

Original Article

Diabetes, a risk factor for both infectious and major complications after percutaneous nephrolithotomy

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Abstract: Background: It is reported that up to one-third of patients might have some postoperative complications after percutaneous nephrolithotomy (PCNL). The predictive factors for infectious and major complications remains conflicted, which was the main objective of this study. Methods: This was a retrospective analysis using data from enrolled 411 patients diagnosed with renal stones underwent PCNL from 2008 to 2013. The correlation between postoperative complications with demographic characteristics, comorbidities and perioperative features was analyzed by Fisher's exact test or Mann-Whitney test. Logistic regression analysis was used for assessment of risk factors associated with infectious and major complications. Results: The mean age of 411 patients included was 53.6 years and male patients occupied 57.9%. Of all the 411 patients enrolled, 145 patients were diagnosed with systemic inflammatory response syndrome (SIRS). The comorbidity of diabetes and complete staghorn calculi were suggested to be independent risk factors for postoperative infectious complications by Logistic regression analysis. The overall complication rate was 31.1% (128/411) and 33 cases (8.0%) was categorized as major complications according to the modified Clavien score. The comorbidity of diabetes and an upper pole tract were risk factors for the occurrence of major complications after PCNL. Conclusions: The comorbidity of diabetes was significantly associated with an increasing incidence of both infectious and major postoperative complications after PCNL.

Keywords: Percutaneous nephrolithotomy, complications, diabetes, risk factor

Introduction

Percutaneous nephrolithotomy (PCNL) is recommended as the first choice of therapeutic strategy for patients with renal stones larger than 2 cm or 1.5 cm (located in the lower pole) by the European Association of Urology Urolithiasis Guidelines [1]. However, it is reported that up to one-third of patients might have some peri-operative complications [2], especially the fever and a urinary tract infection, which occupies about 21-39.8% of all the complications [3]. Among the postoperative complications after PCNL, infection is a potentially devastating one [4] and several studies have suggested sepsis as a leading perioperative cause of death [5]. Numerous established data have assessed several potential perioperative factors affecting postoperative complications [6, 7]. However, until now, no consensus has been obtained about the possible predictive factors, the standardization of complication

score for PCNL and reported outcomes [8, 9]. During the past decades, the improved Clavien classification has got great recognition and been widely used for categorizing and evaluating complications after urological procedures, the grading of life-threatening complications was also included [10, 11]. The criteria for major complications after PCNL were defined by the series include sepsis, admission to the Intensive Care Unit (ICU), adjacent organ injury, hemorrhage requiring transfusion or death [12]. Previous studies have reported that the possible independent risk factors for complications after PCNL include age, horseshoe kidney [13], medial and multiple punctures [14], staghorn calculi [15] and prolonged operative time [16]. The prevalence of diabetes mellitus (DM) has become a worldwide challenge for human's health [17]. The prevalence of type 2 DM (T2DM) all over the world is estimated to be 8.3% reported by the International Diabetes Federation [18]. The impact of T2DM on the

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Table 1. Demographic, clinical and radiological characteristics of patients with or without SIRS

	SIRS (+)	SIRS (-)	P-value
Number	145 (35.3%)	266 (64.7%)	-
Age (years)	55.3±8.8	52.1±7.5	0.011*
Gender			
Male	82 (56.6%)	153 (57.5%)	
Female	63 (43.4%)	113 (42.5%)	0.975
BMI (kg/m ²)	25.6±3.3	25.2±3.6	0.269
Clinical symptoms			
Urinary tract infections	31 (21.4%)	53 (19.9%)	
Hematuria	28 (19.3%)	49 (18.4%)	
Pain	86 (59.3%)	164 (61.7%)	0.895
Preoperative leukocyte count (×10 ⁹ /L)	8.7±1.7	7.4±2.0	0.005*
Comorbidities			
Hypertension	24 (16.6%)	30 (11.3%)	0.142
Diabetes	34 (23.4%)	40 (15.0%)	0.034*
Operative time (min)	113.4±29.8	101.7±33.1	0.021*
Fluoroscopy time (min)	93.2±43.5	88.6±39.9	0.279
Staghorn			
Complete staghorn	35 (24.1%)	34 (12.8%)	0.003*
Partial staghorn	26 (17.9%)	46 (17.3%)	0.871
Multiple tracts	14 (9.7%)	22 (8.3%)	0.635
Upper pole tract	26 (17.9%)	29 (10.9%)	0.046*
Urinary tract anomaly	24 (16.6%)	41 (15.4%)	0.763
Length of hospital stay (d)	4.3±2.0	3.4±2.4	0.011*

SIRS, systemic inflammatory response syndrome; BMI, body mass index. **P* < 0.05 by Fisher's exact test or Mann-Whitney test.

prognosis of infectious and major complications after PCNL still remains conflicted, which was the main objective of this study.

Material and methods

Patients

This retrospective study was approved by the Medical Institutional Ethics Committee of Zhejiang province. A total of 411 patients diagnosed with renal stones underwent PCNL in Ningbo No. 2 hospital from June, 2008 to July, 2013 were enrolled in this study. PCNL was performed in the prone position by 2 surgeons (I.H.B. and T.D.) as described previously with the application of a 3-5 day course of preoperative broad-spectrum antibiotic [19]. For those patients with staghorn stones, a large upper pole stone burden or upper pole calyceal diverticular stones, an upper pole access was used selectively. Taking location of the tract, intraoperative findings, complexity of the stone burden

and correlated examinations (including non-contrast CT, Kidney Ureter Bladder (KUB) plain X-ray, renal ultrasound (US) and nephrotomography) into consideration, the treating urologist chose appropriate postoperative imaging to determine the stone free status (SFS) before hospital discharge.

In this study, the information including demographics, clinical symptoms (hematuria, pain history or urinary tract infections), medical comorbidities, the presence of staghorn calculi was collected and analyzed. Complete staghorn calculi was defined as stone in ≥ 2 calices and ≥ 2 kidney regions and partial staghorn calculi as stone in pelvis, branching into ≤ 2 calices in one region of kidney. As defined by previous studies, perioperative characteristics including operative time, location of tracts, preoperative leukocyte count, use of nephrostomy, dilation device, tube/double J stent, upper pole tract, multiple Tracts length of stay and abnormalities of urinary tract were analyzed [20].

Postoperative information including such as SFS at discharge, stone composition, etc. were included. All patients were followed-up after PCNL and the complications were evaluated using the modified Clavien Score [21]. Major complications were categorized with Clavien score of 3A, 3B, 4A, 4B and 5, while minor complications were categorized with Clavien score of 1 and 2. For those patient with more than one complication, final analysis was performed just with the highest Clavien score [22]. Infectious complications were also evaluated by systemic inflammatory response syndrome (SIRS) criteria and blood cultures. The diagnosis for SIRS required ≥ 2 criteria described below: (1) leukocyte count > 12,000 or < 4000; (2) temperature > 38°C or < 36°C; (3) heart rate > 90/min; (4) respiratory rate > 20/min. Sepsis is defined

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Table 2. Demographic, clinical and radiological characteristics of patients with major or minor complications

	Major complications	Minor complications	P-value
Number	33 (8.0%)	95 (23.1%)	-
Age (years)	57.2±10.8	51.8±9.4	0.003*
Gender			
Male	18 (54.5%)	51 (53.7%)	
Female	15 (45.5%)	44 (46.3%)	0.902
BMI (kg/m ²)	26.0±3.7	24.9±3.9	0.123
Clinical symptoms			
Urinary tract infections	9 (27.3%)	24 (25.3%)	
Hematuria	6 (18.2%)	20 (21.1%)	
Pain	18 (54.5%)	51 (53.7%)	0.93
Preoperative leukocyte count (×10 ⁹ /L)	8.9±2.5	7.2±2.2	0.010*
Comorbidities			
Hypertension	12 (36.4%)	16 (16.8%)	0.019*
Diabetes	16 (48.5%)	19 (20.0%)	0.002*
Operative time (min)	118.6±34.2	103.4±38.3	0.029*
Fluoroscopy time (min)	95.1±40.7	87.3±33.7	0.232
Staghorn			
Complete staghorn	11 (33.3%)	16 (16.8%)	0.045*
Partial staghorn	8 (24.2%)	14 (14.7%)	0.212
Multiple tracts	4 (12.1%)	9 (9.5%)	0.665
Upper pole tract	8 (24.2%)	9 (9.5%)	0.031*
Urinary tract anomaly	5 (15.2%)	14 (14.7%)	0.309
Length of hospital stay (d)	4.5±2.3	3.3±2.7	0.014*

BMI, body mass index. * $P < 0.05$ by Fisher's exact test or Mann-Whitney test.

as SIRS with the presence of a source of infection [23].

Statistical analysis

SPSS 19.0 (SPSS, Inc.) statistical software was used in this study for statistical analysis. Data are presented as number (n) and percentage (%), or mean ± standard error (SD). Fisher's exact test and Mann-Whitney U-test are used respectively for the analysis of categorical variables and continuous variables. The influence of variables for infectious and major complications were evaluated by multivariate logistic regression testing. Each statistical test was two-sided and statistical significance was set at a P value of < 0.05 .

Results

Patient and sample characteristics

During the 5-year period, a total of 437 patients with renal stones were performed with PCNL by

two surgeons in our hospital. Of the 437 patients, 411 were enrolled for the final analysis and 26 were excluded due to incomplete information. The mean age of 411 patients was 53.6 years and male patients occupied 57.9%. 13.1% of the patients were with comorbidity of hypertension and 18.0% were with diabetes. The most common clinical symptoms included pain (250/411, 60.8%), hematuria (77/411, 18.7%) and urinary tract infections (84/411, 20.4%).

Risk factors for postoperative infectious complications

Of all the 411 patients enrolled, 145 patients were diagnosed with SIRS. The comparison of demographic, clinical and radiological variables between patients with and without SIRS was shown in **Table 1**. Those patients with older age, a higher preoperative leukocyte count,

comorbidity with diabetes, a longer operative time or hospital stay, complete staghorn or an upper pole tract seemed more likely to have postoperative infectious complications. As these possible risk factors might be associated with infectious complications, we designed multivariate logistic regression analyses. As shown in **Table 3**, the comorbidity of diabetes and complete staghorn calculi were suggested to be independent risk factors for postoperative infectious complications.

Risk factors for postoperative major complications

In our present study, the overall complication rate was 31.1% (128/411), and 33 cases (8.0%) was categorized as major complications according to the modified Clavien Score. In comparison with patients with minor complications, those with major complications were with an older age, a higher preoperative leukocyte count, a higher incidence of comorbidities (dia-

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Table 3. Multivariate logistic regression analysis for infectious complications (SIRS+)

Parameter	Infectious complications (SIRS+)		
	OR	95% CI	P value
Age	1.02	0.99-1.03	0.34
Preoperative leukocyte count	0.62	0.39-1.01	0.062
Comorbidity of diabetes	1.35	1.01-1.76	0.033*
Operative time	1.48	0.86-2.53	0.19
Complete staghorn	1.93	1.44-2.34	0.012*
Upper pole tract	1.62	0.81-3.12	0.18
Length of hospital stay	1.51	0.78-2.58	0.22

SIRS, systemic inflammatory response syndrome; OR, odds ratio; CI, confidence interval. *Multivariate analysis by logistic regression, $P < 0.05$.

Table 4. Multivariate logistic regression analysis for major complications

Parameter	Major complications (Clavien score $\geq 3a$)		
	OR	95% CI	P value
Age	0.99	0.98-1.01	0.39
Preoperative leukocyte count	1.22	0.59-2.51	0.55
Comorbidity of hypertension	0.87	0.28-2.68	0.84
Comorbidity of diabetes	1.35	1.05-1.72	0.023*
Operative time	1.00	0.99-1.01	0.37
Complete staghorn	1.27	0.96-1.67	0.15
Upper pole tract	1.24	1.12-1.42	0.014*
Length of hospital stay	1.53	0.86-2.81	0.24

OR, odds ratio; CI, confidence interval. *Multivariate analysis by logistic regression, $P < 0.05$.

betes and hypertension), a longer operative time and hospital stay, a higher percentage of complete staghorn and upper pole tract (**Table 2**). As shown in **Table 4**, results from multivariate logistic regression analyses showed that the comorbidity of diabetes and an upper pole tract were risk factors for the occurrence of major complications after PCNL.

Discussion

PCNL has evolved as the first choice of treatment for patients with complex or large renal stone burdens. Numerous studies have certified the safety and efficacy of PCNL for renal stones [24]. The postoperative complications especially infectious and major complications did great damage to the postoperative recovery of patients. Postoperative infectious complications were associated with prolonged hospitalization and additional antibiotic treatment. For those patients with complicated stones, the

incidence of SIRS may develop up to 35% and a small part might progress to sepsis [25]. Numerous studies have concluded that sepsis was the most common cause for the perioperative death after PCNL [5]. Formerly, the evidence of positive blood cultures was always required for the diagnosis of sepsis, however, patients with sepsis sometimes were not with positive results of blood cultures as expected [26]. In recent years, SIRS criteria in urology researches was suggested to be applied instead of fever as the end point in the past [3]. Major complications often became life-threatening with no prediction and intervention in time. The modified Clavien scoring system was recommended to for the evaluation of surgery outcomes and major complications [27]. The determination of major or minor complications in our present study was according to the modified Clavien score system. It is very important to evaluate prognostic factors for infectious and major complications after PCNL.

Recently, diabetes has shown an increasing incidence worldwide. However, the correlation between diabetes and complications after PCNL still remains uncertain. Our study was intended to investigate prognostic factors for infectious and major complications after PCNL in our hospital. Recently, Koras *et al.* reported that 27% of 303 patients in a cohort were with postoperative SIRS and 7.6% of which progressed to sepsis. The majority of SIRS patients have recovered without sequelae [28]. And the incidence of SIRS in this study was 35.3% (145/411), which was much higher than the results reported by Koras. The rigorous use of preoperative prophylactic and culture-directed antibiotics might probably cut down the high rate of SIRS.

As shown in the results, a number of factors including the ages, preoperative leukocyte count, comorbidity of diabetes, complete staghorn calculi, operation time, an upper pole tract

and length of hospital stay were all associated with the development of an infectious complication after PCNL. After multivariate logistic regression analysis, the comorbidity of diabetes and complete staghorn calculi were independently significant predictors of postoperative infectious complications, which was in agreement with prior studies [21]. Patients with complete staghorn calculi always had a higher residual stone rate, and then it might lead to the suffering of postoperative complications. Previous studies have shown that besides a positive preoperative urine culture, the age, preoperative nephrostomy, staghorn calculus and comorbidities of diabetes were all predictive factors for the postoperative fever [29]. Diabetic PCNL patients were with a significantly greater risk of developing urinary tract infections and a fever during the postoperative period [30], and this was quite the same with our study.

The variables including the ages, preoperative leukocyte count, comorbidities (diabetes and hypertension), complete staghorn calculi, operation time, an upper pole tract and length of hospital stay in patients with major complications also significantly differ from patients with minor complications. We found that the factors that could significantly predict a higher Clavien score were an upper pole access and the comorbidity of diabetes. These two factors are maybe directly related to a high rate of major complications or they represent surrogates for other risk factors. Although the Clavien system is a great tool in the immediate postoperative period, it also has a major limitation that it couldn't be used to assess long-term complications. Studies have reported that the incidence of major complications for patients with hypertension, diabetes mellitus or manifestations of metabolic syndrome was much higher [31, 32], which is in agreement with our study. In summary, the comorbidity of diabetes was an independent risk factor for both infectious and major complications after PCNL with unknown involved mechanisms. Recent data in patients with type 2 diabetes have demonstrated that higher CD4 cell counts was observed accompanied with increasing prevalence of advanced glycation end products and elevated glycated HbA1c levels. It was suggested that hyperglycemia may be associated with enhancing CD4 cell counts [33]. The correlation between dia-

betes and immune system attracts a lot in recent years. The overall immune suppression might be a potential explanation why diabetes predisposes to postoperative infection and major complications.

Conclusions

The comorbidity of diabetes was significantly associated with an increasing incidence of both infectious and major postoperative complications after PCNL.

Acknowledgements

All patients included in this study provided written informed consent with signature.

Disclosure of conflict of interest

None.

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