



Risk factors for the fever after percutaneous nephrolithotomy: a retrospective analysis

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Background: It's very common to see the onset of fever after percutaneous nephrolithotomy (PCNL), it's necessary to analyze the risk factors for the fever following PCNL, and to provide evidence for infection prevention after PCNL.

Methods: A total of 546 adult PCNL patients were included as study subjects and retrospective studies were performed. We collected clinical data of patients using a prospectively designed database. Univariate and multivariate logistic regression analyses were performed to identify the potential risk factors for the fever after PCNL.

Results: Of the included 546 PCNL patients, there were 82 fever patients and 464 no-fever patients following PCNL. *Escherichia coli* and *Proteus mirabilis* are the two most common infectious bacteria. Preoperative urinary tract infection (OR =4.38, 95% CI: 1.15–9.53), multiple access (OR =5.31, 95% CI: 1.23–10.75), diabetes (OR =4.97, 95% CI: 1.37–9.86), length of operation ≥ 60 min (OR =5.67, 95% CI: 2.24–13.42), estimated blood loss in PCNL ≥ 500 mL (OR=2.78, 95% CI: 2.32–3.61) were the independent risk factors associated with postoperative infection.

Conclusions: Effective control of urinary tract infection, reduction of access number, strict control of blood glucose, length of operation control, reduction of intraoperative bleeding should be considered as measures to prevent postoperative fever for patients with PCNL.

Keywords: Fever; percutaneous nephrolithotomy (PCNL); risk; retrospective analysis

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Introduction

As a common urological disease, the incidence of urinary tract calculi has significantly increased in recent years, if left untreated, it can severely impair the function of urinary system (1,2). Percutaneous nephrolithotomy (PCNL) has gradually become the preferred choice for the treatment of urinary calculi clinically, and its safety and efficacy have been recognized by patients and clinician (3). However, PCNL can complicate many adverse events. Among them, systemic inflammatory response syndrome (SIRS) is one of

the common complications after urinary calculus surgery (4). Even if preoperative prophylactic treatments have been conducted, the incidence of SIRS caused by infection remains rather high. It's been reported (5,6) that 25.8–39.8% patients get infected after PCNL, and 0.4–3% sepsis rates were found after PCNL. With consideration to the potentially devastating morbidity and up to 50% mortality associated with sepsis (7,8), SIRS compromises the effect and safety of PCNL, and it can result in reduced patient comfort, longer hospital stays, and increased medical costs (9). Therefore, the early observations and preventions

should be established to prevent SIRS.

Fever is one of the most important and timely clinical manifestations of SIRS, the patients with fever may have higher risks of SIRS (10,11). However, the potential reasons and mechanisms related to the onset and development of SIRS remains unclear (12). Furthermore, previous studies (13,14) have indicated that the fever may be a precursor symptom of SIRS, which is an early sign and important factor affecting the prognosis of patients. The observation of fever after PCNL can make important influences on the patients' prognosis. Therefore, it's well-believed that it is necessary to pay attention to the fever after PCNL, and to identify the causes and risk factors of fever to prevent SIRS. Although the factors affecting post-PCNL fever have been extensively evaluated over the years, the main reason for fever and related SIRS after PCNL is not clear. Therefore, in this present study, we retrospectively evaluated the clinical data of patients with fever or no fever following PCNL, aimed to identify the potential risk factors for fever after PCNL, thereby providing evidence for the management of PCNL patients.

Methods

Ethical considerations

The study was approved by the Medical Research Ethics Committee of our hospital (No.20170038) and informed consent was taken from all the patients.

Participants

Between June 2017 and June 2019, a total of 546 adult PCNL patients with completed clinical data were included as study subjects and retrospectively reviewed. The inclusion criteria were as follows: adult patients with age ≥ 18 years old; they underwent single-stage PCNL and were followed in our hospital; the related clinical data were complete. Patients under the age of 18, patients with cancer, heart or kidney failure, patients taking immunosuppressive agents, patients taking two or more-stage PCNL, PCNL combined with another surgery in one operation were excluded from this present study.

All the patient data were collected with a prospectively collected database. Patient assessments included medical history, physical examination, urine analysis, midstream urine and blood culture, complete blood count, renal function tests, abdominal plain film, ultrasonography, and/or drainage urinary tract map. Preoperative abdominal

computed tomography was routinely performed in some patients to determine the position of related organs and the proposed nephrostomy tube. All preoperative patients received a single dose of prophylactic antibiotics during the induction of anesthesia.

PCNL procedures

All the PCNL procedures were performed by the urology surgery team of our hospital. General anesthesia was performed for patients undergoing PCNL. The lithotomy position was taken first, and the ureter was retrogradely inserted into the renal pelvis under the ureteroscope. Then the stent tube was connected with saline to cause artificial hydronephrosis, and the 16F double-lumen catheter was placed through the urethra. Then put patients in prone position, the B ultrasound-guided puncture was performed between the 1st rib or the 12th costal margin or between the posterior tibial line and the lower scapula line, to get into the target renal pelvis, the dilator expanded to 24F to introduce the metal sheath and endoscope. The perfusate was 0.9% NaCl solution, and the flow rate was controlled by a perfusion pump at 200–350 mL/min during the operation, and the ultrasound or pneumatic ballistic lithotripsy was performed. The stone fragments were removed by forceps and irrigation. After the completion of stone removal, one of the F5 double J tubes in the ureter was placed retrogradely, and 14F renal fistula tube was indwelled through the channel. The renal tube was routinely removed 2–4 days after surgery. Antegrade nephrostography was routinely performed before the tube removal to ensure adequate drainage of the collecting system.

Definition of outcomes

Preoperative urinary tract infection was defined as the bacteria is $\geq 10^3$ colony forming units/mL (CFU/mL) in the culture of patients' urinary specimen before PCNL.

The postoperative short-term increase in body temperature below 38.5 °C was identified as normal response to surgery, and in this present study, the body temperature ≥ 38.5 °C was defined as fever. For fever patients after PCNL, the blood and urine specimens were both collected and sent for bacteria culture analyses.

Data collection

We collected the patient's clinical data with prospectively

designed database: age, gender, underlying disease, preoperative urinary tract infection, hydronephrosis, stone status (position, number, size), operation time, the number of PCNL accesses, intraoperative bleeding, length of catheter removal, length of hospital stay, the results of urinary and blood culture, and postoperative fever.

Statistical analysis

All of the statistical analyses were analyzed with SPSS 21.0 (SPSS Inc., Chicago, USA). The categorical variables were analyzed using the χ^2 test or Fisher's exact test, and the continuous variables were analyzed using Student's t test or Mann-Whitney U test, and it were generally presented as means and standard deviation. Multivariate logistic regression analyses were performed using the forward likelihood ratio selection method to identify independent factors of fever and it is presented with an odds ratio (95% confidence intervals, CI). Potential candidate variables were those with $P < 0.05$ in univariate analyses. All of the P values were 2 tailed, and $P < 0.05$ was considered as being statistically significant.

Results

The demographic and clinical characteristics of PCNL patients

The medical records on 546 patients who underwent PCNL were retrospectively collected and analyzed. The overall mean age was 46.3 ± 9.5 years old, and there were 418 male patients and 128 female patients. Of the included 546 PCNL patients, there were 82 fever patients and 464 no-fever patients following PCNL. The demographic characteristics and clinical information of PCNL patients are presented in *Table 1*. There were significant differences in the number of diabetes, preoperative urinary tract infection, PCNL accesses, estimated blood loss in PCNL, length of operation, mean catheter removal between fever and no-fever PCNL patients (all $P < 0.05$), no significant differences were found in the age, gender, hydronephrosis, stone localization, mean stone burden, preoperative creatinine or length of hospital stay between two groups (all $P > 0.05$).

Bacterial species detected in the cultures

The urine culture results of 82 fever patients indicated that

there were 21 cases of *Escherichia coli*, 12 cases of *Proteus mirabilis*, 1 case of *Pseudomonas aeruginosa*, 1 case of *Klebsiella oxytoca*, 3 cases of *Enterococcus faecalis*, and 44 cases of negative results (*Figure 1*).

The blood culture results of 82 fever patients indicated that there were 16 cases of *Escherichia coli*, 7 cases of *Proteus mirabilis* and 59 cases of negative results (*Figure 2*).

Multivariate regression analysis on the of fever after PCNL

An further unconditional logistic multiple regression analysis was further performed on the seven variables with significant differences in univariate analysis, the logistic multiple regression analysis indicated that preoperative urinary tract infection, multiple access, diabetes, length of operation ≥ 60 min, estimated blood loss in PCNL ≥ 500 mL were independent risk factors associated with postoperative infection respectively (*Table 2*).

Discussion

PCNL has gradually become the preferred option for the treatment of most upper urinary calculi in recent years. With the popularity of this technology clinically, more and more complications have been recognized by clinicians. SIRS is one of complications receiving numerous attentions from health care providers, and it's one of the most important and timely clinical manifestations for SIRS (15,16). Therefore, understanding the risk factors affecting postoperative fever after PCNL has important guiding significance for preventing SIRS after PCNL.

The postoperative fever happens frequently in patients with preoperative urinary tract infection, it can be explained by that although antibiotics were used before surgery, the use of the treatment was insufficient and the urinary tract infection was not completely controlled. Besides, for patients with hydronephrosis before surgery, sometimes due to urinary tract obstruction is more serious, after antibiotic treatment, urinary leukopenia. And there may be an illusion that preoperative infection is basically controlled, but the renal pelvis fluid is still turbid and even purulent, and the bacteria in the stones still remain (3,16). Therefore, we believe that patients with preoperative urinary tract infection should be given sufficient attentions, adequate active treatment with sensitive antibiotics to reduce postoperative infection are needed. If the renal sputum is turbid or purulent during surgery, it is necessary to take renal pelvis fluids or stones for bacterial culture and drug

Table 1 The demographic characteristics and clinical information of PCNL patients

Factors	Fever (n=82)	No fever (n=464)	χ^2/t	P
Age(years)	46.5±8.3	46.2±9.7	12.49	0.091
Gender			1.09	0.158
Male	62	356		
Female	20	108		
Diabetes			14.35	0.001
Yes	9	11		
No	73	453		
Preoperative urinary tract infection			10.45	0.005
Yes	68	55		
No	14	409		
Hydronephrosis			1.44	0.190
Yes	40	236		
No	42	228		
Stone localization			5.48	0.122
Pelvis	21	115		
Pelvis + calix	19	93		
Lower pole	12	78		
Upper pole	11	55		
Staghorn	9	62		
Ureter	10	61		
Mean stone burden (mm ²)	450.5±55.4	442.9±64.7	12.08	0.174
Preoperative creatinine (mg/dl)	0.82±0.16	0.82±0.22	1.34	0.190
Access			10.58	0.002
Single	61	436		
Multiple	21	28		
Estimated blood loss in PCNL (mL)			23.50	0.014
<500	57	402		
≥500	25	62		
Length of operation (min)			15.22	0.009
<60	16	385		
≥60	66	79		
Mean catheter removal (day)	3.98±1.01	2.16±0.93	1.42	0.025
Length of hospital stay (day)	4.21±1.28	4.02±1.14	1.75	0.106

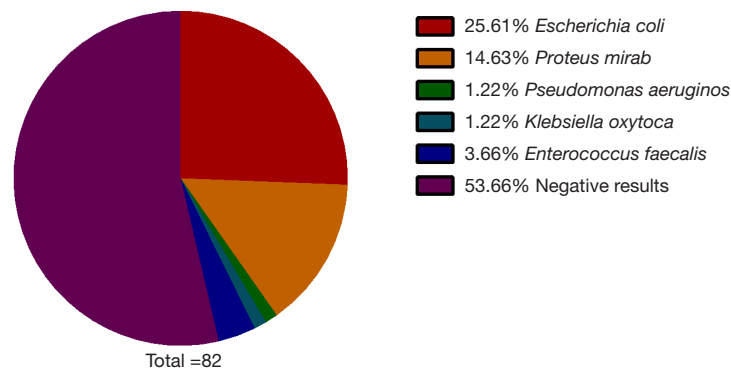


Figure 1 The bacterial distribution of urine culture of 82 fever patients.

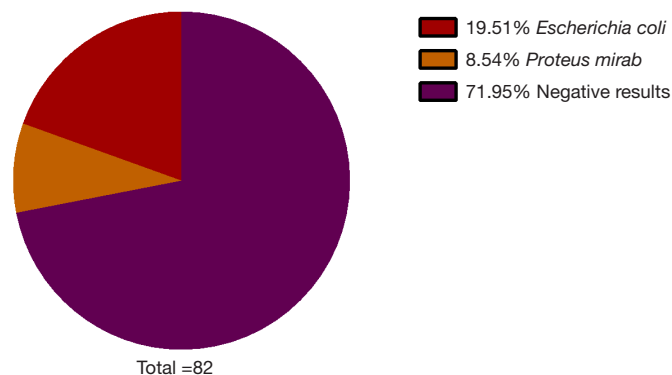


Figure 2 The bacterial distribution of blood culture of 82 fever patients.

Table 2 Multivariate regression analysis on the risk factors of fever after PCNL

Factors	β	SE	OR	95% CI	P	Rank
Preoperative urinary tract infection	0.89	0.29	4.38	1.15–9.53	0.048	1
Multiple access	0.92	0.31	5.31	1.23–10.75	0.031	2
Diabetes	1.03	0.45	4.97	1.37–9.86	0.042	3
Length of operation ≥ 60 min	0.99	0.39	5.67	2.24–13.42	0.019	4
Estimated blood loss in PCNL ≥ 500 mL	1.13	0.11	2.78	2.32–3.61	0.025	5

susceptibility test during surgery, so that sensitive antibiotics can be selected for postoperative fever (17,18).

Previous studies (19-21) have reported that the larger the stone, the more gravel, the greater the chance of stone retention, and the higher risk of postoperative infection. Besides, it increases the possibility of damage to the kidney and renal pelvis mucosa during the crushing process, which in turn causes open blood vessels and increased perfusion fluid absorption (22,23). Therefore, many scholars (24-26) at home and abroad believe that the size and

quantity of stones are closely related to infection and fever, which are not supported by our findings that the size of stone is not related to the postoperative infection. However, the multiple access is independent risk factors associated with postoperative infection. It's understandable that the larger stones are more difficult to pass through the microchannel gravel, it may be necessary to establish multiple accesses, which accordingly increase the duration of operation time and risk of bleeding (27,28).

Univariate and multivariate logistic regression analyses

have showed that length of operation ≥ 60 min and estimated blood loss in PCNL ≥ 500 mL are risk factors for postoperative fever, with OR values of 5.67 and 2.78, respectively. PCNL requires a large amount of normal fluids to maintain perfusion. Nevertheless, the temperature of normal saline is significantly lower than the body temperature, the fluid can take away many heat from the patient and keep the patient in a low body temperature state (29-31). And the longer the operation, the more serious the situation (32,33). Under the condition of hypothermia, the patient's cardiovascular function changes, coagulation function disorder, which can increase intraoperative blood loss and tissue damage (34,35). Meanwhile, when the operation time is prolonged, the amount of perfusate used can accordingly increase, which will lead to the absorption of a large amount of perfusate (36). Several previous studies (34,37-39) have also found that the amount of fluid absorption in PCNL is positively correlated with the perfusion time. With the damage of the renal pelvis mucosa caused by the crushing process, the perfusate easily flows into the blood through the renal sputum, and bacteria or toxins can enter the blood by this pathway easily. The longer the time, the more substances that enter the bloodstream, the greater the possibility of postoperative infection (40). Especially for patients with severe blood vessel damage and massive intraoperative bleeding, the operation should be stopped decisively, the renal fistula should be placed and the hemostasis should be clamped, and the calculus should be treated after 1-2 weeks.

Several limitations must be considered in this present study. Firstly, previous study (41) has reported that the postoperative infection is strongly associated with *A. baumannii* bacteria. Limited by sample size, this present study did not analyze bacterial species and infection correlation. Secondly, we didn't construct a model for predicting the infection after PCNL, which can provide more reference value for clinical use. With more sample included in the future, it's necessary to develop a prediction model for infection prevention after PCNL.

In conclusion, patients with preoperative urinary tract infection, multiple access, diabetes, length of operation ≥ 60 min, estimated blood loss in PCNL ≥ 500 mL potentially risk more for postoperative infection after PCNL. Still, there may be many other factors involved in fever following PCNL that warrants further investigations. Effective control of urinary tract infection, reduction of access number, strict control of blood glucose, length of operation control, reduction of intraoperative bleeding must be

highlighted for the management of patients with PCNL.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tau.2020.03.37>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Medical Research Ethics Committee of our hospital (No.20170038) and informed consent was taken from all the patients.

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