Postoperative infective complications following percutaneous nephrolithotomy

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Abstract Introduction: Percutaneous nephrolithotomy (PCNL) is recommended as the first choice of therapeutic strategy for patients with renal stones larger than 2 cm. It is reported that up to one-third of patients might have some perioperative complications, especially fever and urinary tract infections, which constitutes about 21%–39.8% of all the complications.

Primary and Secondary: The primary aim of the study was to study about the proportion of patients getting post-operative infective complications following PCNL. The secondary aim was to study the patient, stone and procedure related risk factors associated with the infective complications.

Settings and Design: This is an institution-based observational study.

Materials and Methods: All patients who underwent PCNL in the Department of Urology, Medical College, Thiruvananthapuram, during 3 years from September 2016– to August 2019, were included in the study. In this study, the demographic factors and factors related to the patient, stone, and the procedure were collected and analyzed.

Statistical Analysis Used: Data analysis was performed using SPSS version 22.0.

Results: During the 3-year period, a total of 201 patients with renal stones were treated with PCNL in our hospital. Of this 190 cases were taken for analysis. The mean age of patients was 47.7 years, 148 (77.9%) were male, 42 (22.1%) were female, The final outcomes evaluated were episodes of fever, documented urinary tract infection (UTI), pyelonephritis, and sepsis. Thirty-six (18.9%) patients had fever, of which 21 (11.1%) had UTI, 6 (3.1%) had pyelonephritis and 5 (2.6%) developed sepsis.

Conclusions: Post-PCNL complications are more commonly found in patients with history of preoperative UTI, previous history of renal surgeries, large stone burden, operative procedure more than 90 min, and presence of residual calculi.

Keywords: Percutaneous nephrolithotomy, pyelonephritis, sepsis, urinary tract infection

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is recommended as the first choice of therapeutic strategy for patients with renal stones larger than 2 cm. It is also recommended as a treatment option for stones >1 cm in the lower pole and stones in the upper ureter where extracorporeal shock wave lithotripsy (ESWL) has failed or is contraindicated and in upper tracts which are not amenable to retrograde intrarenal surgery (RIRS).^[1] It is reported that upto one-third of patients might have some perioperative complications,^[2] especially the fever and a urinary tract infection, which constitutes about 21%-39.8% of all the complications.[3] Among them 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] Urosepsis has been reported to occur in 0.9%-4.7% of PCNL procedures.^[7] The duration of procedure, bacterial load in the urine, severity of obstruction, and presence of infected stone directly affect the incidence of febrile urinary tract infection (UTI) and/or urosepsis.^[8,9] This study is intended to assess the postoperative infective complications, and to evaluate the patient, stone and procedure related risk factors that affect the incidence of infective complications in PCNL.

MATERIALS AND METHODS

Aims and objectives

Primary

To study about the proportion of patients getting postoperative infective complications following PCNL.

Secondary

To study the patient, stone, and procedure related risk factors associated with infective complications following PCNL.

Study design

This is an institution-based observational study.

Study population

All patients who underwent PCNL in the Department of Urology, Medical College, Thiruvananthapuram, for a period of 3 years September 2016 to August 2019, were included in the study.

After obtaining clearance from Institutional Research Committee and Institutional Ethics Committe, retrospective analysis of the patients who have undergone PCNL in our institution during 3 years from September 2016 to August 2019 were included in the study.

In this study, the information including demographics, clinical symptoms (pain, urinary tract infections), medical comorbidities (diabetes mellitus [DM], systemic hypertension) was collected and analyzed. History of previous surgeries (open, endoscopic, and ESWL within the past 10 years were also taken into account. History of Double J (DJ) stenting or percutaneous nephrostomy (PCN) prior to the surgery was taken into consideration. Laboratory evaluation included Complete Blood Count CBC (Hb, TC, DC and ESR) and renal function test (blood urea and serum creatinine). Radiological evaluation of the stone was done with computerized tomography (CT), and functional evaluation was done with either intravenous urography or CT urogram. Stone characteristics that were assessed included, size (in cm³), staghorn (complete or partial), presence of upper ureteric calculi, presence of hydronephrosis (HDN), and density of the stone. Complete staghorn calculi was defined as stone in ≥ 2 calices 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 (less than or more than 90 min), number of tracts (one or more than one), size of the tracts (≤22 French (Fr), >22Fr), use of nephrostomy, and use of DJ stent were assessed. Preoperatively, sterile urine culture was ensured, and culture-specific antibiotics were given if detected to have positive urine culture. Patients with preoperative fever or positive urine culture were not taken for surgery until unless the fever subsides and urine is sterile. Percutaneous nephrostomy (PCN) tube was placed in patients with pyonephrosis. Prophylactic antibiotics were given for all patients. The second generation cephalosporins or culture-specific antibiotics were given at the induction of anesthesia.

Operative technique

Under general anesthesia, retrograde ureteric catheterization was done on the ipsilateral side. The patient was turned prone, and percutaneous access was obtained under fluoroscopic guidance by the operating surgeon using a diamond tip 18-G puncture needle. A hydrophilic guide wire was passed, over which tract dilatations were done using Alken metal dilators and an Amplatz sheath was placed into system. Stones were fragmented using pneumatic lithoclast and removed. Intraoperative stone clearance was accessed using fluoroscopy. A double J (DJ) stent/ureteric catheter/ nephrostomy tube was placed in most of the cases.

Postoperative period

Patients were admitted for 3-5 days in the ward. During

this period, monitoring of temperature, pulse rate, blood pressure, and total leukocyte count were done daily. Urine culture was done on the 1st postoperative day. Fever was defined as temperature >38°C on any of the postoperative days. The diagnosis of pyelonephritis was given to those patients who developed fever with a raised leukocyte count of 12,000/mm³. The diagnosis for sepsis required ≥ 2 criteria described below: (1) leukocyte count >12,000 or <4000/mm³; (2) temperature >38°C or <36°C; (3) heart rate >90/min; (4) respiratory rate >20/ min. Ultrasound scan and X-ray were used for assessing the residual calculi and calculi more than 8 mm in length on any axis was taken as residual calculi.

Statistical analysis

Quantitative variables were expressed as mean, standard deviation. Qualitative variables were expressed as proportion. Comparison of quantitative variables between two groups were analyzed by Student's *t*-test. The association between qualitative variables was analyzed by Chi-square test. A P < 0.05 was considered statistically significant. Data analysis was performed using SPSS version 22.0 (IBM SPSS Statistics for Windows, Version 22.0. IBM Corp, Armonk, NY, USA).

RESULTS

During the 3-year period, a total of 201 patients with renal stones were performed with PCNL in our hospital. Of this 190 cases were taken for analysis, as the data were incomplete in 11 cases. The mean age of patients was 47.7 years, 148 (77.9%) were male, 42 (22.1%) were female, 108 (56.8%) calculi were on the right side and 82 (43.2%) were left sided. The average size of the calculi was 6 cm³ and average density in CT was 1084.5 Hounse field units [Table 1]. Regarding the comorbidities, 48 (25.3%) were having DM, 64 (33.7%) were hypertensive. Twelve (6.3%) had urinary tract infection (UTI) preoperatively which was treated and urine was made sterile before the procedure. Four (2.1%) had urosepsis before the procedure for which one patient (0.5%) had underwent PCN. Preoperative DJ stenting was done in 38 (20%) patients [Table 2].

Sixty-seven (35.3%) patients had history of open or endoscopic surgery within the last 10 years. Fifty-five (28.9%) were staghorn calculi, and upper calyceal stones were present in 17 (8.9%) and upper ureteral stones were present in 16 (8.4%). Radiological evidence of hydronephrosis was present in 114 (60%) patients. The size of the tract used was less <22Fr in 95 (50%), >22Fr in 50%. The duration of the procedure was <90 min in 109 (57.4%) cases and more than 90 min in 81 (42.6%) cases. Residual calculi were seen in 25 (13.2%) cases. Two patients were readmitted after discharge for managing urinary tract infection.

The final outcomes evaluated were episodes of fever, documented UTI, pyelonephritis, and sepsis. Thirty-six (18.9%) patients had fever, of which 21 (11.1%) had UTI, 6 (3.1%) had pyelonephritis and 5 (2.6%) developed sepsis. Three patients expired [Table 3].

The risk factors for fever include the duration of surgery (>90 min) (P = 0.004), previous episodes of urosepsis (P = 0.004), history of renal surgery in the past (P = 0.033), and presence of residual calculi after the procedure (P = 0.004) [Table 4].

Table 1: Demographic factors

	Mean	SD
Age	47.7	11.8
Size cm ³	6.0	7.8
Density	1084.5	242.5
Male	148	77.9
Female	42	22.1
Right	108	56.8
Left	82	43.2

SD: Standard deviation

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Variable	Number of cases (%)
Flank pain	180 (94.7)
DM	48 (25.3)
HTN	64 (33.7)
History of UTI	12 (6.3)
History of urosepsis	4 (2.1)
Preoperative stenting	38 (20)
Nephrostomy	1 (0.5)
Past history of Surgery	66 (34.7)
Staghorn	55 (28.9)
Multiple	53 (27.9)
Uppercalyx	17 (8.9)
Ureter	16 (8.4)
Hydronephrosis	114 (60)
DJS (on table)	184 (96.8)
Nephrostomy (on table)	149 (78.4)
Puncture - one	163 (85.8)
More than one puncture	27 (14.2)
Tract size <22 Fr	95 (50)
Tract size >22 Fr	95 (50)
Duration <90 MTS	109 (57.4)
Duration >90 MTS	81 (42.6)
Residual calculi present	25 (13.2)

DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, DJS: Double J stenting

Table 3: Outcomes

Outcome	Frequency (%)
ever	36 (18.9)
JTI	21 (11.1)
Pyelonephritis	6 (3.2)
Sepsis	 5 (2.6)

UTI: Urinary tract infection

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	Fe	ver	Р
	Yes (<i>n</i> =36), <i>n</i> (%)	No (<i>n</i> =154), <i>n</i> (%)	
Male	30 (20.3)	118 (79.7)	0.382
Female	6 (14.3)	36 (85.7)	
Right	24 (22.2)	84 (77.8)	0.186
Left	12 (14.6)	70 (85.4)	
<22	14 (14.7)	81 (85.3)	0.139
>22	22 (23.2)	73 (76.8)	
<90	13 (11.9)	96 (88.1)	0.004
>90	23 (28.4)	58 (71.6)	
One puncture	28 (17.2)	135 (82.8)	0.126
>1 puncture	8 (29.6)	19 (71.4)	
Flank pain	35 (19.4)	145 (80.6)	0.458
DM	11 (22.9)	37 (77.1)	0.417
HTN	16 (25)	48 (75)	0.129
UTI	8 (66.7)	4 (33.3)	0.000
Urosepsis	3 (75)	1 (25)	0.004
Stenting	9 (23.7)	29 (76.3)	0.405
Nephrostomy	1 (100)	0 (0)	0.038
History of surgery	18 (27.3)	48 (72.7)	0.033
Staghorn	14 (25.5)	41 (74.5)	0.144
Multiple	8 (15.1)	45 (84.9)	0.399
Uppercalyx	2 (11.8)	15 (88.2)	0.428
Ureter	4 (25)	12 (75)	0.519
Hydronephrosis	21 (18.4)	93 (81.6)	0.821
DJS	35 (19)	149 (81)	0.885
Nephrostomy	28 (18.8)	121 (81.2)	0.917
Residual calculi	10 (40)	15 (60)	0 004

DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, DJS: Double J stenting

Table 5: Association between outcome and variables

	U	ITI	Р
	Yes (<i>n</i> =21), <i>n</i> (%)	No (<i>n</i> =169), <i>n</i> (%)	
Male	18 (12.2)	130 (87.8)	0.360
Female	3 (7.1)	39 (92.9)	
Right	15 (13.9)	93 (86.1)	0.152
Left	6 (7.3)	76 (92.7)	
<22	8 (8.4)	87 (91.6)	0.247
>22	13 (13.7)	82 (86.3)	
<90	6 (5.5)	103 (94.5)	0.005
>90	15 (18.5)	66 (81.5)	
One puncture	16 (9.8)	147 (90.2)	0.182
>1 puncture	5 (18.5)	22 (81.5)	
DM	5 (10.4)	43 (89.6)	0.871
HTN	9 (14.1)	55 (85.9)	0.346
UTI	3 (25)	9 (750	0.111
Urosepsis	2 (50)	2 (50)	0.012
Stenting	4 (10.5)	34 (89.5)	0.908
Nephrostomy	1 (100)	0 (0)	0.004
History of surgery	11 (16.7)	55 (83.3)	0.072
Staghorn	9 (16.4)	46 (83.6)	0.136
Multiple	4 (7.5)	49 (92.5)	0.338
Uppercalyx	0(0)	17 (100)	0.128
Ureter	2 (12.5)	14 (87.5)	0.847
Hydronephrosis	14 (12.3)	100 (87.7)	0.508
DJS	21 (11.4)	163 (88.6)	0.380
Nephrostomy	18 (12.1)	131 (87.9)	0.389
Residual calculi	7 (28)	18 (72)	0.004

DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, DJS: Double J stenting

The risk factors for urinary tract infection include duration of surgery more than 90 min (P = 0.005), history of

preoperative urosepsis (P = 0.012), and presence of residual calculi (P = 0.004) [Table 5].

Significant risk factor for pyelonephritis was found to be the presence of staghorn calculi (P = 0.038) [Table 6]. Those who developed sepsis had incidence of UTI (P = 0.002) in the past as one of the important risk factors [Table 7]. The only patient who had a preoperative nephrostomy for pyonephrosis had fever with pyelonephritis and features of sepsis in the post-operative period.

DISCUSSION

PCNL is still the most commonly performed surgery for large and complex renal stones. Though the safety and efficacy of the procedure has been defined, infectious complications are still the dangerous ones. Postoperative infectious complications were associated with prolonged hospitalization and additional antibiotic treatment. Numerous studies have concluded that sepsis is the most common cause for the perioperative death after PCNL.^[5] The incidence of fever in our study was 18.9%, UTI 11.1%, pyelonephritis 3.2% and sepsis 2.6%. The prospective study conducted by Rivera et al.[10] in 227 patients had infectious complications in 37 (16%) patients: 11 (5%) UTI/ pyelonephritis, 21 (9%) systemic inflammatory+ response syndrome (SIRS), 2 (0.9%) sepsis. In an even larger study investigating postoperative fever after PCNL Gutierrez et al.^[5] utilizing the CROES (Clinical Research Office of the Endourological Society) data and found that 10.4% of the 5,313 patients with pre- and post-operative data developed a fever (>38.5°C). In a study published by Sharma et al. patients with renal failure (serum creatinine >1.4 mg/ dl), staghorn stone, severe preoperative HDN, higher number of puncture, and longer duration of surgery were found to be significant factors associated with infectious complications.^[11] Similar to our study, DM and complete staghorn calculus were found to be the major risk factors for infective complications in a study by Wei et al.^[12] In a study by Yang et al. they observed that urine WBC and stone size were two risk factors for both fever and SIRS. The postoperative complication rates were 12.2% for fever and 27.4% for SIRS, respectively, in this study.^[13] Some other studies also found that the stone burden, history of recurrent urinary tract infections were independent risk factors for infectious complications.^[4,14] Studies showed that patients with recurrent urinary tract infections had a higher risk of developing SIRS after PCNL.^[3] Besides, existing urinary tract infection would increase the risk of postoperative fever.^[15] The number of punctures, size of the tract, preoperative stenting and the presence of

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	Pyelon	ephritis	Р
	Yes (<i>n</i> =6), <i>n</i> (%)	No (<i>n</i> =184), <i>n</i> (%)	
Male	4 (2.7)	144 (97.3)	0.501
Female	2 (4.8)	40 (95.2)	
Right	3 (2.8)	105 (97.2)	0.731
Left	3 (3.7)	79 (96.3)	
<22 Fr	2 (2.1)	93 (97.9)	0.407
>22 Fr	4 (4.2)	91 (95.8)	
<90 min	2 (1.8)	107 (98.2)	0.226
>90 min	4 (4.9)	77 (95.1)	
One puncture	5 (3.1)	158 (96.9)	0.861
>1 puncture	1 (3.8)	26 (96.2)	
DM	3 (6.3)	45 (93.8)	0.156
HTN	3 (4.7)	61 (95.3)	0.390
UTI	3 (25)	9 (75)	0.000
Urosepsis	2 (50)	2 (50)	0.000
Stenting	1 (2.6)	37 (97.4)	0.836
Nephrostomy	1 (100)	0 (0)	0.000
History of surgery	2 (3)	64 (97)	0.942
Staghorn	4 (7.3)	51 (92.7)	0.038
Multiple	0(0)	53 (100)	0.122
Uppercalyx	0 (0)	17 (100)	0.435
Ureter	0 (0)	16 (100)	0.450
Hydronephrosis	4 (3.5)	110 (96.5)	0.735
DJS	6 (3.3)	178 (96.7)	0.653
Nephrostomy	5 (3.4)	144 (96.6)	0.766
Residual calculi	2 (8)	23 (92)	0.137

DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, DJS: Double J stenting

Table 7: Association between outcome and variables

	Se	psis	Р
	Yes (<i>n</i> =5), <i>n</i> (%)	No (<i>n</i> =185), <i>n</i> (%)	
Male	4 (2.7)	144 (97.3)	0.908
Female	1 (2.4)	41 (97.6)	
Right	2 (1.9)	106 (98.1)	0.441
Left	3 (3.7)	79 (96.3)	
<22	2 (2.1)	93 (97.9)	0.650
>22	3 (3.2)	92 (96.8)	
<90	1 (0.9)	108 (99.1)	0.087
>90	4 (4.9)	77 (95.1)	
One puncture	4 (2.5)	159 (97.5)	0.707
>1 puncture	1 (3.8)	26 (96.2)	
DM	3 (6.3)	45 (93.8)	0.070
HTN	3 (4.7)	61 (95.3)	0.207
UTI	2 (16.7)	10 (83.3)	0.002
Urosepsis	2 (50)	2 (50)	0.000
Stenting	0(0)	38 (100)	0.257
Nephrostomy	1 (100)	0 (0)	0.000
History of surgery	1 (1.5)	65 (98.5)	0.483
Staghorn	3 (5.5)	52 (94.5)	0.121
Multiple	1 (1.9)	52 (98.1)	0.690
Uppercalyx	0 (0)	17 (100)	0.477
Ureter	0(0)	16 (100)	0.492
Hydronephrosis	3 (2.6)	111 (97.4)	1.000
DJS	5 (2.7)	179 (97.3)	0.682
Nephrostomy	5 (3.4)	144 (96.6)	0.235
Residual calculi	1 (4)	24 (96)	0.646

DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, DJS: Double J stenting

hydronephrosis were not found to be significant risk factors in our study. One patient had preoperative nephrostomy and that patient had developed fever, pyelonephritis, and later developed sepsis. Three patients expired in the postoperative period, 1 due to sepsis, and 2 due to pulmonary embolism and acute myocardial infarction, respectively. In contrast to other studies our study showed that previous history of renal surgery is one of the risk factors for fever and sepsis.

CONCLUSIONS

Post-PCNL complications are more commonly found in patients with a history of preoperative UTI, previous history or renal surgeries, large stone burden, operative procedure more than 90 min and presence of residual calculi. The number or size of the tracts was not associated with significant risk. The main fallacy of our study was its retrospective nature. This study was conducted in a single institute with different surgeons performing the same procedure.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Türk C, Neisius A, Petrik A, Seitz A, Skolarikos A, Thomas K, *et al.* Urolithiasis [Internet] EAU; 2000. Available from https://uroweb. org/guideline/urolithiasis/. [Last updated 2020; cited 2020 May 3].
- Tefekli A, Ali Karadag M, Tepeler K, Sari E, Berberoglu Y, Baykal M, et al. Classification of percutaneous nephrolithotomy complications using the modified clavien grading system: Looking for a standard. Eur Urol 2008;53:184-90.
- Draga RO, Kok ET, Sorel MR, Bosch RJ, Lock TM. Percutaneous nephrolithotomy: Factors associated with fever after the first postoperative day and systemic inflammatory response syndrome. J Endourol 2009;23:921-7.
- Bozkurt IH, Aydogdu O, Yonguc T, Koras O, Sen V, Yarimoglu S, et al. Predictive value of leukocytosis for infectious complications after percutaneous nephrolithotomy. Urology 2015;86:25-9.
- de la Rosette J, Assimos D, Desai M, Gutierrez J, Lingeman J, Scarpa R, *et al.* The clinical research office of the endourological society percutaneous nephrolithotomy global study: Indications, complications, and outcomes in 5803 patients. J Endourol 2011;25:11-7.
- Labate G, Modi P, Timoney A, Cormio L, Zhang X, Louie M, *et al.* The percutaneous nephrolithotomy global study: Classification of complications. J Endourol 2011;25:1275-80.
- Michel MS, Trojan L, Rassweiler JJ. Complications in percutaneous nephrolithotomy Eur Urol 2007;51:899-906.
- Mariappan P, Tolley DA. Endoscopic stone surgery: Minimizing the risk of post-operative sepsis. Curr Opin Urol 2005;15:101-5.
- Mariappan P, Smith G, Moussa SA, Tolley DA. One week of ciprofloxacin before percutaneous nephrolithotomy significantly reduces upper tract infection and urosepsis: A prospective controlled study. BJU Int 2006;98:1075-9.
- 10. Rivera M, Viers B, Cockerill P, Agarwal D, Mehta R, Krambeck A.

Pre- and postoperative predictors of infection-related complications in patients undergoing percutaneous nephrolithotomy. J Endourol 2016;30:982-6.

- Sharma K, Sankhwar NS, Goel A, Singh V, Sharma P, Garg Y. Factors predicting infectious complications following percutaneous nephrolithotomy. Urol Ann 2016;8:434-8.
- 12. Wei W, Leng J, Shao H, Wang W. Diabetes, a risk factor for both infectious and major complications after percutaneous nephrolithotomy. Int J Clin Exp Med 2015;8:16620-6.
- 13. Yang T, Liu S, Hu J, Wang L, Jiang H. The evaluation of risk factors

for postoperative infectious complications after percutaneous nephrolithotomy. Biomed Res Int 2017;2017:1-7.

- Dogan HS, Guliyev F, Cetinkaya YS, Sofikerim M, Ozden E, Sahin A. Importance of microbiological evaluation in management of infectious complications following percutaneous nephrolithotomy. Int Urol Nephrol 2007;39:737-42.
- Mirheydar HS, Palazzi KL, Derweesh IH, Chang DC, Sur RL. Percutaneous nephrolithotomy use is increasing in the United States: An analysis of trends and complications. J Endourol 2013;27:979-83.