Midstream Urine Culture Had a Higher Predictive Value of Post-PNL SIRS in Patients Without Upper Urinary Tract Obstruction

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Abstract

Introduction:

Systemic inflammatory response syndrome (SIRS) is a common complication of percutaneous nephrolithotomy (PNL). Midstream urine culture (MUC) is reported to be associated with postoperative SIRS, but this correlation is uncertain, as MUC may not represent infection of obstructed urine in patients with upper urinary tract obstruction (UUTO). Instead, for patients without UUTO, positive MUC may be an indicator of intrarenal infection. The aim of this study was to investigate whether MUC had a higher predictive value in patients without UUTO.

Materials and Methods

The data of 175 patients who underwent PNL between September 2015 and June 2016 were retrospectively reviewed. Preoperative and intraoperative factors including MUC were collected and analyzed. The primary endpoint was development of SIRS. Subgroup analysis according to the presence of UUTO was conducted.

Results

Generally, patients who suffered SIRS had a higher incidence of positive MUC (56%[25/45] vs. 32%[41/130], $p=0.005$). Subgroup analysis showed that among patients without UUTO, positive MUC (75%[13/17] vs. 33%[13/39], $p=0.003$) was still associated with development of SIRS. Among patients with UUTO, however, there was no obvious correlation between positive MUC and SIRS. Multivariate analysis controlling for age, previous ipsilateral kidney surgery, multiple tracts, and blood creatinine conducted in patients without UUTO demonstrated that positive MUC (odds ratio [OR] = 6.419, 95% confidence interval [CI]: 1.424-28.942, $p=0.016$) was still associated with development of SIRS. The rate of positive urine culture was 37.7% (66/72), 72 isolates of 24 species were reported, including 6 patients with mixed infection and 2 patients with fungi infection. Gram-negative bacteria accounted for a large proportion of all isolates (68.1%), and *Escherichia coli* was the most common bacteria (34.7%).

Conclusions

MUC had a higher predictive value of post-PNL SIRS in patients without UUTO.

1. Introduction

Percutaneous nephrolithotomy (PNL), first described in 1976 by Fernstrom and Johansson [1], has become the standard treatment for larger and complicated renal stones [2]. Infectious complications usually occurred after PNL, specifically, the incidence of fever was 10-30%, systemic inflammatory response syndrome was 35% and sepsis was 0.9%-9.3% [3–5]. Sepsis rarely occurred after PNL, but it will deteriorate to fetal septic shock with a mortality rate of 50–66% [6]. Due to its high mortality, judging which patients are susceptible to develop sepsis is necessary. For the close association with sepsis and clear diagnostic criteria, systemic inflammatory response syndrome (SIRS) is a commonly used endpoint to evaluate infection-related complications following PNL [7].

Traditionally, midstream urine culture (MUC) was suggested as a potential factor to predict postoperative infection-related complications and guidance of perioperative antibiotic selection. But several studies indicated that MUC failed to identify patients who develop sepsis post-PNL [8–10]. MUC was shown to have a 15% positive predictive value for SIRS in one study [10]. A possible explanation for the low predictive value of MUC is midstream urine sample do not accurately represent infection of obstructed urine in patients with upper urinary tract obstruction (UUTO). Instead, for patients without UUTO, positive MUC may be an accurate indicator of intrarenal infection.

The aim of the present study was to test the hypothesis that UUTO may impair the correlation between MUC and SIRS in patients underwent percutaneous nephrolithotomy and to further investigate whether MUC had a higher predictive value in patients without

UUTO.

2. Materials And Methods

After obtaining institutional review board approval, we reviewed all patients who underwent PNL at our institution between September 2015 and June 2016.

Patients' demographics and preoperative variables were collected, including age, gender, presence of diabetes mellitus, placement of ureteral stent, previous ipsilateral kidney surgery. Laboratory tests including midstream urine culture, blood creatinine, blood glucose as well as image examination including ultrasound and CT scan without contrast were performed. Intraoperative variables including operative time, presence of tachycardia, simultaneous ureteroscopy, multiple tracts, size of the tracts, placement of nephrostomy and blood transfusion were collected.

Inclusion criteria were: greater than 18 years of age, underwent PNL, clinical data was complete. Exclusion criteria were: history of malignancy and/or renal failure and/or heart failure, taking immunosuppressant, fever/tachycardia prior to surgery, two-stage PNL.

Previous ipsilateral kidney surgery included previous PNL, ureteroscopy, retrograde intrarenal surgery, partial nephrectomy, pyeloplasty. UUTO was defined as hydronephrosis and/or hydrocalycosis reported by radiologist according to CT scan. A positive midstream urine culture was defined as culture showing growth > 100,000 colony-forming units (CFUs) of a bacterial species. Operative time was measured as the time from skin incision to placement of nephrostomy or suture. Tachycardia was defined as intraoperative heart rate > 100/min. 24F tract was defined as standard tract, compared to 16F tract.

All patients received antibiotic prophylaxis 48h prior to PNL, this typically involved recommended drug by urine culture or ciprofloxacin 500mg for patients with negative urine culture.

Endpoint

The primary endpoint for this study was the development of SIRS in the postoperative hospitalization stay. SIRS was defined as having two of the following: temperature $\geq 38^{\circ}\text{C}$ or $\leq 36^{\circ}\text{C}$, heart rate $> 90/\text{minute}$, respiratory rate $> 20/\text{minute}$, or WBC count $> 12,000 \text{ cells}/\mu\text{L}$ or $< 4000 \text{ cells}/\mu\text{L}$ [11]. At our institution, vitals were measured every 4 hours for the first 24 hours and every 6 hours thereafter.

Statistical analysis

Statistical analysis was performed using SPSS software (version 19). Mann-Whitney test was used to compare continuous variables, and the Chi square or Fisher's exact tests were used to compare categorical data between groups with and without SIRS. Multivariate analysis was used to study the relationship between MUC and SIRS controlling for other factors. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were used to evaluate the ability of MUC to identify patients at increased risk for developing SIRS. All tests were performed at a significance level of 0.05.

3. Results

The final analysis included 175 patients who met study criteria. Of those patients, 45 (25.7%) individuals experienced SIRS during the postoperative hospital stay, 119 (68.0%) patients were combined with UUTO. For patients with UUTO, the incidence of SIRS was 23.5% (28/119). Among patients without UUTO, the incidence was 30.4% (17/56) (Table 1).

Table 1
Demographic data and univariate analysis of risk factors for development of SIRS

	Total (n=175)			with UUTO (n=119)			without UUTO (n=56)		
	SIRS+ (n=45)	SIRS- (n=130)	P value	SIRS+ (n=28)	SIRS- (n=91)	P value	SIRS+ (n=17)	SIRS- (n=39)	P value
Age,median (IQR),years	47(41-54)	52(42-58.25)	0.031	44.5(41-50)	51(42-58)	0.027	51(38-58)	52(39-60)	0.515
Gender,% (No.)			0.115			0.186			0.554
Male	49%(23)	65%(84)		50%(14)	65%(59)		53%(9)	64%(25)	
Female	51%(22)	35%(46)		50%(14)	35%(32)		47%(8)	36%(14)	
Previous history									
Diebetes Mellitus,% (No.)	4%(2)	16%(21)	0.070	0%(0)	15%(14)	0.061	12%(2)	18%(7)	0.854
Placement of ureteral stents,% (No.)	11%(5)	10%(13)	1.000	14%(4)	11%(10)	0.890	6%(1)	8%(3)	1.000
Previous ipsilateral kidney surgery,% (No.)	36%(16)	22%(29)	0.112	43%(12)	23%(21)	0.041	24%(4)	21%(8)	1.000
Preoperative laboratory tests and image examination									
UUTO,% (No.)	62%(28)	70%(91)	0.335	/	/	/	/	/	/
Positive PMUC,% (No.)	56%(25)	32%(41)	0.005	43%(12)	31%(28)	0.259	76%(13)	33%(13)	0.003
Blood creatinine,median (IQR),umol/L	76(66-90)	73.5(62-85)	0.344	74(58.75-89.75)	75(64-87)	0.785	78(66-133)	69(59-81)	0.032
Blood glucose,median (IQR),mmol/L	5.24(4.845-5.61)	5.23(4.82-5.72)	0.941	5.08(4.81-5.35)	5.22(4.83-5.63)	0.206	5.59(5.21-6.19)	5.23(4.80-5.92)	0.203
Intraoperative factors									
Operative time,median (IQR),min	80(62.5-100)	70(50-90)	0.072	80(65-100)	70(55-95)	0.284	80(57.5-102.5)	65(50-80)	0.081
Tachycardia,% (No.)	18%(8)	9%(12)	0.171	25%(7)	11%(10)	0.123	6%(1)	5%(2)	1.000
Simultaneous ureteroscopy,% (No.)	11%(5)	10%(13)	1.000	18%(5)	10%(9)	0.419	0%(0)	10%(4)	0.420
Multiple tracts% (No.)	38%(17)	22%(28)	0.047	39%(11)	25%(23)	0.231	35%(6)	13%(5)	0.114
24F tracts,% (No.)	100%(45)	96%(125)	0.415	100%(28)	97%(88)	1.000	100%(17)	95%(37)	1.000
Placement of nephrostomy,% (No.)	100%(45)	93%(121)	0.155	100%(28)	93%(85)	0.368	100%(17)	93%(36)	0.546

	Total (n=175)		with UUTO (n=119)			without UUTO (n=56)			
Blood transfusion,% (No.)	4%(2)	2%(2)	0.585	7%(2)	1%(1)	0.138	0%(0)	3%(1)	1.000

Generally, patients who suffered SIRS had a higher incidence of positive MUC (56%[25/45] vs. 32%[41/130], $p=0.005$), were younger than the other patients (47[41-54] vs. 52[42-58.25], $p=0.031$), and were more likely to received multiple tracts surgery (38% [17/45] vs. 22%[28/130], $p=0.047$). Other factors including gender, previous history, preoperative laboratory tests, operative time and blood transfusion showed no difference between groups ($p>0.05$) (Table 1).

Among patients with UUTO, the incidence of positive MUC was similar between patients with and without SIRS (43%[12/28] vs. 31%[28/91], $p=0.259$). Meanwhile, younger age (44.5[41-50] vs. 51[42-58], $p=0.027$) and previous ipsilateral kidney surgery (43% [12/28] vs. 23%[21/91], $p=0.041$) were associated with development of SIRS (Table 1).

Among patients without UUTO, positive MUC (76%[13/17] vs. 33%[13/39], $p=0.003$) as well as elevation of blood creatinine (78[66-133] vs. 69[59-81], $p=0.032$) were associated with development of SIRS. Unlike the entire sample, there was no difference could be seen in age ($p>0.05$) (Table 1).

Positive MUC had sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 55.6%, 68.5%, 37.9%, and 81.7%, respectively, for development of SIRS of all patients.

When the effect of UUTO was excluded, among patients without UUTO, the sensitivity increased to 76.5%, specificity remained similar at 66.7%, PPV increased to 50.0%, and NPV increased to 86.7%.

Multivariate analysis was conducted to test stability of the relationship between MUC and development of SIRS among patients without UUTO, controlling factors including age, previous ipsilateral kidney surgery, multiple tracts and blood creatinine. Result showed that positive MUC (odds ratio [OR] = 6.419, 95% confidence interval [CI]: 1.424-28.942, $p=0.016$) was still associated with development of SIRS (Table 2).

Table 2
Multivariate analysis of risk factors for development of SIRS among patients without UUTO

Variables	β value	S.E.	Wals	<i>P</i> value	OR	95% C.I.	
						Lower	Upper
Age,years	-.015	.028	.290	.590	.985	.932	1.041
Positive PMUC	1.859	.768	5.855	.016	6.419	1.424	28.942
Previous ipsilateral kidney surgery	-.923	1.004	.845	.358	.397	.055	2.844
Multiple tracts	1.160	.901	1.657	.198	3.189	.546	18.645
Blood creatinine	.031	.014	4.934	.026	1.031	1.004	1.059
Constant	-3.723	1.896	3.854	.050	.024		

Among 175 patients included in this study, 66(37.7%) patients had positive urine culture, yielding 72 isolates of 24 species. Mixed infection (two kinds of bacteria) appeared in 6 patients, including three patients infected with *Escherichia coli* and *Enterococcus faecalis*, one patient infected with *Escherichia coli* and *Stenotrophomonas maltophilia*, one patient infected with *Escherichia coli* and *Klebsiella pneumoniae*, and one patient infected with *Enterococcus faecalis* and *Citotobacter bureli*. Gram-negative bacteria accounted for a large proportion of all isolates, with the percent of 68.1% (49/72). *Escherichia coli* was the most common bacteria (34.7%), followed by *Proteus mirabilis* (13.9%), *Enterococcus faecalis* (11.1%), *Pseudomonas aeruginosa* (4.2%), *Klebsiella pneumoniae* (4.2%), *Streptococcus agalactiae* (2.8%), *Staphylococcus haemolyticus* (2.8%), *Streptococcus mitis* (2.8%) and *Staphylococcus epidermidis* (2.8%) (Figure 1). It should be noted that fungal infection occurred in two patients (3.0%), including

one 49-year-old male patient infected with *Candida parapsilosis* and one 27-year-old female patients infected with *Candida glabrata*, and both of them developed SIRS postoperatively.

4. Discussion

Infectious complication usually emerges after PCNL, which could deteriorate to fatal urosepsis. Several studies have reported preoperative and intraoperative risk factors for the development of SIRS following PNL, including stone burden, hydronephrosis, staghorn stone, multiple tracts, longer operative time, the presence of purulent substance obtained on puncture, positive pelvic urine culture, positive stone culture and so on [12, 13].

Pathogenic microorganisms colonized in urinary tract are source of infection. So, urologists emphasize the importance of bacterial culture. Due to convenience and easiness to collect, urine culture is routinely performed before PNL to ensure sterility, and appropriate antibiotics were used for patients with infection, but urosepsis is still a serious complication in patients undergoing PNL [10, 14]. Comparing to higher predictive value of stone culture and pelvic urine culture [15], midstream urine culture is reported as a poor predictor for development of SIRS following lithotripsy [8–10], one study by Dogan et al [16] showed that 66% of 82 patients with SIRS had negative urine culture.

This poor predictive value of midstream urine culture could possibly be explained that midstream urine sample do not accurately represent infection of obstructed urine in patients with upper urinary tract obstruction. Felix Cheung et al. [17] reported that Bacteria on urine microscopy was not associated with other markers of systemic infection and may largely represent a contaminant. Similar conclusion was also made by Paramanathan Mariappan et al. [18], they found that in obstructive uropathy secondary to a stone midstream urine culture was a poor predictor of infected urine proximal to the obstruction and infected stones. But no research has investigated whether midstream urine culture could predict postoperative infectious complications more accurately in the absence of UUTO.

The results of our study verified the hypothesis that UUTO impaired the correlation between MUC and SIRS pre and post. On the one hand, positive MUC had a higher predictive value without the effect of UUTO, on the other hand, positive MUC was not associated with development of SIRS among patients with UUTO. Multivariate analysis controlling for other related factors showed that UUTO still correlated with the development of SIRS after PNL.

Our study brought several reported risk factors into analysis, the result showed that positive MUC, multiple tracts, ipsilateral kidney surgery, and blood creatinine were associated with development of SIRS, which was in accord with previous studies [12, 19, 20]. We also found that patients suffered SIRS was younger than the other patients, narrow age range of patients may account for this result, and some studies also reported that age was not a significant factor [21, 22].

Escherichia coli was reported as the most common bacteria associated with urinary tract infection, with the prevalence of 50.0%-82.8% [23–26]. But for patients with stones, data from China reported relative lower prevalence of *Escherichia coli*, which ranged from 29.3–48.7% [27–29], and was in accord with our results. This discrepancy may be explained by difference of bacteria distribution in different population and regions.

There are several limitations of our study. UUTO was defined as hydronephrosis and/or hydrocalycosis in this study, this was a major confounding factor, because in cases with hydrocalycosis pelvic urine could flow to bladder, so MUC could partly represent upper urinary tract infection. Second, this was a retrospective study, only data were important enough to be recorded could be analyzed. Third, the effects of other potential covariates on developing SIRS after PNL such as, prophylactic antibiotic administration, previous history of urinary tract infection, stone burden, and irritation pressure were not taken into account in this study.

5. Conclusions

Upper urinary tract obstruction could impair the relationship between preoperative midstream urine culture and post-PNL SIRS. Midstream urine culture had a higher predictive value of post-PNL SIRS in patients without upper urinary tract obstruction.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics board of Peking University People's Hospital Review Board and all patients signed the preoperative informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no conflicts of interest to declare.

Funding

Not applicable.

Authors' contributions

L.A. collected the data and wrote the manuscript. L.X. edited the manuscript. Q.X. managed the data. X.H. developed the project. All authors reviewed the manuscript.

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Figures

Figure 1

Among 175 patients included in this study, 66(37.7%) patients had positive urine culture, yielding 72 isolates of 24 species. Mixed infection (two kinds of bacteria) appeared in 6 patients, including three patients infected with *Escherichia coli* and *Enterococcus faecalis*, one patient infected with *Escherichia coli* and *Stenotrophomonas maltophilia*, one patient infected with *Escherichia coli* and *Klebsiella pneumoniae*, and one patient infected with *Enterococcus faecalis* and *Citotobacter bureli*. Gram-negative bacteria accounted for a large proportion of all isolates, with the percent of 68.1% (49/72). *Escherichia coli* was the most common bacteria (34.7%), followed by *Proteus mirabilis* (13.9%), *Enterococcus faecalis* (11.1%), *Pseudomonas aeruginosa* (4.2%), *Klebsiella pneumoniae* (4.2%), *Streptococcus agalactiae* (2.8%), *Staphylococcus haemolyticus* (2.8%), *Streptococcus mitis* (2.8%) and *Staphylococcus epidermidis* (2.8%)