

## Original Article

# Analysis on the risk factors for septic shock following minimally invasive percutaneous nephrolithotomy

Xiaojie Yang, Dong Zhang, Youfang Li, Tie Chong, Peng Zhang

Department of Urology, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an City 710004, Shaanxi Province, P. R. China

Received February 28, 2018; Accepted March 26, 2018; Epub May 15, 2018; Published May 30, 2018

**Abstract:** Objective: To examine the risk factors for septic shock following minimally invasive percutaneous nephrolithotripsy (PCNL). Methods: From January 2009 to June 2017, 700 patients who underwent PCNL in our hospital were included in this prospective and their clinical records were pooled for analysis. Univariate and multivariate logistic regression analyses were employed for clarification of the risk factors for post-PCNL septic shock, and the patients with the disease received active anti-infective and anti-shock care. Results: Fifteen of the 700 patients had post-PCNL septic shock. Multivariate logistic regression analysis revealed that women (adjusted odds ratio (OR)=1.719,  $P<0.001$ ) and diabetes mellitus (adjusted OR=4.217,  $P=0.002$ ) were independent risk factors for post-PCNL septic shock. After active treatment, the 15 patients were all cured and discharged from the hospital. Conclusion: Women and diabetes mellitus are the risk factors for the onset of post-PCNL septic shock, and prognosis is favorable in the patients after early and effective treatment.

**Keywords:** Percutaneous nephrolithotripsy, upper urinary calculi, septic shock, prevention, treatment

## Introduction

Urolithiasis is a common urologic disorder clinically treated by lithotripsy [1, 2]. There are a variety of techniques for lithotripsy. Recently, with the advances in urology-associated minimally invasive surgeries, percutaneous nephrolithotomy (PCNL) has been increasingly applied to treat urolithiasis in the upper urinary tract [3]. PCNL is advantageous over the conventional methods of lithotripsy in smaller trauma, fewer postoperative complications, more rapid recovery, and more acceptability [4, 5].

However, after PCNL, some patients may develop septic shock due to severe infection. In spite of a low incidence, septic shock adversely affects the patients' life [6-8]. Therefore, how to effectively prevent post-PCNL septic shock has become the focus of urologists.

In this prospective study, we analyzed the clinical records of 15 patients with septic shock, aiming to reduce the morbidity and mortality of septic shock in patients and get a better understanding of the risk factors for PCNL-septic sh-

ock. In this way, the patients can get timely prevention and treatment, and better prognosis.

## Materials and methods

### Patients

This study got approval from the Hospital Ethics Committee, and each enrolled patient gave written informed consent. From January 2009 to June 2017, seven hundred patients who underwent minimally invasive PCNL admitted to our hospital were recruited in this prospective study. Patients older than 18 years old were eligible for enrollment if they received the initial unilateral minimally invasive PCNL, and had no contraindications to PCNL. Patients were excluded if they had urolithiasis of bilateral upper urinary tracts, congenital renal malformations, malignancy, took immunosuppressive agents, or had heart failure. All the patients were treated with the prophylactic second-generation cephalosporin antibiotics before PCNL. The patients with positive urine culture received sensitive antibiotics for at least 2 weeks until the results became negative.

## Risk factors for septic shock following invasive percutaneous nephrolithotomy



**Figure 1.** Image of PCNL in patients with right renal calculi. The single arrow denotes the ureteral catheter and the double arrows denote the puncture needle. The ureteral catheter was inserted into the right ureter under the direct vision of the ureteroscope. The renal pelvis was successfully punctured on the B-ultrasound.

### Operative procedures

All the patients were placed in a semi-supine lithotomy position under general anesthesia. A ureteral catheter was inserted into the ureter under direct vision of the ureteroscope. The renal pelvis was successfully punctured under the B-ultrasound guidance, and dilated by a fascia dilator. The external sheath was positioned in place; then the ureteroscope was further advanced via the sheath. Subsequently, lithotripsy was performed with the 65 W holmium laser. The double J tubes were placed after the completion of lithotripsy. After removal of the ureteroscope, one renal fistulae was placed, sutured and fixed, as shown in **Figure 1**. The patients' vital signs were monitored and the patients were administered routine antibiotics for anti-infection.

### Diagnostic criteria for post-PCNL septic shock

Diagnostic criteria were bacteremia or clinically suspected sepsis, systemic inflammatory res-

**Table 1.** Baseline characteristics of the patients (n)

Variable	SSG	NSSG	$\chi^2$	P
Case	15	685		
Male/Female	1/14	430/255	17.230	<0.001
Age (> 60 years)	6	166	1.969	0.161
Hypertension	5	147	1.217	0.270
DM	9	117	18.319	0.000
UTI	12	487	0.217	0.641
RI	3	91	0.138	0.710
PUC	4	151	0.013	0.911
Left/Right	6/9	349/336	0.704	0.401

Note: DM, denotes diabetes mellitus; UTI, urinary tract infection; RI, renal insufficiency; PUC, positive urine culture; SSG, septic shock group; and NSSG, non-septic shock group.

ponse syndrome, refractory hypotension, with systolic blood pressure <90 mmHg or 40 mmHg lower than the original base value, the mean arterial pressure <65 mmHg, and the presence of visceral hypo-perfusion [9, 10].

### Treatment of post-PCNL septic shock

The patients were treated with anti-shock therapy immediately after they were diagnosed with post-PCNL septic shock, with the goals of resuscitation including mean arterial pressure  $\geq 65$  mmHg, central venous pressure of 8-12 mmHg, the urine volume  $\geq 0.5$  ml/kg/h, oxygen saturation > 70% or mixed venous oxygen saturation > 65% in the superior vena cava [11, 12]. Prior to disclosure of the results of urine culture and blood culture, Tienam or mepem empiric therapy was applied for anti-infection. After disclosure of the culture results, sensitive antibiotic therapy was utilized. The antibiotic therapy was recommended for a period of 7 to 10 days. To maintain a stable internal microenvironment, 5% sodium bicarbonate was added, and blood pressure was stabilized with the use of proper dopamine and other cardiovascular active agents.

### Statistical analysis

All the statistical data were analyzed with the application of the SPSS software, version 21. Count data were expressed as percentage, with the chi-square test for comparisons of baseline characteristics and intraoperative parameters of the patients between the septic shock group and the non-septic shock group.

## Risk factors for septic shock following invasive percutaneous nephrolithotomy

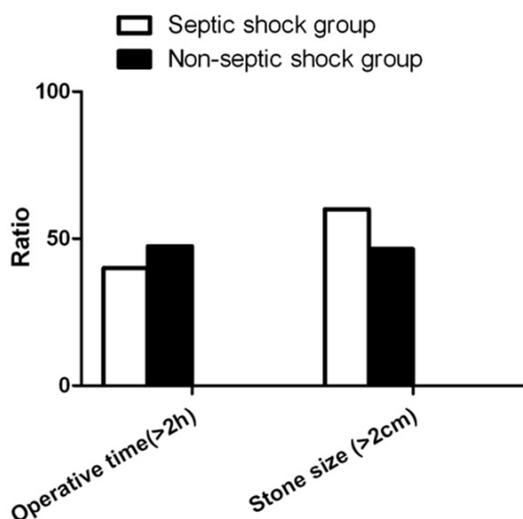


Figure 2. Intraoperative indexes of the patients

Table 2. Risk factors for post-PCNL septic shock on univariate logistic regression analysis

Variable	OR	95% CI	P
Gender	1.023	1.015-1.087	<0.001
Age	0.679	0.318-1.867	0.405
Hypertension	0.652	0.191-2.139	0.362
DM	3.198	1.179-8.012	0.011
UTI	3.226	0.816-10.162	0.072
RI	1.277	0.292-5.794	0.495
UC	0.784	0.361-2.093	0.466
OS	0.511	0.175-1.205	0.086
OT	1.438	0.624-3.951	0.317
SS	1.098	0.447-2.736	0.481

Note: DM, denotes diabetes mellitus; UTI, urinary tract infection; RI, renal insufficiency; UC, urine culture; OS, operative site; OT, operative time; and SS, stone size.

Univariate and multivariate logistic regression analyses were utilized for exploring the factors associated with post-PCNL septic shock. The variables for multivariate logistic regression were selected by the forward step method, with the inclusion criteria set at  $\alpha=0.05$  and the exclusion criteria set at  $\alpha=0.10$ .  $P<0.05$  was deemed as statistically different.

### Results

#### Baseline characteristics of the patients

Septic shock occurred in 15 patients of the 700 patients who had undergone PCNL. Ac-

cordingly, the 700 patients were subdivided into the septic shock group and the non-septic shock group. The differences in age, gender, underlying diseases and the affected sites between the two groups are shown in **Table 1**. The proportions of women and the patients with diabetes mellitus were remarkably larger among the patients with septic shock than those without septic shock (both  $P<0.001$ ).

#### Intraoperative outcomes

Among the patients in the non-septic shock group, the duration of PCNL longer than 2 h was reported in 325 patients, and the stone size larger than 2 cm in 318 patients; by contrast, among the patients in the septic shock group, the time for PCNL longer than 2 h was seen in 6 patients and the stone size larger than 2 cm in 9 patients. The rates of patients with over-2h PCNL ( $X^2=0.518$ ,  $P=0.472$ ) and those of patients with over-2cm stone ( $X^2=1.087$ ,  $P=0.297$ ) were mildly different between the two groups (both  $P > 0.05$ , **Figure 2**).

#### Univariate and multivariate logistic regression analyses

On univariate logistic regression analysis, age, hypertension, urinary tract infection, renal insufficiency, urine culture, operative site, operative time and the stone size were insignificantly associated with post-PCNL septic shock (all  $P > 0.05$ ); conversely, women (odds ratio (OR)=1.023,  $P<0.001$ ) and diabetes mellitus (OR=3.198,  $P=0.011$ ) were risk factors for post-PCNL septic shock, and the difference was statistically significant, **Table 2**).

Moreover, multivariate logistic regression analysis also demonstrated that women (adjusted OR=1.719,  $P<0.001$ ) and diabetes mellitus (OR=4.217,  $P=0.002$ ) were risk factors for post-PCNL septic shock, and the difference was statistically significant, **Table 3**).

#### Results of septic shock treatment

After timely anti-infective and anti-shock treatment, stable vital signs, normal urine volume, improved general conditions, no complications like multiple organ dysfunction syndrome (MODS) were observed among the 15 patients with PCNL-septic shock. At 48 h, vasopressors

## Risk factors for septic shock following invasive percutaneous nephrolithotomy

**Table 3.** Risk factors for post-PCNL septic shock on multivariate logistic regression analysis

Variable	OR	95% CI	P
Gender	1.719	1.524-5.132	<0.001
Age	7.096	0.411-12.628	0.677
Hypertension	0.795	0.304-2.318	0.162
Diabetes mellitus	4.217	0.769-10.425	0.002
Urinary tract infection	0.371	0.145-1.761	0.242
Renal insufficiency	1.115	0.242-5.119	0.872
Urine culture	1.272	0.515-4.002	0.526
Operative site	4.382	0.571-13.179	0.081
Operative time	1.122	0.384-3.295	0.774
Stone size	1.553	0.494-4.391	0.545

(dopamine) were gradually discontinued in the patients; the results of blood culture indicated that escherichia coli infection occurred in 10 patients and bacterial culture failed in 5 patients. On the third day after the body temperature of patients became normal, antibiotics were discontinued after twice negative findings of blood culture and urine culture. All the 15 patients were cured and discharged from the hospital.

### Discussion

Post-PCNL septic shock has a low morbidity in clinical practice, but it is characteristic of fast onset, rapid development and high mortality. As a result, post-PCNL septic shock has still been a major concern for clinical urologic surgeons. It is reported that puncture and lithotripsy during the PCNL procedure induce drainage of bacteria and their endotoxins into the systemic circulation via renal tubules reflux, the renal vein-lymphatic system or the damaged calyx [13]. In case of uncontrolled infection, septic shock may occur under the action of bacteria and their endotoxins. Therefore, it is clinically paramount to explore the risk factors for post-PCNL septic shock and the strategies for its prevention and treatment.

The risk factors for post-PCNL septic shock include diabetes mellitus, positive urine culture, renal insufficiency, and women [14, 15]. In the current study, the factors affecting post-PCNL septic shock covered age, sex ratio, hypertension, urinary tract infection, renal insufficiency, urine culture, diabetes mellitus, operative site, operative time and stone size.

The results revealed that most of the patients with post-PCNL septic shock were women and had diabetic mellitus. Additionally, the univariate and multivariate logistic regression analyses demonstrated that women and diabetes mellitus were independent risk factors for the presence of post-PCNL septic shock. This is consistent with the result reported by Sharifi Aghdas et al. [16]. In the current study, we held that female patients might be susceptible to infections due to their anatomic characteristics of the urinary system such as short

urethra, and diabetes mellitus is the pathological basis for damaging humoral immunity and cellular immunity. According to Sachwani et al., the blood glucose under strict control is associated with lower risks for septic shock [17]. The results of the current study also suggested that the infectious bacteria in patients with post-PCNL septic shock were escherichia coli, which are gram-negative bacilli, and have high resistance, which corresponds to the reports regarding the previous studies [18, 19]. If the patients have concomitant underlying diseases which lower their resistance, they are subject to severe infection by various bacteria in the course of anesthesia and surgery, and septic shock under the action of bacterial toxins, which is difficult to control. Accordingly, the general health and immunity and resistance of patients should be improved actively.

Based on the current study, we suggest the following measures be adopted for effective prevention and treatment of post-PCNL septic shock: renal trauma and laceration should be minimized; bacterial culture and drug sensitivity tests should be conducted on the urine in renal pelvis for antibiotics adjustment after surgery; renal pelvis hypo-perfusion (<20 mmHg) should be maintained during surgery to avoid bacteria and endotoxins draining into the systemic circulation; the operative time should be under control to avoid absorption of bacterial urine [20]. If a patient has post-PCNL septic shock, the patient should maintain adequate circulating blood volume and airway patency, monitor the central venous pressure and maintain the balance of the internal environment and electrolytes, so as to avoid aggravation of

## Risk factors for septic shock following invasive percutaneous nephrolithotomy

the disease, even progressing into MODS. In the current study, none of the 15 patients with post-PCNL septic shock progressed into MODS, and they were all cured and discharged from the hospital after active treatment.

In summary, septic shock is one of the severe complications after the PCNL procedure; women and diabetes mellitus are risk factors for post-PCNL septic shock. For patients with high risk factors, the perioperative measures of prevention and treatment should be enhanced to reduce the postoperative complications. Early detection and timely treatment are essential to successful management of post-PCNL septic shock. Nevertheless, this study is not free of limitations, such as few selected samples, single-center, and a non-randomized and non-controlled study in nature. Therefore, additional studies including more complicated factors are required to delve into the risk factors for post-PCNL septic shock, so as to provide more evidence for clinical prevention and treatment of the disease.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Peng Zhang, Department of Urology, The Second Affiliated Hospital of Xi'an Jiaotong University, No. 157, West 5th Road, Xi'an City 710004, Shaanxi Province, P. R. China. Tel: +86-029-87679533; Fax: +86-029-87679436; E-mail: pengzhang83@163.com

### References

- [1] Yamashita S, Kohjimoto Y, Hirabayashi Y, Iguuchi T, Iba A, Higuchi M, Koike H, Wakamiya T, Nishizawa S and Hara I. Upper urinary tract stone disease in patients with poor performance status: active stone removal or conservative management? *BMC Urol* 2017; 17: 103.
- [2] Yang B, Ning H, Liu Z, Zhang Y, Yu C, Zhang X, Pan D and Ding K. Safety and efficacy of flexible ureteroscopy in combination with holmium laser lithotripsy for the treatment of bilateral upper urinary tract calculi. *Urol Int* 2017; 98: 418-424.
- [3] Karakan T, Kilinc MF, Bagcioglu M, Doluoglu OG, Yildiz Y, Demirbas A, Bozkurt S and Resorlu B. Comparison of ultra-mini percutaneous nephrolithotomy and micro-percutaneous nephrolithotomy in moderate-size renal stones. *Arch Esp Urol* 2017; 70: 550-555.
- [4] Abdelhafez MF, Wendt-Nordahl G, Kruck S, Mager R, Stenzl A, Knoll T and Schilling D. Minimally invasive versus conventional large-bore percutaneous nephrolithotomy in the treatment of large-sized renal calculi: Surgeon's preference? *Scand J Urol* 2016; 50: 212-215.
- [5] Antonelli JA and Pearle MS. Advances in percutaneous nephrolithotomy. *Urol Clin North Am* 2013; 40: 99-113.
- [6] Wang Y, Jiang F, Wang Y, Hou Y, Zhang H, Chen Q, Xu N, Lu Z, Hu J, Lu J, Wang X, Hao Y and Wang C. Post-percutaneous nephrolithotomy septic shock and severe hemorrhage: a study of risk factors. *Urol Int* 2012; 88: 307-310.
- [7] Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL and Vincent JL. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008; 36: 296-327.
- [8] Liu C, Zhang X, Liu Y and Wang P. Prevention and treatment of septic shock following mini-percutaneous nephrolithotomy: a single-center retrospective study of 834 cases. *World J Urol* 2013; 31: 1593-1597.
- [9] Seymour CW and Rosengart MR. Septic shock: advances in diagnosis and treatment. *JAMA* 2015; 314: 708-717.
- [10] Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, Angus DC, Rubenfeld GD and Singer M. Developing a new definition and assessing new clinical criteria for septic shock: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016; 315: 775-787.
- [11] Berger RE, Rivers E and Levy MM. Management of septic shock. *N Engl J Med* 2017; 376: 2282-2285.
- [12] Rowan KM, Angus DC, Bailey M, Barnato AE, Bellomo R, Canter RR, Coats TJ, Delaney A, Gimbel E, Grieve RD, Harrison DA, Higgins AM, Howe B, Huang DT, Kellum JA, Mouncey PR, Music E, Peake SL, Pike F, Reade MC, Sadique MZ, Singer M and Yealy DM. Early, goal-directed therapy for septic shock—a patient-level meta-analysis. *N Engl J Med* 2017; 376: 2223-2234.
- [13] Wollin DA and Preminger GM. Percutaneous nephrolithotomy: complications and how to deal with them. *Urolithiasis* 2018; 46: 87-97.
- [14] Gravas S, Montanari E, Geavlete P, Onal B, Skolarikos A, Pearle M, Sun YH and de la Rosette J. Postoperative infection rates in low risk patients undergoing percutaneous nephrolithotomy with and without antibiotic prophylax-

## Risk factors for septic shock following invasive percutaneous nephrolithotomy

- is: a matched case control study. *J Urol* 2012; 188: 843-847.
- [15] Bootsma AM, Laguna Pes MP, Geerlings SE and Goossens A. Antibiotic prophylaxis in urologic procedures: a systematic review. *Eur Urol* 2008; 54: 1270-1286.
- [16] Sharifi Aghdas F, Akhavidadegan H, Aryanpoor A, Inanloo H and Karbakhsh M. Fever after percutaneous nephrolithotomy: contributing factors. *Surg Infect (Larchmt)* 2006; 7: 367-371.
- [17] Sachwani GR, Jaehne AK, Jayaprakash N, Kuzich M, Onkoba V, Blyden D and Rivers EP. The association between blood glucose levels and matrix-metalloproteinase-9 in early severe sepsis and septic shock. *J Inflamm (Lond)* 2016; 13: 13.
- [18] Gutierrez J, Smith A, Geavlete P, Shah H, Kural AR, de Sio M, Amón Sesmero JH, Hoznek A, de la Rosette J; CROES PCNL Study Group. Urinary tract infections and post-operative fever in percutaneous nephrolithotomy. *World J Urol* 2013; 31: 1135-1140.
- [19] Tavichakorntrakool R, Prasongwattana V, Sungkeeree S, Saisud P, Sribenjalux P, Pimratana C, Bovornpadungkitti S, Sriboonlue P and Thongboonkerd V. Extensive characterizations of bacteria isolated from catheterized urine and stone matrices in patients with nephrolithiasis. *Nephrol Dial Transplant* 2012; 27: 4125-4130.
- [20] Mariappan P, Smith G, Bariol SV, Moussa SA and Tolley DA. Stone and pelvic urine culture and sensitivity are better than bladder urine as predictors of urosepsis following percutaneous nephrolithotomy: a prospective clinical study. *J Urol* 2005; 173: 1610-1614.