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The outcome of urine culture positive and culture negative staghorn calculi after minimally invasive percutaneous nephrolithotomy

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Abstract The purpose of this study was to compare the treatment outcomes of staghorn stones using minimally invasive percutaneous nephrolithotomy (MPCNL) in patients who had positive preoperative urine culture to patients with negative urine culture. The records of 284 patients with staghorn calculi, who underwent MPCNL in our center from January 2012 to January 2013, were retrospectively analyzed. Patients were divided into positive and negative group, according to the result of preoperative urine culture. Staghorn stones with negative culture received a single dose of broad spectrum antibiotic prophylaxis, whereas stones with positive culture were treated for at least 72 h according to antibiogram. The perioperative findings and postoperative outcomes were compared between the two groups. There were 70 (24.6 %) patients with positive and 214 (75.4 %) patients with negative preoperative urine culture who underwent MPCNL. There were no statistical differences in the duration of hospital stay, operative time, estimated blood loss, final stone free rate (SFR) as well as the incidence of the following infectious complications such as fever, systemic inflammatory response syndrome and septic shock, between both groups. Our retrospective study showed that MPCNL was a safe and effective modality in the treatment of staghorn stones. The morbidity, complication, and SFR were similar between patients with positive and negative preoperative urine cultures, once the culture positive infections were adequately controlled.

Keywords Urine culture · Staghorn calculi · MPCNL · SIRS

Abbreviations

MPCNL	Minimally invasive percutaneous nephrolithotomy
PCNL	Percutaneous nephrolithotomy
SIRS	Systemic inflammatory response syndrome
SFR	Stone free rate
CBC	Routine complete blood count
SWL	Shock wave lithotripsy
KUB	Kidneys, ureters and bladder
CT	Computed tomography

Introduction

Staghorn calculi are large, branched stones that fill all or part of the renal pelvis and extend into the majority of the

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renal calices [1]. Staghorn calculi were traditionally called infection stones as infection was thought to be the underlying cause for the majority of these stones. There was a strong association between the infected staghorn stones and the urea splitting uropathogens. The composition of these stones often contained magnesium ammonium phosphate (struvite) or calcium carbonate apatite [2].

Percutaneous nephrolithotomy (PCNL) has become a widely accepted treatment option for staghorn calculi. It has a track record of acceptable morbidity, high success rate and reasonable operative time [3].

Minimally invasive PCNL (MPCNL) is a modified PCNL technique using a small caliber endoscope through an 18Fr. or less nephrostomy tract to perform the procedure. We have been using this technique for most of staghorn calculi in our center with outcomes similar to those reported for standard PCNL [4].

During any kind of PCNL, the presence of bacteriuria or stones may cause a variety of infectious complications. These complications can increase the morbidity and mortality of the procedure as well as increase the medical cost and hospital stay. Some literatures reported that positive preoperative urine culture was one of the most important predictors for the development of postoperative complications [5, 6].

The design of this study was to compare the treatment outcome and infectious complications: fever, systemic inflammatory response syndrome (SIRS) and septic shock, between staghorn stone patients who underwent MPCNL with positive and negative preoperative urine culture.

Patients and methods

Patients

All patients treated for staghorn calculi using the MPCNL technique at the Department of Urology of the First Affiliated Hospital of Guangzhou Medical University from January 2012 to January 2013, were retrospectively reviewed.

Staghorn calculi was defined as stones that fill the renal pelvis and branching into several or all of the calices. Based on the result of preoperative urine culture, patients were divided into two groups: positive culture group and negative culture group.

We defined the positive culture as a clean catch midstream urine specimen that grew out greater than 10^4/ml of a single microbial organism or mixed flora with a predominant species. For catheterized specimen the threshold, was lowered to greater than 10^3/ml.

Negative urine culture was defined as no growth, insufficient growth, or a mixed microbial flora with no predominant organism.

Patients with positive preoperative urine culture were treated with suitable antibiotics based on the culture sensitivity result for at least 72 h before MPCNL. Patients who had mixed flora but with a predominant organism on urine culture, antibiotic selection was based on this organism. Patients who had negative urine culture received a single dose of broad spectrum antibiotic prophylaxis (usually a second-generation cephalosporin) just prior to the procedure.

The stone surface area was calculated by measuring the length of the stone in the greatest left–right and cephalad–caudal axis on the radiological images then multiplying these two values.

Surgical technique

Our technique of MPCNL has been described in detail elsewhere [4, 7] and is summarized herein. Under general anesthesia, a 5Fr. open-ended ureteral catheter was inserted into the target ureter using either ureteroscope or cystoscope in a lithotomy position. A Foley catheter was placed into the bladder to provide drainage during the procedure. The patient was then turned in the prone position. Percutaneous access was achieved using an 18-gauge coaxial needle to puncture the desired calyx under fluoroscopic or ultrasonic guidance. Middle pole calyx was the most often initial puncture site for the staghorn stones. A 0.035″ flexible tip guide wire was inserted through the needle. Nephrostomy tract dilatation was accomplished by using fascial dilators up to 18Fr. A matching peel away sheath was advanced into the renal collecting system. Lithotripsy was performed using either pneumatic lithotriptor or holmium laser. Stone fragments were removed using pulsatile irrigation and grasping forceps through an 8/9.8Fr. semi-rigid ureteroscope. When multiple nephrostomy tracts were necessary to remove the stones, same technique was employed for each of the tracts. At the end of procedure, the 5Fr. ureteral catheter was replaced by a 5Fr. double-J stent. An 18Fr. drainage tube was left in each of the nephrostomy tracts.

Patients was examined with kidneys, ureters and bladder (KUB) and ultrasound 24–48 h after surgery. For patients with radiolucent stones, CT(Computed tomography) was performed when necessary. Routine complete blood count, serum chemistry were monitored pre- and postoperatively.

In patients whose stone clearance was less than optimal, a second-look MPCNL through the same nephrostomy tract(s) or repeat MPCNL (re-MPCNL) by establishing new nephrostomy tract(s) was performed 5–7 days after the first session. Patients with residual stone ≤1.5 cm, shock wave lithotripsy (SWL) and/or flexible ureterorenoscopy were used as alternative ancillary procedure. Complete stone-free status was defined as no stones visible on plain KUB and ultrasound images on the postoperative follow-up. The nephrostomy tubes were removed 5–6 days after the procedures when the drainage had become clear. The indwelling double-J stents were removed with cystoscope under local anesthesia 4 weeks as outpatients. All patients were followed up again in 3 months.

Data collection

Data was collected from retrospective reviews of the hospital and clinic records of the patients. Patients' demographics, operative factors and postoperative outcome of both groups were compared.

Complication was defined as any adverse event occurred intraoperatively or ≤30 days postoperatively. Complication included fever, SIRS, septic shock, extravasations, bleeding necessitating transfusion, and severe bleeding necessitating selective renal artery embolization. The grade of complication was determined according to the modified Clavien classification for percutaneous procedures [8].

The fever was defined as body temperature ≥38 °C. The SIRS was diagnosed by meeting at least two of the following four criteria: body temperature ≥38 or ≤36 °C; heart rate >90 bpm; respiratory rate >20 breaths/min or $PaCO_2$ <32 mmHg (<4.3 kPa); leukocyte count >12,000 or <4,000/dL or immature forms >10 %. Septic shock was defined as hypotension despite of adequate fluid resuscitation and the presence of perfusion abnormalities [9].

Statistical analysis

Differences between the two groups were tested for significance using the *t* test, Pearson χ^2 and Fisher exact test. A two-sided $p < 0.05$ was considered to be statistically significant. Statistical analysis was performed using SPSS 13.0 software.

Result

A total of 284 patients with staghorn calculi were treated with MPCNL in our center between January 2012 and January 2013. Positive preoperative urine culture was found in 24.6 % of patients (70 cases). *Escherichia coli* was the most common organism. There were only eight cases of *Proteus mirabilis* infection in all staghorn calculi.

Stone analyses were available in all patients. Infection stones were defined as calculi with any components of calcium carbonate apatite, magnesium ammonium phosphate (struvite) or ammonium urate. The composition of stones which were calcium oxalate, calcium phosphate, uric acid or a mixture of them were defined as metabolic stones [2]. Infection stones and metabolic stones were detected in 133 (46.8 %) and 151 (53.2 %) patients, respectively. Positive urine cultures were found in only 29.3 % of the infection stones and in 20.5 % of the metabolic stones ($p = 0.064$). (Table 1).

Table 1 Predominant pre-operative urine culture results

	Infected stone	Metabolic stone	*p* value
No. positive urine culture (%)	39 (29.3)	31 (20.5)	0.064
Escherichia coli	13 (33.3)	19 (61.3)	
Proteus mirabilis	8 (20.5)		
Klebsiella pneumoniae	5 (12.8)	4 (12.9)	
Enterococcus faecalis	2 (5.1)	3 (9.7)	
Acinetobacter bowmannii	3 (7.7)	1 (3.2)	
Staphylococcus species	3 (7.7)	1 (3.2)	
Morganella morganii	1 (2.6)	2 (6.5)	
Enterobacter aerogenes		1 (3.2)	
S.agalactiae	2 (5.1)		
Aerococcus viridans	1 (2.6)		
Citrobacter koseri	1 (2.6)		

The patient and stone are characteristics were presented in Table 2. Female patients were more likely to have positive preoperative urine culture, 55 out of the 70 positive cultures (78.6 %, $p < 0.001$). The two groups were similar in terms of mean age, mean stone size and co-morbidities.

Comparison of single versus multiple tracts for the two groups is shown in Table 2. There were no significant differences in the use of multiple nephrostomy tracts during MPCNL.

Operative time was defined as the interval from commencing the percutaneous access to the placement of nephrostomy drainage tube. There was no significant difference between these two groups in terms of mean operative time, hospital stay and duration of nephrostomy drainage (Table 2).

Table 3 showed postoperative complications for these two groups. The infectious complications including fever, SIRS and septic shock were not significantly higher in patients with positive urine culture than the negative culture. 34.3 % of patients with positive urine culture and 24.8 % of patients with negative culture had occurred SIRS. There was a patient (1.4 %) with positive urine culture and 4 (1.9 %) patients with negative culture that developed clinical septic shock. There was no difference in the rate of perioperative blood transfusion between two groups. Three (1.4 %) patients with negative urine culture required selective renal artery embolization for severe hemorrhage.

The initial stone free rate (SFR) and the final SFR (after second-look MPCNL, re-MPCNL or other ancillary procedures) showed no significant difference between these two groups ($p = 0.216$ and $p = 0.738$, respectively) (Table 2).

Table 2 Demographic, stone and operative characteristics of the study population

Variable	Positive preoperative urine culture	Negative preoperative urine culture	*p* value
Total number	70	214	–
Mean age, years (range)	52.26 (19–79)	51.18 (19–82)	0.075
Gender, female, *n* (%)	55 (78.6)	110 (51.4)	<0.001*
Side, left, *n* (%)	37 (52.9)	114 (53.3)	0.952
Mean stone size, mm^2 (range)	2607.07 (420–6148)	2440.41 (408–11500)	0.214
Previous open surgery, *n* (%)	5 (7.1)	33 (15.4)	0.077
Comorbidities			
Hypertension, *n* (%)	12 (17.1)	52 (24.3)	0.214
Diabetes mellitus, *n* (%)	6 (8.6)	17 (7.9)	0.867
No. of tracts, (%)			
Single	45 (64.3)	138 (64.5)	0.976
Multiple	25 (35.7)	76 (35.5)	
Mean operative time, min	103.5	96.6	0.653
Mean decrease in hemoglobin, g/dL	1.87	1.68	0.535
Mean hospitalization time, days	16.29	15.31	0.226
Mean nephrostomy removal time, days	9.11	8.92	0.124
Stone free, *n* %			
Primary	18 (25.7)	72 (33.6)	0.216
With second-look MPCNL	39 (55.7)	114 (53.3)	0.722
With re-MPCNL	40 (57.1)	131 (61.2)	0.546
With any auxiliary procedure	55 (78.6)	164 (76.6)	0.738

*Statistically significant

Table 3 postoperative complications for positive and negative preoperative urine culture

	Clavien grade	Positive preoperative urine culture, *n* (%)	Negative preoperative urine culture, *n* (%)	*p* value
Fever (>38 °C)	I	21 (30.0)	56 (26.2)	0.531
SIRS	II	24 (34.3)	53 (24.8)	0.120
Blood transfusion	II	7 (10.0)	20 (9.3)	0.871
Extravasation treated conservatively	II	5 (7.1)	9 (4.2)	0.505
Embolization	IIIa	–	3 (1.4)	–
Septic shock	IVa	1 (1.4)	4 (1.9)	1.000

SIRS Systemic Inflammatory Response Syndrome

[a] Some cases had more simultaneous complications

Discussion

In the past staghorn calculi were thought to be composed of primarily struvite and carbonic apatite. These stones were also referred to as infection stones because of their strong association with urinary tract infection caused by the urea-splitting organisms [1]. In our study only about half of the staghorn calculi (46.8 %) were infection stones according to the postoperative stone analyses. Furthermore, positive preoperative urine culture was found in only 24.6 % of patients (70 cases). Conversely 20.5 % of our non-infection (metabolic) stones had positive preoperative urine culture. An important explanation might be that negative preoperative urine culture did not correlate well with infection presented in the upper urinary tract [10]. It was possible where the stones or pelvic urine were infected and yet the bladder urine showed negative culture. Mariappan and his colleagues [10] reported that renal pelvic urine culture and positive calculus culture were better predictors for potential urosepsis than bladder urine. These specimens, however, can only be collected intraoperatively or postoperatively. It may not be very helpful in planning the preoperative treatment of staghorn calculi.

In our patients with positive urine cultures, *E. coli* was the most common organism, which accounted for 45.7 % of the positive cultures. On the other hand, *Proteus mirabilis* only accounted for 11.4 % of the positive culture. One of the likely reasons was the fact that in the recent years the proportion of metabolic stones had increased in the staghorn stones [2].

We have relatively low incidence of positive urine cultures. This could be because we set the threshold for positive urine culture too high. Many of the mixed flora cultures might represent true infections. Nevertheless we found it was impractical to treat mixed bacterial flora and retrospectively we did not find the treatment results to be much different from the "no growth" patients. It was also plausible that our low rate of positive culture was due to the poor correlation between upper urinary tract infections or infected stones and bladder urine specimens, especially in the cases of high, grade obstruction or poorly functioning kidneys [10, 11].

It is important to identify and manage the risk factors to minimize infectious complications in MPCNL. Positive preoperative urine is an important prognostic indicator for the development of postoperative infectious complication [5]. Gutierrez et al. [12] reported that a positive preoperative urine culture was strongly associated with postoperative fever. Therefore, it is paramount to control urinary tract infection prior to any surgical intervention to reduce postoperative fever and other complications. Eradication of urinary tract infection with appropriate antibiotic therapy and the use of prophylaxis in patients with sterile urine were the principle preventive measures for sepsis [13]. In the present series, our patients who had positive preoperative urine culture were treated with appropriate antibiotics based on the culture sensitivity for at least 72 h before the MPCNL, whereas the culture with negative patients were treated with a single dose of broad spectrum preoperative antibiotics as prophylaxis. We found with this protocol as the incidence of infectious complications (fever, SIRS and septic shock) was similar in both groups. In addition, we did not find preoperative urine analysis helpful in patient management, for most of our patients with staghorn stones had large number of leukocytes and erythrocytes.

SIRS, an inflammatory cascade caused by bacteremia or endotoxemia, which could progress to septic shock [9]. We generally started parenteral therapy including both fluid resuscitation and antibiotics therapy as soon as SIRS or sepsis was recognized. After obtaining blood and urine culture, patients were started on broad spectrum antibiotics pending the culture results. Carbapenems was the most often used empirical antibiotics based on our local bacterial spectrum and their susceptibility pattern. The duration of the therapy was usually 10 days and antibiotics were adjusted according to culture results. Adjunctive treatment for cardiovascular, endocrine, and glucose metabolism complications were instituted as needed. In our series, SIRS following MPCNL for staghorn stones were quite common; however, only few cases advanced to septic shock. We do believe early recognition and treatment of SIRS is the key to prevent the development of septic shock.

In addition to infectious complications, other complications such as intraoperative and postoperative bleeding were found to be higher if preoperative urine cultures were positive. In a study by EI-Nahas et al. [6], positive preoperative urine culture was an independent risk factor for development of complications. Keoghane et al. [14] reported that the risk of transfusion after PCNL was associated with the presence of a positive preoperative middle stream urine sample. Possible explanations for these findings included distorted anatomy secondary to edema and the hyperemic nature of the inflamed urothelium [14]. In our study, the mean drop in Hb levels, transfusion rate and arterial embolization rate were all similar in patients with positive or negative preoperative culture once the positive urine culture were appropriately treated.

We used MPCNL in all staghorn calculi patients, a modified procedure using smaller scope and percutaneous nephrostomy tract. In patients with large stone bulk, multiple tracts and second-stage procedures were often used. SWL and flexible ureterorenoscopy were utilized for residual stones $\leq$1.5 cm after MPCNL. We found that the presence of positive preoperative urine culture did not influence the SFR. No significant differences were found in the initial SFR and the final SFR between the two groups.

Not surprisingly, the final SFR in patients with staghorn stones was relatively low (78.6 and 76.6 %). This could be easily explained by the large stone burden in our series; more than half of our cases had stone surface area >2000 mm^2. Our result was comparable to the CROES study in which the SFR in patients with staghorn stones was 56.9 % [15].

Matlaga et al. [16] reported that the patients with preoperative urinary tract infections had longer hospitalization. Although patients with positive urine culture had received antibiotic treatment for at least 72 h before surgery in our center, we did not find that patients with positive urine culture experienced longer hospitalization (16.29 vs. 15.31 days, $p = 0.226$). However, we tended to have much longer hospital stay than many other countries. This was due to the unique re-imbursement policy set by our government. All preoperative evaluation, including laboratory examinations and imaging studies had to be done as inpatient in order to get government reimbursement. Meanwhile, most of our second stage procedures were performed 5–7 days after the first session during the same hospitalization due to the unique culture in our society where it was unacceptable to the patients to go home with drainage catheter in place or to receive intravenous antibiotic therapy on an outpatient setting. Furthermore, many of our patients came from other cities and provinces. It was prudent if not requested by patients to observe them for 1–2 days after removal of nephrostomy tube.

Conclusion

Our retrospective study showed MPCNL was safe and effective treatment for staghorn calculi. The morbidity and complication as well as SFR were similar between patients with positive and negative preoperative urine culture once the culture positive infections were adequately controlled. It was noted that 53 % of our staghorn stones were metabolic stones per definition whether with or without positive urine culture. This change in stone composition had also been observed by others [2]. There was no statistical difference in the preoperative urine culture between infection and metabolic stones. Furthermore, most common organism found in our staghorn stone patients was still *E. coli* with *P. mirabilis* accounted for only a minority. Staghorn stones with negative preoperative urine culture could safely undergo surgical intervention with a single dose of broad spectrum antibiotic prophylaxis. SIRS following MPCNL was common in all staghorn calculi patients,34.3 % in patient with positive and 24.8 % in patients with negative preoperative urine culture. However, with early intervention, only on rare occasion would it progress to septic shock.

Conflict of interest The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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