Original Article

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Impact of Renal Stone Clearance in Patients of Chronic Kidney Disease: A Prospective Observational Study from a Tertiary Care Centre

Surgery Section

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ABSTRACT

Introduction: Varying degrees of renal insufficiency is associated with renal stone disease. The incidence of Chronic Kidney Disease (CKD) in renal stone is around 0.8 to 17.5%. There is limited data on the outcomes of Percutaneous Nephrolithotomy (PCNL) in CKD patients like improvement in Glomerular Filtration Rate (GFR), Effective Renal Plasma Flow (ERPF), postoperative complications, morbidity like dialysis dependence and mortality and various other factors.

Aim: To study the impact of PCNL in patients of urolithiasis with CKD.

Materials and Methods: A prospective observational study was conducted on 100 patients of chronic kidney disease seeking operative treatment during June 2017 to September 2019 in the Department of Urology, Superspeciality Hospital and Government Medical College (GMC), Nagpur, Maharashtra, India. All suspected patients underwent a plain Computed Tomography (CT) scan. Patients were classified into three groups; group 1 included stage III, group 2 included stage IV and group 3 included stage V CKD patient. Patients with Acute Kidney Injury (AKI) underwent urine diversion first. Both short term impact like hospital stay, need for blood transfusion, AKI, sepsis, fever and long term impact like change in renal function, stage migration were studied. Statistical analysis was done using Kruskal Wallis Test (age distribution); Chi-squared test (gender and AKI); Fisher's exact test (stone Composition and transfusion); Kruskal Wallis Test {Body Mass Index (BMI), hospital stay, Effective Renal Plasma Flow (ERPF) and Estimated Glomerular Filtration Rate (eGFR)}.

Results: A total of 55 patients were of Grade III CKD, 31 were of Grade IV CKD and 14 patients were of stage V CKD and classified into groups 1, 2 and 3, respectively. Age and gender distribution were not significantly different among various groups. There was no significant difference in BMI (Kg/m^2) or diabetes in the groups. The most common stone composition was calcium oxalate dihydrate (53%). Among 100 patients, urine culture was sterile in 77 patients. No significant difference was found in the incidence of urinary tract infection (p-value=0.629). Group 3 presented with significantly higher incidence of AKI (p-value=0.001). Stone free rate was not significantly different among groups (p-value=0.252). Blood transfusion rates was not statistically different in these groups (p-value=0.066). Mean hospital stay was significantly higher with higher stages of CKD (p-value <0.001). Change in renal function was evaluated by change ERPF and eGFR. ERPF significantly increased by 1.96±4.87 (p-value=0.001) after surgery. Similarly, there was significant increase in eGFR over time (p-value=0.037).

Conclusion: PCNL in patients of chronic kidney disease has a minor but significant improvement in GFR with good clearance rates.

Keywords: Acute kidney injury, Estimated glomerular filtration rate, Percutaneous nephrolithotomy, Urolithiasis

INTRODUCTION

Chronic renal failure implies continuing renal deterioration in nephron function or number and is typically categorised among Chronic Kidney Disease (CKD) stages III to V [1]. Varying degrees of renal insufficiency is associated with renal stone disease [2,3]. In chronic renal failure patients, the cause of renal stones includes renal obstruction, recurrent urinary tract infections, surgical interventions, and other co-morbidities. The incidence of chronic kidney disease in renal stone is around 0.8% to 17.5% [4,5].

Co-morbid conditions associated with chronic kidney disease may increase the operative risk, the incidence of postoperative complications and decrease the success rate. CKD in the surgical setting does not only have a higher risk of anaesthetic complications, but also a greater risk of post-procedure complications [6]. The presence of urinary tract infections tended to affect Glomerular Filtration Rate (GFR) negatively. There is limited data on the outcomes and factors affecting outcome in patients with CKD with urolithiasis. There is a need for a thorough prospective study since there is limited data on the outcomes of Percutaneous Nephrolithotomy (PCNL) in CKD patients like improvement in GFR, Effective Renal Plasma Flow (ERPF), postoperative complications, morbidity like dialysis dependence and mortality and various other factors.

The primary objective of the study was to study the impact of PCNL in patients of urolithiasis with CKD. Secondary objective was to assess the complication rates among various grades of CKD.

MATERIALS AND METHODS

This prospective observational study was performed between June 2017 to September 2019, after obtaining permission from the appropriate authority within the institute. A total of 100 consecutive patients of chronic kidney disease visiting Department of Urology, Superspeciality Hospital and Government Medical College, Nagpur, Maharashtra, India, and seeking operative treatment for urolithiasis were included. Written informed consent was obtained from all the patients. Sample size was calculated by nMaster 1.0 Sample size software developed by Christian Medical College, Vellore, Tamil Nadu, India. Patients were evaluated for their demographics like age, sex, weight, co-morbidity, significant medical and surgical history.

Inclusion and Exclusion criteria: All suspected patients underwent a plain CT scan. Patients less than 18 years of age or more than

70 years, immunodeficient patient, patient with bleeding disorders, patient with anatomic anomalies of kidney like horseshoe kidney, patients with prior renal surgery were excluded from the study. However, patients with co-morbidities like hypertension and diabetes were not excluded. All the CKD patients with the urolithiasis were included.

The included patients were classified into three groups; group 1 included stage III CKD patients, group 2 included stage IV CKD patients and group 3 stage included stage V CKD patient. All patients underwent an Technetium-99m ethylene dicysteine renal scan (EC scan) to look at the functional status of each kidney.

Study Procedure

Patients with the features of obstruction and Acute Kidney Injury (AKI) underwent urine diversion with either PCN insertion or Double J stent (DJ stenting) till nadir serum creatinine was reached, before posting the patient for surgery. Stone analysis was done using the X-ray diffraction technique. The GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) (2009) equation [7]. CKD was defined according to the eGFR as outlined by the National kidney foundation [8]. ERPF was calculated by measuring change in the gamma radiation of the radionucleotide 99mTm EC (Technetium-99m Ethylene Dicysteine) over fixed time using computer. After the surgery, the complete stone clearance was defined as the non visualisation of residual fragments in X-ray or ultrasound.

All PCNLs were performed in prone position. Initially a retrograde pyelogram was done and calyx was selected for renal puncture. Following renal puncture, a guidewire was parked in the renal pelvicalyceal system. Over the guidewire, the tract was dilated upto 24 to 26 F. Using 22F nephroscope the stone was visualised and broken with pneumatic lithoclast. A 6/26 DJ stent was kept in all cases.

In the perioperative period, all patients undergoing PCNL were monitored for short term parameters like blood transfusion, urinary tract infection with fever and sepsis, the incidence of AKI, hospital stay, residual calculus, stone composition. Long term impact was studied by the change in estimated Glomerular Filtration Rate (eGFR), Estimated Renal Plasma Flow (ERPF), stage migration, need for renal replacement therapy, and mortality.

In the long term impact of PCNL on renal function, eGFR levels were measured before surgical intervention and three months postsurgery. EC scan was repeated after three months in all the patients. All patients underwent an Ultrasound (USG) scan to look for the residual stone.

STATISTICAL ANALYSIS

All statistical tests were done using Statistical Package for the Social Sciences (SPSS) version 27. 0. Statistical test applied were Kruskal Wallis Test for Age distribution, Chi-square test for gender distribution and frequency of AKI. Fisher's-exact test was used for stone composition and distribution of diabetes, need for transfusion. Kruskal Wallis Test was used for the distribution of BMI, hospital stay, change in ERPF and eGFR. Stuart-Maxwell test was used to assess stage migration of CKD. Paired Wilcoxon test was used to explore the difference in ERPF and eGFR. Wilcoxon rank-sum test (Mann-Whitney U test) was used to compare the change in renal function with diabetes.

RESULTS

In patients enrolled in the study, 55 patients were Grade III CKD, 31 were Grade IV CKD and 14 patients were of stage V CKD and classified into groups 1, 2 and 3, respectively [Table/Fig-1]. The mean age of patients was 47.05, 46.0, 43.79 years in groups 1,2 and 3, respectively. Age distribution was not significantly different among these groups (p-value=0.968). The male to female ratio was 4:1. There is no significant difference in gender distribution among the three groups (p-value= 0.177). Thirteen patients were suffering from diabetes mellitus. There was no significant difference between these groups in terms of the distribution of diabetes (p-value=0.178). There was no significant difference between the groups in terms of BMI (Kg/m^2) (p-value=0.626). The mean preoperative creatinine in non diabetic was 2.85±0.99 and in diabetic was 2.86±0.81.

Parameters	Group 1 (n=55) (n,%)	Group 2 (n=31) (n,%)	Group 3 (n=14) (n,%)	p-value
Age (years)	47.05±9.83	46.00±10.08	43.79±14.21	0.968[1]
Gender (female)	9 (16.4%)	10 (32.3%)	2 (14.3%)	0.177[2]
Creatinine (Preoperative)	2.33±0.32	3.15±0.75	4.27±1.34	<0.001[1]
Stone composition				
Calcium oxalate dihydrate	30 (54.5%)	13 (41.9%)	10 (71.4%)	0.476[3]
Calcium oxalate monohydrate	13 (23.6%)	7 (22.6%)	4 (28.6%)	
Phosphate	2 (3.6%)	4 (12.9%)	0 (0.0%)	
Urate	2 (3.6%)	1 (3.2%)	0 (0.0%)	
Uric acid	6 (10.9%)	6 (19.4%)	0 (0.0%)	
Xanthine	2 (3.6%)	0 (0.0%)	0 (0.0%)	
Effective renal plasma flow (mL/min) (preoperative)	71.41±19.18	47.71±20.71	27.79±4.53	<0.001[1]
Diabetes mellitus (present)	5 (9.1%)	7 (22.6%)	1 (7.1%)	0.178[3]
eGFR (mL/min/m^2) (Preoperative)	37.80±6.19	23.11±5.01	11.43±2.77	<0.001[1]
Body mass index (Kg/m^2)	23.92±3.83	23.40±3.99	23.19±3.61	0.626[1]
Blood transfusion done	1 (1.8%)	3 (9.7%)	2 (14.3%)	0.066[3]
Urine culture				
No growth	41 (74.5%)	25 (80.6%)	11 (78.6%)	0.318[3]
E.Coli	5 (9.1%)	1 (3.2%)	1 (7.1%)	
Klebsiella	1 (1.8%)	1 (3.2%)	2 (14.3%)	
P. Aurgenosa	8 (14.5%)	4 (12.9%)	0	

[Table/Fig-1]: Association between Group and preoperative characteristics.
***Significant at p<0.05, 1: Kruskal Wallis test, 2: Chi-squared test, 3: Fisher's-exact test

The most common stone composition was calcium oxalate dihydrate (53%). Other stone compositions were calcium oxalate monohydrate (24%), phosphate (6%) and uric acid (12%). There was no difference in stone composition (p-value=0.476) in the three groups. Urine was sterile in 77% of the patient. The most common organism in infected urine was *Pseudomonas aeruginosa* (12%) followed by *E. coli* (7%) and *Klebsiella* (4%).

For the short term impact of PCNL, we evaluated hospital stay, blood transfusion, the incidence of AKI, urinary tract infection, residual stones [Table/Fig-2]. Around nine patients developed urinary tract infection with fever and sepsis. No significant difference was found with Fisher's-exact test in the incidence of urinary tract infection in these groups (p-value=0.629). Around 26% of patients developed AKI in the postoperative period with patients in group 3 having significantly higher incidence (p-value=0.001). A 9% of patients had residual stones after surgery. Stone free rate was not significantly different among these groups (p-value=0.252). Blood transfusion rates were similar in these groups (p-value=0.066). Mean hospital stay was 2.38, 3.55, 4.00 days in groups 1, 2 and 3, respectively. Mean hospital stay was significantly higher with higher stages of CKD (p-value <0.001). Mean hospital stay was also found to be higher with larger stone load and multiple punctures. Staghorn calculus involving 2 or more calyx required 2 or more punctures, had longer operating time and hospital stay.

Parameters	Group 1 (n=55)	Group 2 (n=31)	Group 3 (n=14)	p-value
Hospital stay (days)	2.38 (0.83)	3.55 (1.55)	4.00 (1.04)	<0.001##
Blood transfusion (1 Unit PCV)	1 (1.8%)	3 (9.7%)	2 (14.3%)	0.066#
Fever/Sepsis (n,%)	4 (7.3%)	3 (9.7%)	2 (14.3%)	0.6293#
Acute kidney injury (n,%)	7 (12.7%)	11 (35.5%)	8 (57.1%)	0.001*
Residual calculus (n,%)	3 (5.5%)	5 (16.1%)	1 (7.1%)	0.252*

[Table/Fig-2]: Short term impact of Percutaneous Nephrolithotomy on short term parameters.
*Chi-squared test frequency of AKI; #Fisher's-exact test ##Kruskal Wallis test

Change in renal function was evaluated by change ERPF and eGFR. The ERPF significantly increased by 1.96±4.87 (p-value=0.001) after surgery. Change in ERPF after surgery in groups 1, 2 and 3 were 1.43, 1.9, 4.15, respectively. All three groups showed a statistically significant increase in ERPF [Table/Fig-3]. Also, there was a significant difference in change in ERPF (mL/min) over time between the three groups. Mean eGFR significantly increased by 1.08±2.69 (p-value=0.001) after surgery. Change in eGFR after surgery in group 1, 2 and 3 were 1.38, 0.99, 0.07, respectively. three groups showed a statistically significant increase [Table/Fig-4]. Also, the overall p-value for comparison of the change in eGFR over time between the three groups (Generalised Estimating Equations Method) is 0.033.

ERPF (mL/min)	Group			p-value*
	Group 1 Mean (SD)	Group 2 Mean (SD)	Group 3 Mean (SD)	
Preoperative	71.41 (19.18)	47.71 (20.71)	27.79 (4.53)	<0.001
Postoperative	72.84 (20.10)	49.61 (21.42)	31.94 (4.15)	0.001
p-value (Wilcoxon Test)	0.012	0.016	<0.001	

[Table/Fig-3]: Change in Estimated Renal Plasma Flow (ERPF) after PCNL.
Kruskal Wallis test and Paired Wilcoxon test
Effective Renal Plasma Flow (ERPF), *p-value for comparison of the three groups at each of the time points (Kruskal Wallis Test)

eGFR (mL/min/m²)	Group			p-value*
	1	2	3	
	Mean (SD)	Mean (SD)	Mean (SD)	
Preoperative	37.80 (6.19)	23.11 (5.01)	11.43 (2.77)	<0.001
Postoperative	39.18 (6.53)	24.10 (6.18)	11.50 (2.98)	<0.001
p-value (Wilcoxon test)	0.002	0.028	0.017	

[Table/Fig-4]: Change in estimated Glomerular Filtration Rate (eGFR) values after PCNL.
Kruskal Wallis Test and Wilcoxon Test; *p-value for comparison of the three groups at each of the time points (Kruskal Wallis Test)

Change in ERPF in DM was 5.75 and non diabetic was 1.39 [Table/Fig-5]. This change was statistically significant (p-value=0.009). Change in eGFR in DM was 2.14 and non diabetic was 0.92. There was a significant difference in the trend of eGFR (mL/min/m²) over time in both groups (p-value=0.037). Stage migration was seen as not statistically different among these stages of CKD

Variables	Diabetes mellitus			
	Present		Absent	
	eGFR Mean (SD)	ERPF Mean (SD)	eGFR Mean (SD)	ERPF Mean (SD)
Preoperative	29.78 (8.78)	54.81 (27.31)	29.52 (11.62)	58.43 (24.08)
Postoperative	31.92 (8.64)	60.56 (26.92)	30.44 (12.35)	59.82 (24.24)
Overall p-value for comparison over time between the two groups (Generalised Estimating Equations Method)	0.037 (eGFR) 0.009 (ERPF)			

[Table/Fig-5]: Outcomes in renal function concerning diabetes.
Wilcoxon rank-sum test (Mann Whitney U test); estimated Glomerular Filtration Rate (eGFR) - mL/min/m², Effective Renal Plasma Flow (ERPF) -mL/min

(p-value=0.321) [Table/Fig-6]. A total of 21% of patients had a history of Haemodialysis (HD) during their presentation with AKI. A 5% patient posted for surgery required perioperative HD. During follow-up for one year 7% patient required Maintenance HD. There was no perioperative mortality. However, during the follow-up for one year three patients succumbed to death secondary to the complications of chronic kidney disease.

Stage of CKD		Preoperative				Stuart-Maxwell test
		Stage 3	Stage 4	Stage 5	Total	p-value
Postoperative	Stage 3	52 (52.0%)	8 (8.0%)	0 (0.0%)	60 (60.0%)	0.321
	Stage 4	3 (3.0%)	20 (20.0%)	3 (3.0%)	26 (26.0%)	
	Stage 5	0 (0.0%)	3 (3.0%)	11 (11.0%)	14 (14.0%)	
	Total	55 (55.0%)	31 (31.0%)	14 (14.0%)	100 (100.0%)	

[Table/Fig-6]: Chronic Kidney Disease (CKD) stage migration after surgery.
Stuart-Maxwell test

In one patient with 2 cm pelvic calculus was taken for PCNL but initial puncture in PCS could not be made even after multiple attempts and PCNL couldn't be performed. Patient died on postoperative day 3 after developing complications of CKD. No patient was lost to follow-up.

DISCUSSION

A 73% of patients presented with AKI and required some form of diversion. Of these patients, more than 95.9% of patients were not known CKD patients but were diagnosed as CKD on serial follow-up. Around 14% of patients presented with severe CKD (stage V). Renal stones contribute to poor renal function but the exact contribution of stone on renal function is less defined [9]. Age and gender were equally distributed among different CKD groups. Mean creatinine value was slightly high in diabetic patients and the difference was not significant. Diabetes may be associated with early presentation of these patients and therefore, would compensate for the overall equivalent renal functions in these patients. Staghorn calculus is a large renal calculus that fills the whole pelvis with one renal calyx or pelvis into multiple calyces [10-12]. Staghorn calculus is associated with progressive renal deterioration [13]. CKD patients have overall higher infectious complications [9]. Similarly, in the present study, the overall incidence of postoperative fever and sepsis was higher with increasing stage of CKD. The difference was, however, not significant owing to a lower number of recruited patients. The most common urinary infection is E. coli [14] but owing to the diversion in hospital setting pseudomonas was found to be of higher incidence. Similar to the findings of Clinical Research Office of the Endourological Society (CROES) PCNL Global Study the mean hospital stay was significantly greater in higher stages of CKD [9]. Blood transfusion rates were higher in the higher stage CKD patients. The perioperative blood transfusion may be more influenced by the poor nutrition status and anaemia in these patients, stone load and operative time rather than the CKD stage itself. Gopalakrishnan G and Prasad GS stated greater haemolytic tendency, thinned out parenchyma, lower tamponade effect as a more important factor for perioperative blood transfusion [15]. Higher blood transfusion rates did not amount to increased residual calculus with higher stages of CKD contradicting the findings of Gambaro G et al., who stated increased risk of residual stone and repeat PCNL with higher CKD stage [16]. Numerous studies suggested that removal of stones in CKD patients may prevent renal deterioration [4,17,18]. Overall the detrimental effect of PCNL appears to be balanced with no perioperative mortality in the present study. Both mean eGFR and ERPF show a significant increase after surgery. The improvement eGFR was significantly different among the three stages of CKD. The ERPF improvement was, however, better in higher stages of CKD. But the clinical impact of this improvement appears to be

insignificant. Kurien A et al., demonstrated, better the renal function preoperatively, the more will be the improvement after surgery [19]. Although these studies elaborate that the need for haemodialysis can be deferred with aggressive surgery [20] but comment could not be made in the present study due to shorter follow-up.

Limitation(s)

Limitations of the study included limited number of patients. A prospective randomised control trial would have made the results of the study more impactful. This study will pave the path for future research in the area and it will help in decision making for management of renal stones in CKD patients.

CONCLUSION(S)

The PCNL in patients of chronic kidney disease has a minor but significant improvement in GFR with good clearance rates. Urinary infection and stone composition do not affect improvement in GFR. In diabetic patients also, PCNL appears to have a positive impact on GFR improvement in CKD patients.

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