preop creatinine	0.91	0.40	2.09	0.823
Stone number	1.02	0.82	1.27	0.849
Stone size	1.19	0.92	1.54	0.177
Staghorn stone				
No	Reference			
Yes	1.20	0.30	0.74	0.794
Diabetes mellitus				
No	Reference			
Yes	4.59	1.10	19.06	0.036
Positive urine culture				
No	Reference			
Yes	16.48	1.98	137.34	0.010
Number of access points				
=1	Reference			
>1	3.84	0.67	22.06	0.132
Access tract				
Upper pole	Reference			
Middle pole	1 (empty)			
Lower pole	0.90	0.17	4.66	0.898
Point access				
Supracostal	Reference			
Subcostal	0.33	0.08	1.33	0.119
History of previous PCNL				
No history of surgery	Reference			
History of PCNL	1 (empty)			
History of NL	0.91	0.18	4.67	0.907
Blood loss	1.00	1.00	1.01	0.842
Transfusion				
No	Reference			
Yes	6.71	1.38	32.74	0.018
Postoperative fever				
No	Reference			
Yes	5.47	0.66	45.38	0.116
Stone free				
Stone free	Reference			
Retain stone	0.70	0.18	2.74	0.605
LOS	1.22	1.01	1.48	0.037

PCNL = percutaneous nephrolithotomy, NL = nephrolithotomy, MDR = multidrug resistant, LOS = length of stay (days)

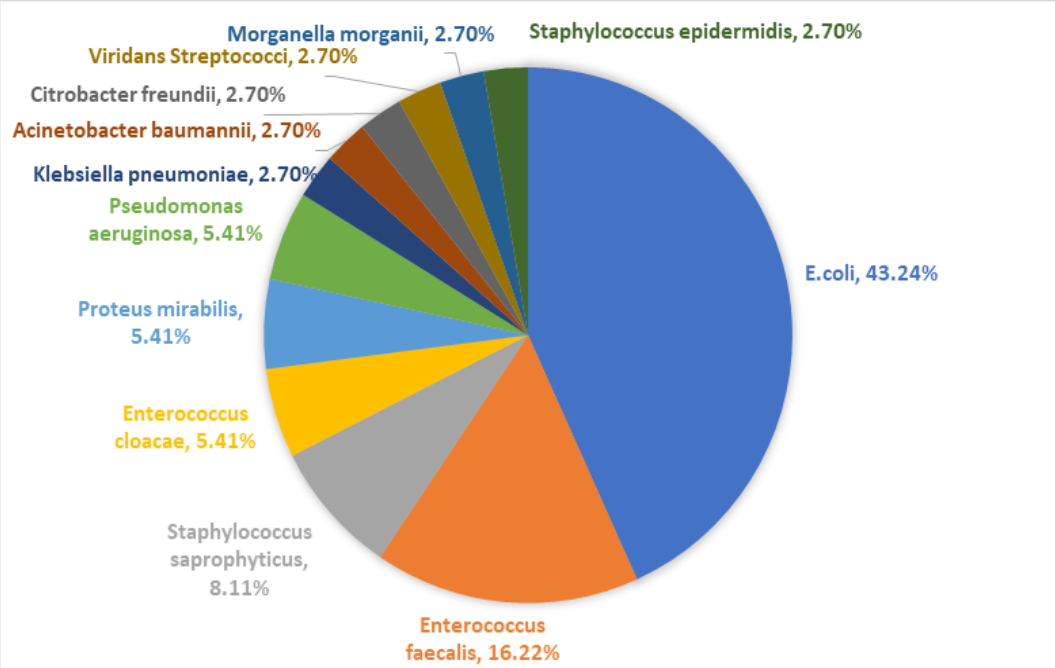

Figure 1. Multidrug resistant (MDR) pathogens

Table 3. Multivariable analysis for postoperative sepsis complications

Parameters	Odds ratio	95 % C.I. for odds		P-value
		Lower	Upper	
Sex				
Male	Reference			
Female	0.03	0.001	0.75	0.033
Preop creatinine	0.34	0.06	1.96	0.229
Stone number	1.28	0.84	1.93	0.246
Stone size	1.30	0.90	1.87	0.160
Staghorn stone				
No	Reference			
Yes	1.80	0.19	17.49	0.611
Diabetes mellitus				
No	Reference			
Yes	1.54	0.14	17.16	0.724
Blood loss	0.99	0.98	1.00	0.094
Positive MDR				
No MDR	Reference			
MDR	15.21	1.59	145.35	0.018
Postoperative fever				
No	Reference			
Yes	3.05	0.16	57.47	0.457
Stone free				
Stone free	Reference			
Retain stone	0.24	0.02	2.66	0.243
LOS	1.93	0.94	3.99	0.074

MDR = multidrug resistant, LOS = length of stay (days)

itself might be or become the cause of a persistent bacterial infection, in which case it would be wise to proceed with the PCNL with empirical antibiotic treatment. Counselling the patient about possible complications in either scenario is important. For patients without a previous history of preoperative urine cultures, assessing the prevalence of organisms can assist in determining the appropriate use of prophylactic antibiotics.

This study has some limitations. Some data was incomplete due to the retrospective nature of the study. The data was also only collected from a single-center limiting the generalization of the findings which would also be affected by the sample size being relatively small.

Conclusion

The prevalence of MDR bacteriuria in patients who underwent PCNL in our study was relatively high. This study found that female gender is a prophylactic factor, and also that preoperative MDR bacteriuria is a strong predictor of postoperative sepsis complications. Therefore, extra care and precautionary measures should be taken in treating male patients and those with positive MDR bacteriuria.

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Conflict of Interest

The authors declare no conflict of interest.

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