Preoperative Urine Analysis is An Effective Tool to Predict Fever After Miniaturized Percutaneous Nephrolithotomy on Large Renal Stones

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Purpose: To investigate the preoperative and intraoperative potential risk factors associated with miniaturized percutaneous nephrolithotomy (mPCNL) fever in the treatment of patients with large renal stones.

Materials and Methods: All patients with renal stones larger than 2.5 cm, who had undergone mPCNL, were included in the period between April 2018 and September 2019. Logistic regression analyses were performed to identify clinical variables associated with post-operative fever (>38°C).

Results: A total of 53 patients were enrolled for whom the median maximal stone length was 3.08 cm. 24 (45%) patients had a fever after mPCNL. Significantly more patients with urine WBC $\geq$ 27(/HPF) had a fever after surgery ($p = 0.004$). No significant between-group differences in urine cultures were found for the fever and non-fever groups ($p = 0.094$). Stepwise and multivariable logistic regression analyses all revealed that urine WBC $\geq$ 27(/HPF) is the only risk factor for developing post-mPCNL fever. Based on the highest body temperature, all of the patients were assigned into no fever, mild fever (37.5 $\leq$ Temp < 38.0), and fever groups, and an ordinal logistic regression analysis still supported the premise that the result of urine analysis is strongly associated with post-mPCNL fever.

Conclusion: Large renal stones are challenging to treat and associated with severe complications. Approximately 45% of large renal stone patients treated via mPCNL developed a fever. Urine WBC can easily and directly predict the risk of fever.

Keywords: renal stone; urolithiasis; percutaneous nephrolithotomy; urine analysis; urinary tract infection; fever; sepsis

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the standard of care for the treatment of large renal stones, defined as larger than 2cm[1]. Although PCNL is considered to be the most effective therapy, it is definitely associated with high risks of complication. Some publications have even reported complication rates up to 83% following PCNL[2]. High complication rates contributed to less than 4% nonendourologists performing this surgery[3]. PCNL carries two major concerns for complications. Bleeding accounts for most of the PCNL complications, and the incidence of blood transfusion has been reported from 5.5% to 18%[4,5]. Given the advancement in surgical techniques and equipment, miniaturized PCNL (mPCNL) was developed in an effort to reduce bleeding related to standard PCNL. According to UAA (Urology Association of Asia) guidelines[6], mPCNL is recommended for renal stones size < 3.0-3.5cm with good surgical outcome and less morbidity. However, relatively small tract size restricted the efficacy of stone removal and therefore increased the risks of post operation fever[7]. In consideration of infectious complications, few studies have used mPCNL to treat large renal stones, which was defined as "partial or complete renal stones filling the renal pelvis and one or more calices with diameter of at least 3 cm"[1,8]. Even utilizing PCNL on large renal stones, experienced urologists didn't have universal consensus on preoperative antibiotics strategies to prevent infection[8]. In this retrospective study, we aimed to investigate the preoperative and intraoperative potential risk factors associated with post-mPCNL fever in the treatment of patients with large renal stones.

MATERIAL AND METHODS

Study Design and Population

We retrospectively recruited reviewed patients from a single tertiary referral medical center between April 2018 and September 2019. The patients who fulfilled the definition of large renal stones and underwent mPCNL were included[8]. The reviewed data included patient demographics, body weight, and height on the admission day, and systemic diseases on medical records (e.g., diabetes mellitus (DM), hypertension (HTN), and cardiovascular disease). Preoperative laboratory investigations included urine analysis, midstream urine culture, complete blood count, renal, liver function tests, and electrolytes. Differentiation of white blood cells was also done on preoperative survey. The plate-

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Table 1. Demographics and baseline characteristics of the patients.

	Non fever (N=29) n (%)	Fever (N=24) n (%)	*p* value [a]
Age (years)			
median (IQR)	62.00 (55.00, 65.00)	63.00 (55.00, 66.50)	0.642
Gender			
Male	19 (65.52)	11 (45.83)	0.246
Female	10 (34.48)	13 (54.17)	
BMI (kg/m^2)			
< 25.0	13 (44.83)	11 (45.83)	1.000
≥ 25.0	16 (55.17)	13 (54.17)	
median (IQR)	25.60 (22.70, 29.99)	25.05 (22.95, 26.98)	0.655
Stone size			
< 30	12 (41.38)	12 (50.00)	0.726
≥ 30	17 (58.62)	12 (50.00)	
median (IQR)	30.84 (25.58, 38.09)	30.73 (23.60, 42.52)	0.964
Operation time			
< 120	9 (31.03)	3 (12.50)	0.202
≥ 120	20 (68.97)	21 (87.50)	
median (IQR)	130.00 (110.00, 180.00)	120.00 (175.00, 180.00)	0.123
Urine WBC(/HPF)			
< 27	20 (68.97)	6 (25.00)	0.004
≥ 27	9 (31.03)	18 (75.00)	
median (IQR)	19.00 (6.00, 33.00)	87.00 (22.50, 278.00)	0.007
WBC			
< 10000	28 (96.55)	20 (83.33)	0.164
≥ 10000	1 (3.45)	4 (16.67)	
median (IQR)	6500.00 (5100.00, 7600.00)	7250.00 (6250.00, 7950.00)	0.133
GFR			
< 90	13 (44.83)	12 (50.00)	0.921
≥ 90	16 (55.17)	12 (50.00)	
median (IQR)	96.14 (72.35, 107.66)	87.43 (63.45, 115.39)	0.480
PLR			
<110	11 (37.93)	7 (29.17)	0.705
≥ 110	18 (62.07)	17 (70.83)	
median (IQR)	125.83 (92.05, 173.27)	157.37 (106.57, 226.79)	0.085
NLR			
<5	28 (96.55)	18 (75.00)	0.038
≥5	1 (3.45)	6 (25.00)	
median (IQR)	1.91 (1.43, 2.68)	2.01 (1.34, 4.62)	0.416
Hydronephrosis			
No	13 (44.83)	7 (29.17)	0.376
Yes	16 (55.17)	17 (70.83)	
HU 900			
No	7 (24.14)	6 (25.00)	1.000
Yes	22 (75.86)	18 (75.00)	
Diabetes mellitus			
No	25 (86.21)	20 (83.33)	1.000
Yes	4 (13.79)	4 (16.67)	
UC			
No	25 (86.21)	15 (62.50)	0.094
Yes	4 (13.79)	9 (37.50)	

[a]chi-square test or Fisher's exact test for categorical variables / Mann-whitney U test for continuous variables.

let-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) were defined as the ratios of the absolute platelet, lymphocyte, and neutrophil counts, respectively. At the last outpatient clinics visit before surgery, midstream urine culture was collected from all the patients. All the patients were admitted one day before surgery. If the urine culture was negative, prophylactic intravenous (IV) broad-spectrum antibiotic was given after admission based on the recommendations from American Urology Association guideline[9]. In our hospital, cefuroxime is given as prophylactic antibiotics prior to operation in a negative urine culture patient. The patients who had positive urine culture were given with appropriate oral form or IV form antibiotics for 7 days according to sensitivity tests.

All the patients had at least one abdominal computed tomography (CT) before surgery. The maximal stone length was calculated based on CT images by the operator, and in cases of multiple stones, the stone length was calculated by adding the length of the longest axis of each stone. The mean attenuation levels in Hounsfield units (HUs) were measured by CT. We used the biggest circular diameters to cover the stone and calculated the average HU values. Stone clearance was assessed intraoperatively by direct renoscopy and postoperatively by radiography images. All patients underwent a plain abdominal film one month after mPCNL to see any residual stones. Stone free was defined as either complete clearance or clearance with insignificant residual fragments less than 4 mm in size on the follow-up imaging[10].

Operation details

All the operations were performed by the same experienced surgeon at our hospital using a 1- stage procedure. After induction of general anesthesia, a ureter occlusive catheter was retrogradely placed to the target kidney by cystoscopy. Percutaneous access was performed using an 18-gauge needle under combined echo and fluoroscopic assistance. After successful access, a guidewire was inserted into the collecting system and

Table 2. Results of operations.

	Crude OR (95 % CI)	*p*-value	Adjusted OR [a] (95 % CI)	*p*-value	Adjusted OR [b] (95 % CI)	*p*-value	Adjusted OR [c] (95 % CI)	*p*-value
Age (years)	1.02 (0.97-1.08)	0.412						
Age (per 10 years)	1.24 (0.74-2.06)	0.412						
Gender								
Male	Ref.							
Female	2.25 (0.74-6.81)	0.153						
BMI (kg/m^2)	0.93 (0.80-1.08)	0.334						
BMI								
<25.0	Ref.							
≥25.0	0.96 (0.32-2.85)	0.942						
Stone size	1.01 (0.96-1.06)	0.723						
Stone size								
<30	Ref.							
≥30	0.71 (0.24-2.10)	0.531						
Operation time	1.01 (0.99-1.02)	0.217						
Operation time								
< 120	Ref.				Ref.			
≥ 120	3.15 (0.74-13.34)	0.119			5.30 (1.02-27.55)	0.047		
Urine WBC	1.00 (0.99-1.00)	0.860						
Urine WBC (/HPF)								
< 27	Ref.		Ref.		Ref.		Ref.	
≥ 27	6.67 (1.98-22.44)	0.002	5.48 (1.57-19.10)	0.008	5.08 (1.39-18.60)	0.014	8.86 (2.35-33.42)	0.001
WBC	1.00 (1.00-1.00)	0.094						
WBC								
< 10000	Ref.							
≥ 10000	5.60 (0.58-53.94)	0.136						
GFR	0.99 (0.98-1.01)	0.406						
GFR								
< 90	Ref.							
≥ 90	0.81 (0.28-2.40)	0.707						
PLR	1.01 (0.99-1.02)	0.121						
PLR								
< 110	Ref.							
≥ 110	1.48 (0.47-4.72)	0.503						
NLR	1.20 (0.87-1.66)	0.261						
NLR								
< 5	Ref.		Ref.		Ref.			
≥ 5	9.33 (1.04-84.02)	0.046	5.82 (0.58-58.46)	0.135	5.22 (0.48-56.94)	0.175		
Hydronephrosis								
No	Ref.							
Yes	1.97 (0.63-6.20)	0.245						
HU 900								
No	Ref.							
Yes	0.95 (0.27-3.35)	0.942						
Diabetes mellitus								
No	Ref.							
Yes	1.25 (0.28-5.63)	0.771						
UC								
No	Ref.				Ref.			
Yes	3.75 (0.98-14.33)	0.053			1.52 (0.27-8.58)	0.633		

[a] Multivariable logistic regression analysis of variables (*p*-value < 0.05 in univariate logistic regression analysis). AIC: 65.61
[b] Multivariable logistic regression analysis of variables (*p*-value < 0.1 in univariate logistic regression analysis). AIC: 67.45
[c] Stepwise logistic regression for variables entry in model $p < 0.1$ $p < 0.05$ & stay in model $p < 0.1$ $p < 0.05$. AIC: 63.97

the tract was dilated using balloon dilators until an 18 Amplatz sheath can be placed. Mini-nephroscopy (12 Fr Richard Wolf) was inserted into the Amplatz sheath and stones were disintegrated using Holmium laser. Holmium:yttrium-aluminum-garnet (Ho:YAG) laser 60 W is generated by Sphinx 60(LISA Laser, Pleasanton, CA, USA) with setting of energy from 0.5-1.5J and frequency from 6-20 Hz for fragmentation[(11)]. The stone fragments were removed with forceps. After the completion of stone extraction, a 6 Fr double J catheter was inserted. A 14F nephrostomy tube was placed at the end of each surgery. The operative time was calculated from the insertion of the cystoscopy to the completion of nephrostomy tube placement.

Fever definition and management

Ear temperatures were recorded every 2 hours after surgery on all patients. Fever was defined as body temperature > 38 °C. For every patient, the highest body temperatures were recorded. The normal range of ear temperature is between 35.7 to 37.5 degree[(12)]. Based on the highest body temperature, we further separated non-fever group into no fever and mild fever group (37.5 ≤ Temp < 38.0).

All fever patients are treated with IV form antibiotics which are adjusted by urine culture results. The choices of definite antibiotics in fever group are listed in supplementary data. The treatment duration is 7 to 14 days with oral or IV form antibiotics according to European Association of Urology (EAU) infections guidelines[(13)]. If there are no available culture results, antibiotics is given with second or third generation of cephalosporin by EAU guidelines recommendation[(13)].

Table 3. Difference in clinical features and laboratory findings of mPCNL patients subsequently happening fever (Temp ≥ 38.0), mild fever (37.5 ≤ Temp < 38.0) or not (Temp < 37.5).

	Non fever (N=21) n (%)	Mild fever (N=8) n (%)	Fever (N=24) n (%)	*p* value[a]
Age (years)				
median (IQR)	58.00 (52.00, 65.00)	62.50 (57.50, 66.50)	63.00 (55.00, 66.50)	0.661
Gender				
Male	15 (71.43)	4 (50.00)	11 (45.83)	0.232
Female	6 (28.57)	4 (50.00)	13 (54.17)	
BMI (kg/m^2)				
< 25.0	8 (38.10)	5 (62.50)	11 (45.83)	0.570
≥ 25.0	13 (61.90)	3 (37.50)	13 (54.17)	
median (IQR)	25.90 (23.92, 30.08)	23.65 (22.62, 26.40)	25.05 (22.95, 26.98)	0.512
Stone size				
< 30	11 (52.38)	1 (12.50)	12 (50.00)	0.156
≥ 30	10 (47.62)	7 (87.50)	12 (50.00)	
median (IQR)	27.77 (23.50, 36.93)	36.14 (31.65, 42.28)	30.73 (23.60, 42.52)	0.160
Operation time				
< 120	7 (33.33)	2 (25.00)	3 (12.50)	0.246
≥ 120	14 (66.67)	6 (75.00)	21 (87.50)	
median (IQR)	120.00 (110.00, 155.00)	160.00 (115.00, 240.00)	175.00 (120.00, 180.00)	0.130
Urine WBC (/HPF)				
< 27	15 (71.43)	5 (62.50)	6 (25.00)	0.006
≥ 27	6 (28.57)	3 (37.50)	18 (75.00)	
median (IQR)	15.00 (5.00, 33.00)	24.50 (9.00, 101.50)	87.00 (22.50, 278.00)	0.016
WBC				
< 10000	20 (95.24)	8 (100.00)	20 (83.33)	0.355
≥ 10000	1 (4.76)	0 (0.00)	4 (16.67)	
median (IQR)	6600.00 (4800.00, 8500.00)	6000.00 (5450.00, 6650.00)	7250.00 (6250.00, 7950.00)	0.188
GFR				
< 90	11 (52.38)	2 (25.00)	12 (50.00)	0.430
≥ 90	10 (47.62)	6 (75.00)	12 (50.00)	
median (IQR)	88.56 (72.35, 110.80)	100.32 (71.58, 105.49)	87.43 (63.45, 115.39)	0.671
PLR				
< 110	8 (38.10)	3 (37.50)	7 (29.17)	0.798
≥ 110	13 (61.90)	5 (62.50)	17 (70.83)	
median (IQR)	121.22 (89.56, 165.01)	145.98 (94.22, 180.08)	157.37 (106.57, 226.79)	0.188
NLR				
< 5	20 (95.24)	8 (100.00)	18 (75.00)	0.091
≥ 5	1 (4.76)	0 (0.00)	6 (25.00)	
median (IQR)	1.78 (1.36, 2.50)	2.31 (1.69, 3.19)	2.01 (1.34, 4.62)	0.519
Hydronephrosis				
No	9 (42.86)	4 (50.00)	7 (29.17)	0.440
Yes	12 (57.14)	4 (50.00)	17 (70.83)	
HU 900				
No	3 (14.29)	4 (50.00)	6 (25.00)	0.136
Yes	8 (85.71)	4 (50.00)	18 (75.00)	
Diabetes mellitus				
No	18 (85.71)	7 (87.50)	20 (83.33)	1.000
Yes	3 (14.29)	1 (12.50)	4 (16.67)	
UC				
No	19 (90.48)	6 (75.00)	15 (62.50)	0.094
Yes	2 (9.52)	2 (25.00)	9 (37.50)	

[a] chi-square test or Fisher's exact test for categorical variables / Kruskal-Wallis Test for continuous variables.

Statistical analysis

All categorical variables were analyzed by chi-square test or Fisher's exact test. The Mann-Whitney U test was used to compare continuous variables. For the comparison of three groups, Kruskal-Wallis tests were used to analyze continuous variables. Multiple logistic regression analysis was used to determine any risk factors associated with fever. The variables were selected if their p values were less than 0.10 in univariate logistic regression analysis. For the comparison of three groups, ordinal logistic regression analysis was conducted.

All analyses were conducted using SPSS statistical software (versions 16; SPSS Inc., Chicago, CA, USA). Two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

A total of 53 patients were enrolled and 56.6% of them were male. The median maximal stone length was 3.08 cm (95% CI=2.98 to 3.57). Most of the patients were above 60 years old (58.5%). The mean age was 59.91 years old (SD=10.99). The overall stone-free rate was 67.9 % (36 of 53 patients). 45.3% (24 of 53 patients) patients had fever after the operation. We compared the baseline characteristics between the fever and the non-fever groups (**Table 1**). The demographic characteristics were generally similar in each group. Only urine WBC was significantly different between the two groups. Among all, only 9 patients didn't have pyuria before surgery. Significantly more patients with urine WBC ≥ 27 had fever after surgery ($p = 0.004$). No significant difference in urine culture was found between the two groups ($p = 0.094$). The logistic regression analysis (**Table 2**) indicated that urine WBC ≥ 27(/HPF) is the risk factor for developing post-mPCNL fever. The association between urine culture and post-mPCNL fe-

Table 4. Ordinal logistic regression analysis of risk factors for fever among mPCNL patients.

	Crude OR (95 % CI)	*p*-value	Adjusted OR [a] (95 % CI)	*p*-value	Adjusted OR [b] (95 % CI)	*p*-value	Adjusted OR [c] (95 % CI)	*p*-value
Age (years)	1.03 (0.98-1.08)	0.236						
Age (per 10 years)	1.34 (0.83-2.17)	0.236						
Gender								
Male	Ref.				Ref.			
Female	2.48 (0.86-7.11)	0.091			1.83 (0.54-6.13)	0.331		
BMI (kg/m^2)	0.91 (0.79-1.05)	0.210						
BMI								
< 25.0	Ref.							
≥ 25.0	1.28 (0.46-3.55)	0.639						
Stone size	1.02 (0.98-1.08)	0.347						
Stone size								
< 30	Ref.							
≥ 30	1.04 (0.37-2.88)	0.944						
Operation time	1.01 (0.99-1.02)	0.116						
Operation time								
< 120	Ref.						Ref.	
≥ 120	2.86 (0.81-10.13)	0.104					5.29 (1.24-22.57)	0.025
Urine WBC	1.00 (0.99-1.00)	0.611						
Urine WBC (/HPF)								
< 27	Ref.		Ref.		Ref.		Ref.	
≥ 27	5.70 (1.88-17.25)	0.002	4.16 (1.29-13.36)	0.017	3.83 (1.18-12.48)	0.026	8.26 (2.43-28.02)	0.001
WBC	1.00 (1.00-1.00)	0.150						
WBC								
< 10000	Ref.							
≥ 10000	4.93 (0.56-43.54)	0.152						
GFR	1.00 (0.98-1.01)	0.542						
GFR								
< 90	Ref.							
≥ 90	1.05 (0.38-2.91)	0.921						
PLR	1.01 (0.99-1.02)	0.104						
PLR								
<110	Ref.							
≥110	1.42 (0.48-4.16)	0.525						
NLR	1.22 (0.89-1.69)	0.217						
NLR								
<5	Ref.		Ref.		Ref.			
≥5	8.43 (1.00-71.13)	0.050	3.78 (0.41-34.89)	0.241	4.59 (0.47-44.82)	0.190		
Hydronephrosis								
No	Ref.							
Yes	1.68 (0.59-4.82)	0.336						
HU 900								
No	Ref.							
Yes	0.66 (0.20-2.17)	0.492						
Diabetes mellitus								
No	Ref.							
Yes	1.19 (0.29-4.95)	0.813						
UC								
No	Ref.		Ref.		Ref.			
Yes	4.03 (1.08-15.06)	0.038	1.81 (0.40-8.20)	0.439	1.40 (0.28-6.87)	0.681		

[a] Multivariable logistic regression analysis of variables (p-value < 0.05 in univariate logistic regression analysis). AIC: 103.91
[b] Multivariable logistic regression analysis of variables (p-value < 0.10 in univariate logistic regression analysis). AIC: 104.98
[c] Stepwise logistic regression for variables entry in model $p < 0.10$ $p < 0.05$ & stay in model $p < 0.10$ $p < 0.05$. AIC: 99.18

ver revealed a marginal trend toward significance before adjustment ($p = 0.053$). However, the significance blunted after adjustment ($p = 0.369$). In ordinal logistic regression analysis (**Table 4**), urine culture and NLR revealed significance in univariate analysis, but there was no statistical significance in multivariable logistic regression analysis. Stepwise and multivariable logistic regression analysis also suggested that urine WBC ≥ 27(/HPF) is still the risk factor for developing post-mPCNL fever. According to Akaike information criterion (AIC) which is listed in Table 2 and Table 4, stepwise logistic regression is the best-fit model. Based on the highest body temperature, all the patients were assigned to no fever, mild fever, and fever groups (Table 3). Only 8 patients were in the mild fever group. Most clinical characteristics were not significantly different. Only urine WBC was significantly different between the three groups. We used ordinal logistic regression analysis to find any risk factors for developing fever (**Table 4**). Only urine WBC ≥ 27(/HPF) could predict whether the patients had fever after mPCNL. The area under the curve for WBC ≥ 27 (/HPF) was 0.72 (**Figure 1**). Using the cutoff of WBC ≥ 27 (/HPF), the sensitivity was 75% and specificity 69%, with an odds ratio of 6.67 (1.98-22.44; p value = 0.002).

The bacteria type of urine culture and stone composition of those patients are listed in supplementary table. Gram-negative bacteria, such as Proteus mirabilis, Klebsiella pneumoniae and Escherichia coli were the most common pathogens from urine culture. In both fever and non-fever groups, calcium oxalate stone was the leading composition from stone analysis.

In fever group, average fever lasting days was 1.67 days, only 4 patients had fever lasting more than two days including the operation day, and the onset day of fever was on post-operative day (POD) 0 and 1 in most

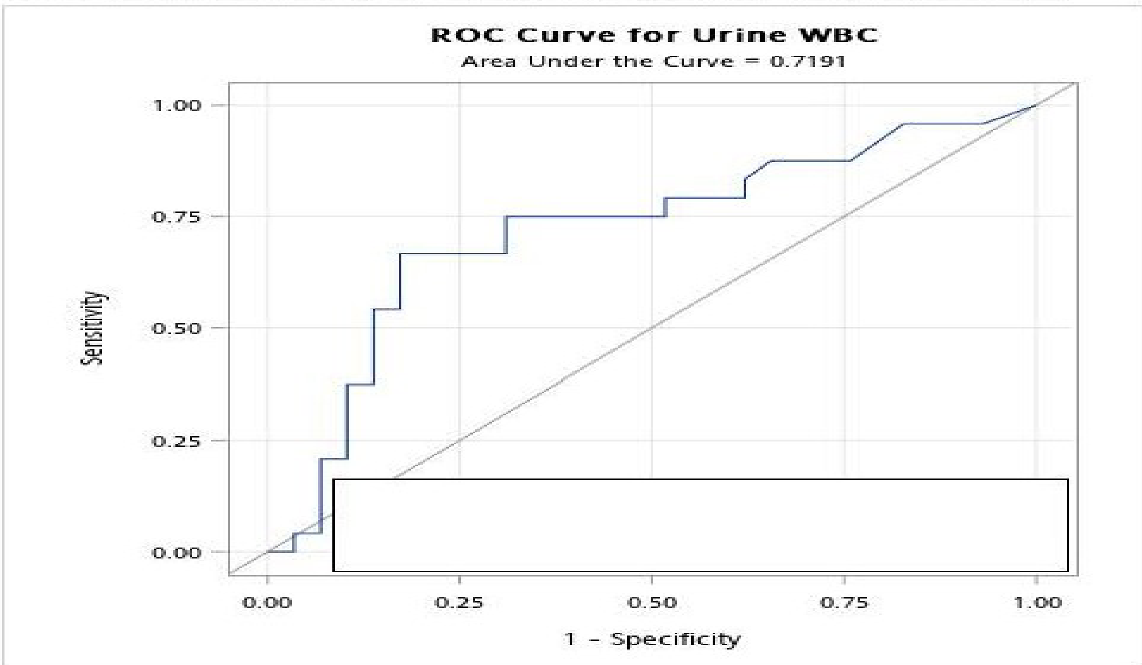

Figure 1. ROC curve of urine WBC on post-mPCNL fever. AUC, area under curve.

cases. The details fever pattern were listed in supplementary table.

DISCUSSION

In the current study, we analyzed the risk factors for developing fever after mPCNL treatment on large renal stones. Numerous studies have studied the contributing factors for infectious complications after PCNL, but few aimed at mPCNL. Lai et al. had conducted a meta-analysis on 2018 and a total of 24 studies were recruited, of which 12 were prospective and 12 were retrospective[14]. In all the prospective studies, preoperative urine culture, intraoperative renal pelvic urine culture, and stone culture have been associated with fever after PCNL. Only preoperative urine culture and stone culture were found to be significantly associated with infection of all the retrospective studies. However, stone culture is not a common preoperative exam in all medical facilities. Besides, the exam should rely on urinary tract stone specimens, which are usually taken from surgery. Therefore, it is unlikely to have results soon after surgery. Taken together, although the stone culture appears to be the strongest risk factor on literature, stone culture is only available after PCNL and, therefore, cannot be used to prevent infectious complications.

Urine cultures, including preoperative midstream urine and intraoperative renal pelvis urine, are also associated with post PCNL infectious complications[15,16]. Even some studies found that intraoperative renal pelvis urine was more predictable than preoperative urine culture [17,18]. The finding was offset by the meta-analysis results[14]. Besides, intraoperative renal pelvis urine culture was performed during operation and the culture may take 5 days to have the results, which indicates that intraoperative renal pelvis urine culture was not a practical tool for predicting post-PCNL fever. Preoperative midstream urine culture is a common practice to detect latent bacteria in the urinary tract in most facilities. However, the accuracy of midstream urine culture for predicting infectious complications after PCNL is always questioned. A prospective study revealed near half positive stone culture patients had negative preoperative midstream urine culture. Consequently, the author concluded that although preoperative midstream urine culture should be collected, neither a positive nor a negative midstream urine culture influences the risk of postoperative systemic inflammatory response syndrome (SIRS). In the current study, we only had the results of midstream urine culture rather than stone culture or renal pelvis urine culture. No matter in univariable or multivariable analysis, the result of midstream urine culture can't be the predictor to distinguish whether the patient will have fever after mPCNL or not. In contrast, the result of urine analysis can strongly predict post mPCNL fever even by the use of stepwise logistic regression. In analysis of mild fever and fever groups, urine WBC ≥ 27 was still strongly associated with post-surgery fever using ordinal logistic regression. All the solid evidence above highly suggested that urine WBC alone can reliably predict the risk of post-mPCNL fever.

The first introduction of the technique of mPCNL was in 1997, which was using an 11~15Fr sheath on pediatric stone patients by Jackman et al. and Helal et al[19,20]. Afterward, mPCNL is generally accepted as tract sizes between 14 Fr and 22 Fr, although a clear definition remains controversial[21]. Echo, fluoroscopy or combined guided tract creation are applied in mPCNL currently[22]. In our hospital protocol, we combine ultrasound and fluoroscopy guidance to create tract. The first step is ultrasound guided needle placement, and then position confirmation by fluoroscopy. Ultrasonography guided calyx access has been proved feasibility, but some pitfalls have been found such as minimal hydronephrosis, superior pole approach or high lying kidneys[23] with bare ultrasound guidance. A prospective and randomized trial[22] showed combined ultrasonographic and fluoroscopic guidance for percutaneous renal access in mini-percutaneous nephrolithotomy is safe and effective especially in complex renal stone. Ultrasonic and pneumatic lithotripsy devices have showed efficacy and safety in PCNL[24]

Due to narrow working channel of nephroscopes in mPCNL, Holmium laser (Sphinx 60, LISA Laser, Pleasanton, CA, USA) is applied in our institute. However, small diameter dual energy lithotripsy has showed comparable stone clearing in mPCNL[25]. It needs further investigations and large size studies in the future.

Most available evidence support the role of mPCNL is more suitable for smaller rather than larger renal stones >20 mm[21]. The main reasons for the limitations are increased operation time[26] and concerning infectious complications. In the literature, fever occurred in 21%-39.8% of patients who underwent PCNL, but small number of patients progressed to sepsis or even mortality[27]. During any endoscopic surgeries, irrigation is always requested to maintain a clear visual field. High intrapelvic pressure (IPP) caused by irrigation can lead to pyelovenous and pyelolymphatic backflow, which will transmit bacteria and endotoxin into the systemic circulation and infectious complications develop(28). Comparing with standard PCNL, miniaturized percutaneous sheath restricted efficient circulation of irrigation fluid and then IPP increased during mPCNL (29). Theoretically, mPCNL could be prone to have post-surgery fever, and a study confirmed this hypothesis with the result of nearly two times higher incidence of fever after mPCNL compared with the standard[7]. In our results, near half of the patients had fever episodes after mPCNL, but only 4 patients (7.5%) persisted fever more than two days after the operation (including the operation day). None of them had septic shock or sepsis. The findings can be explained by the hypothesis mentioned above that transient peak IPP leads to fever but is soon ameliorated under an adequate control of outflow with a JJ catheter insertion or nephrostomy tube placement. There are limited studies assessing mPCNL on large renal stones until very recently. Kandemir et al. and Güler et al. all introduced the outcomes of mPNL in the treatment of renal stones ≥ 3cm[30,31]. The stone free rate (SFR) reported in two studies were 75.0% and 76.5%, respectively. In discordance with the literature, we have found an obvious lower SFR (67.9%). The reasons for the different results obtained in the present study might be that 8 of them (15.0%) were cases with complete staghorn stones. Accumulative evidence suggests that staghorn stones are the most difficult to achieve stone clearance. Besides, the number of cases enrolled in the present cohort is relatively small. The difference in a few cases could easily affect the proportion of the outcome.

There are some limitations to this study. First, the study was based on retrospective patient data from a single center. Large-scale and prospective design studies will be needed for further analysis. Second, we did not discuss the relationship between fever and residual stone. Besides, the stone sizes in the current study ranged too wide, which would limit the specificity of the analysis. In contrast, it is worthy to mention that this is the first study to analyze the possible factors contributing to fever after mPCNL in the treatment of kidney stones larger than 3cm. Our investigation is also the first one to use the peak body temperature to ordinally evaluate post-mPCNL infectious complications rather than fever or not. The ordinal logistic regression analysis definitely strengthens our findings.

CONCLUSIONS

In patients with large renal stones, mPCNL is associated with adequate stone clearance rate but high incidence of post-surgery fever. Urine WBC alone rather than urine culture can reliably predict the risk of post-mPCNL fever. Using the cutoff of WBC ≥ 27, the predictive sensitivity was 75% and specificity was 69%.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

APPENDIX

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