

Original Research Article

Urolithiasis related renal failure: outcome following surgery and factors influencing outcome

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Abstract: Urolithiasis accounts for 5 to 10% of all the urological conditions. Neglected urolithiasis is fraught with multiple complications such as recurrent urinary tract infections, pyonephrosis and eventual end stage renal damage. Urolithiasis in a patient with renal failure requires a tailor made management. The approach is multifaceted and requires the combined effort of the surgeon and the nephrologist. There are multiple factors which influence the recovery of the renal function post-operatively in these situations. This study aims at studying the outcome of patients with urolithiasis and renal failure. The factors which influence outcome shall also be assessed in this study. Patients with urolithiasis related renal failure (Serum creatinine >1.5mg/dl for men more than 3 months and serum creatinine >1.4mg/dl for 3 months in women) were included in the study. All patients were either stented or underwent percutaneous nephrostomy under ultrasound guidance. Baseline creatinine (<2mg/dl, 2to4mg/dl, >4mg/dl), stone burden (maximal stone size <3cm and >3cm), duration of symptoms (<6 months, >6 months), presence of post-operative UTI, presence of pyonephrosis, trend of creatinine and post obstructive diuresis and parenchymal thickness (<5mm versus >5mm) were the variables assessed. The patients were followed up for 9 months post-operatively. Nephrology consultation was done regarding the presence and management of uremia. 74 patients were included in our study. We found a baseline creatinine >4mg/dl, stone burden >3cm, renal parenchymal thickness <5mm and duration of symptoms >6 months to be factors which influence outcome adversely. A baseline serum creatinine >4mg/dl, renal parenchymal thickness <5mm, duration of symptoms >6 months, presence of post-operative UTI were all detrimental to post-operative renal function.

Keywords: Renal parenchymal thickness, eGFR, chronic kidney disease, uremia, urinary tract infection, renal replacement therapy

INTRODUCTION

Urolithiasis accounts for 5 to 10% of all the urological conditions [1]. It is one of the most common afflictions of the modern society. The natural history of stone is to eventually cause stone related symptoms owing to stone growth and subsequent renal damage [2]. This is more so in case of staghorn calculi with 50% incidence of renal function loss in a time span of 2 years if no intervention is done [3, 4]. The past decade has seen a boom in the usage of computerized tomography for the diagnosis of stone disease along with significant advancement in the development of minimally invasive techniques for the management of stone disease. Early detection results in prompt removal of the stone before it has caused significant damage. The overall morbidity and mortality associated with

stone disease has decreased progressively. Despite these advances neglected urolithiasis remains a common in developing countries [8]. Neglected urolithiasis is fraught with multiple complications such as recurrent urinary tract infections, pyonephrosis and eventual end stage renal damage [7-10]. Studies conducted in India have shown urolithiasis to be the 2nd most common cause of renal failure [11]. The possible reason for this may be due to chronic negligence of symptoms, ignorance, poverty and delayed administration of appropriate management.

Urolithiasis in a patient with renal failure requires a tailor made management. The approach is multifaceted and requires the combined effort of the surgeon and the nephrologist. There are multiple factors

which influence the recovery of the renal function post-operatively in these situations [12, 13]. The patient may be relieved of pain and infection post-operatively but renal function may not recover. Prior to intervention, it is essential to be aware about the potential recoverability of the kidneys. The knowledge of these factors can help us in counselling the patient pre-operatively. Currently very few studies are available in Indian patients and further research is needed to strategize a protocol for the management of these patients. This study aims at understanding the surgical management of patients with urolithiasis related renal failure. The study also aims at understanding the various factors which play a role in determining the final long term outcome with regards to renal function. An attempt has also been made to identify the best possible predictor.

MATERIALS AND METHODS

This study is a prospective observational study conducted from January 2015 to January 2017 and included 74 patients. Patients with urolithiasis and renal failure (serum creatinine > 1.4 mg/dl in females and serum creatinine > 1.5 mg/dl in males for a period greater than or equal to three months) admitted for intervention were included in the study. All patients underwent DJS or PCN prior to the intervention in order to stabilize the renal function. Patients with known medical renal disease were excluded from the study. Patients will be subjected to preoperative hemodialysis or peritoneal dialysis if advised by nephrologist.

Patient workup

Detailed history was taken from all the patients along with physical examination. Routine blood investigations (Complete blood count, Serum Urea, and Serum creatinine and serum electrolytes) and urinary examination was done for all patients. X ray KUB (plain and digital) was done to assess the maximal stone size. USG (Ultrasonography) KUB was done to assess renal size, parenchymal thickness, corticomedullary differentiation and infective hydronephrosis. All patients underwent an NCCT of the KUB region. Intravenous urography was done wherever possible. Creatinine clearance estimation using MDRD e GFR formula ($175 \times (\text{serum creatinine})^{-1.154} \times (0.742 \text{ in females})$). Post percutaneous nephrostomy urinary volume, urinary pH, urinary Na, creatinine clearance, Serum creatinine was estimated. Serum creatinine was done daily for the first week and was repeated weekly until definitive surgery is done

Follow up protocol

Patients were followed up for 9 months. Post-operatively BUN, S creatinine, S electrolytes was done

every alternate day until discharge and was done weekly 1st month post op and 3 monthly until 9 months. Creatinine clearance was estimated at the 3rd month, 6th month and 9th month. Post-operative urine culture was done at the 3rd month postoperatively following stent removal.

Variables to be analyzed

1. USG findings- parenchymal thickness
Division of groups will be done into groups with parenchymal thickness greater than or less than 5 mm.
2. Baseline Serum creatinine (< 2 mg/dl, 2 to 4 mg/dl, > 4 mg/dl)
Post PCN or DJS –
 - i. Patients to be divided into groups with post PCN creatinine fall greater than or less than 50%
 - ii. Urinary pH less than or greater than 6 (in sterile urine culture)
 - iii. Post PCN urine output less than or greater than 2 l
 - iv. Stone burden (maximum stone size > or < 3 cm)- The stone burden of the kidney with the better parenchymal thickness was taken as the baseline maximal stone size.
 - v. Presence or absence of pyonephrosis
 - vi. Presence of functional or anatomical solitary kidney
 - vii. Duration of uremic symptoms (greater than or less than 6 months)

Statistical analysis

1. Means and averages
2. Analysis will be done using the chi square test with p value < 0.05 being considered as significant. The statistical software being used will be SPSS 20.0

RESULT AND ANALYSIS

There were total 74 patients with 64 males and 10 females. After 9 months of follow-up total 28 patients were found to have persistent uremic symptoms. The procedures and the number of patients in each procedure are listed in TABLE 1. On evaluating the baseline serum creatinine, 16 patients had a baseline creatinine < 2 mg/dl (no patient was uremic post-operatively). 26 patients had a baseline creatinine between 2 to 4 mg/dl (4 symptomatic and 22 non symptomatic post-operatively). 32 patients had a baseline creatinine > 4 mg/dl (24 symptomatic and 8 non symptomatic post-operatively). On applying chi square test, a p-value of 0.003 was obtained (significant).

Table 1: Procedures Performed

Procedure performed	Number of patients
B/I open pyelolithotomy	16
U/I open pyelolithotomy	9
B/I open ureterolithotomy	10
U/I PCNL with opposite side pyelolithotomy	12
U/I URSL with opposite side pyelolithotomy	8
B/I URSL	4
U/I URSL with opposite side PCNL	7
B/I PCNL	4
U/I URSL with opposite side ureterolithotomy	2
U/I URSL	2

On assessing parenchymal thickness 24 patients were found to have a parenchymal thickness <5mm (22 – symptomatic and 2-asymptomatic post-operatively) and 50 patient were found to have a parenchymal thickness > 5mm (44- asymptomatic and 6- symptomatic) .On applying chi square test a p value<0.005 was obtained (significant).Infected hydronephrosis was seen in 6 patients(4 symptomatic postoperatively). A p value of 0.156 was obtained using the chi square test (non- significant)

Duration of uremic symptoms was divided into 2 groups (<6 months and>6 months). 43 patients had symptoms <6 months(12-symptomatic and 31 non symptomatic).31 patients had symptoms > 6 months(16-symptomatic and 15 non symptomatic). On applying the chi square test a p value<0.0345 was obtained (significant). Post-operative urine culture was found to be positive in 28 patients (15 – symptomatic and 13-non symptomatic post-operatively) .On applying the chi square test, a p value < 0.0292 was obtained (significant). Baseline stone burden was assessed by measuring the maximal stone size of the kidney with better parenchymal thickness in a plain X ray KUB film. 44 patients were found to have a baseline maximal stone size> 3cm (24- symptomatic,20-asymptomatic). 30 patients were found to have baseline maximal stone burden<3cm (4- symptomatic and 26 – asymptomatic post-operatively).On applying the chi square test a p value <0.003 was obtained (significant).

Solitary kidney was seen in 12 cases. 3 patients were asymptomatic post-operatively and 9 patients were symptomatic. On applying the chi square test, a p value of 0.033 was obtained (significant). Following PCN or DJS diuresis, natreuresis and acidification of urine was seen in 52 patients (42-asymptomatic and 10- symptomatic post-operatively). On applying the chi square test a p value<0.05 was obtained (significant).

DISCUSSION

The mean baseline creatinine in the patients with complete recovery was 3.3mg/dl (group1) and in the symptomatic group was 4.7mg/dl (group 2). The

post-operative creatinine for the 1st group was 1.5mg/dl and for the 2nd group was 2.8mg/dl. The mean preoperative creatinine clearance of the group with complete recovery was 23.3 ml/min (grade 4 CKD) and the post-operative creatinine clearance was 57.7ml/min (grade 3a). 15.5ml/min (grade 5 CKD) and the post-operative creatinine clearance of this group was 23.4ml/min (grade 4 CKD).

In the group with improvement of symptoms and salvage of kidney function the post-operative creatinine clearance did not warrant a nephrology consultation and showed a relatively low risk of progression as per national kidney foundation guidelines. In the group with symptom persistence the post-operative creatinine clearance warranted nephrology consultation and showed a high risk of progression as per national kidney foundation guidelines [5]. The above data clearly shows that our definition and selection of patients as CKD due to urolithiasis is correct as per guidelines and recommendations. The post-operative classification of patients as CKD is also correct as per national kidney foundation recommendations. Our study included 74 patients in a span of 2 years. 28 patients remained symptomatic with persistent uremia and need for renal replacement therapy. There were 64 males and 10 females in our study. The increased presence of males in our study is similar to other studies. The possible reason for this may be due to the overall high prevalence of urolithiasis in males compared to females. Symptoms persisted in 26 males (40.6%) and 2 females (20%) post operatively. Statistical analysis however did not show any significant relation of gender with poor post-operative outcome.

The age of our patients ranged from 12 to 68. Majority of our patients were from the 3rd, 4th and 5th decade. This finding corresponds to other studies which show high prevalence in the 3rd and 4th decade of life [1]. We are unable to evaluate the difference in outcome between pediatric and adult patients because of paucity of children in our study. This may be because of most of the children with stone disease are managed in our institute by the department of pediatric surgery. There

were only 2 pediatric patients in our study (12 years, 14 years) and both had a successful outcome.

We performed B/I open pyelolithotomy in 16 cases, U/I open pyelolithotomy in 9 cases, B/I open ureterolithotomy in 10 cases, U/I PCNL with opposite side pyelolithotomy in 12 cases, U/I URSL with opposite side open pyelolithotomy in 8 cases, B/I URSL in 4 cases, U/I URSL with opposite side PCNL in 7 cases, B/I PCNL in 4 cases, U/I URSL with opposite side ureterolithotomy in 2 cases and U/I URSL in 2 cases. Total open surgery and open surgery with endoscopic assistance was done in 57(77%) of our patients with total endoscopic clearance being done in only 17(23%) cases. The possible reason for the increased use of open surgery in our cases may be due to the fact that these cases had a large stone burden with increased chance of incomplete clearance using endoscopic techniques. PCNL in these cases required multiple punctures which increased the chance of bleeding in such patients [14, 15]. Endoscopic procedures in such patients were associated with a prolonged operating time which resulted in a high chance of urosepsis in the post-operative period. Endoscopic surgery may be associated with an increased fluid load which may result in increased post-operative morbidity in patients with compromised renal function.

The significance of baseline creatinine was assessed in our study. The baseline creatinine in our study was defined as the lowest prevailing value within one month of presentation. For statistical analysis, the patients were classified in 3 groups (<2 mg/dl, 2 to 4 mg/dl, > 4 mg/dl). The number of patients in <2mg/dl,

2 to 4 mg/dl and > 4 mg/dl groups were 16, 26 and 32 respectively. Successful outcome was seen in 16(100%), 22(84.6%) and 8(25%) patients in >2mg/dl, 2 to 4 mg/dl, > 4mg/dl groups respectively. On statistical analysis, significant difference was seen between group 1 and group 3 as well as between group 2 and 3. However, no significant difference was seen between group 1 and group 2. This finding of ours is identical to other studies [16]. The possible reason for this may be because a higher baseline serum creatinine implies extensive parenchymal damage and may predict poor chance of recovery.

Ultrasound plays a major role in renal evaluation. Multiple parameters such as renal parenchymal thickness, renal length and cortical echogenicity may help in determining the potential of renal recovery post-operatively [17, 18]. Renal parenchymal thickness is defined as the distance from the outer renal cortical margin to the outer border of the sinus echoes. In our study the renal parenchymal thickness of the better kidney was taken as the representative value (Figure 1). We had 24 patients with a parenchymal thickness of less than 5mm. Out of them only 2 were symptom free and 22 continued to have symptoms. We had 50 patients with a parenchymal thickness greater than 5mm. Out of them 44 patients were symptom free and 6 patients were dialysis dependent. On statistical analysis, significant difference was seen between the two groups (p value<0.05). Parenchymal thickness is inversely proportional to parenchymal and tubular atrophy [19, 20]. Thinned out parenchyma implies significant thinning and loss of renal tissue. Multiple studies support our findings [20].

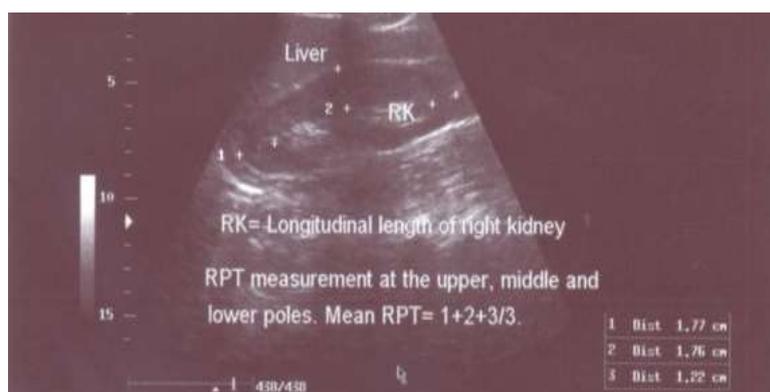


Fig 1: Renal parenchymal thickness is defined as the distance from the outer renal cortical margin to the outer border of the sinus echoes

Infected hydronephrosis may complicate stone disease. Patients are usually ill with associated fever, chills, flank pain and tenderness. Pyonephrosis refers to infected hydronephrosis associated with suppurative destruction of renal parenchyma [1]. Pyonephrosis may be associated with total loss of renal function. USG

shows internal echoes within the dilated pelvicalyceal system. Focal areas of decreased cortical echogenicity and thinning of the renal parenchyma within a hydronephrotic parenchyma are suggestive of pyonephrosis. In our study, infected hydronephrosis was diagnosed in 6 patients based on clinical findings

and USG evaluation. These patients were treated with IV antibiotics and decompression with either DJS or PCN was done wherever indicated. Post-operatively 4 patients (66.6%) were found to be symptom free and 2(33.4%) patients were found to be symptomatic. Statistical analysis however did not show the presence of infected hydronephrosis to be a significant factor in determining the post-operative outcome. There is however studies which show infected hydronephrosis to be a significant risk factor [21]. The possible reason for this may be the high incidence of extensive pyonephrosis in these studies which results in loss of functional renal tissue. In our study the patients who were symptomatic were patients who had pyonephrosis and complete loss of function of the affected kidney.

Symptom duration may influence outcome of surgery [22]. The symptom duration refers to the duration of patient's presenting complaints, which could be flank pain, vomiting, fever, fatigue, pedal edema and decreased urine output. Multiple studies have shown that a delayed presentation with symptoms may be associated with a poor outcome. We divide our patients into 2 groups based on symptom duration (< 6 months and > 6 months). 31 patients had symptoms for more than 6 months and out of them 16 patients (51.6%) continued to remain symptomatic following surgery. Statistical analysis showed symptomatic duration more than 6 months to be a significant risk factor. Delayed presentation is associated with

prolonged duration of obstruction and infection. This results in extensive baseline renal insult and damage. This is the reason for the poor post-operative outcome. Delayed presentations noted in our present study could be attributed to various factors including delayed diagnosis, limited access to healthcare, unavailability of appropriate medical expertise, time taken for transportation to referral center, and financial constraints.

Early relief of obstruction may result in a significant chance of renal recovery (Figure 2) [23, 24]. Certain clinical and biochemical parameters may help in identifying patients with a chance of recovery with surgical management. Measurement of urine output, urinary ph, creatinine clearance, serum creatinine and natriuresis post PCN have proven to be sensitive indicators of recoverability [25]. In our study all patients underwent DJS or PCN preoperatively. We assessed urine output, urinary ph, serum creatinine and creatinine clearance on the 1st day and then repeated it every alternate day on the 1st week. Subsequently, the parameters were assessed weekly until the definitive surgery was performed. Fall in serum creatinine by 50% by the end of the first week, acidic urinary ph (ph<6) and post-obstructive diuresis (u/o>2l) was seen in 52 patients. Out of them 42(91.3%) were symptom free post-operatively. On statistical analysis these parameters were found to be significant in determining the post-operative outcome.



Fig 2: Depicting preoperative stenting for right sided Staghorn stone and left sided ureteric stone

Diuresis and natreuresis are the normal physiological response to combat fluid overload. On relief or bypass of obstruction the presence of diuresis indicates a viable kidney with intact blood flow with potential salvagability. Chronic obstruction may be associated with impaired distal tubular function and acidification. The presence of acidic urine following

bypass of obstruction indicates reversal of distal tubular defect which implies the presence of functional renal tissue.

Stone burden has been found to a significant factor in determining the post-operative outcome [26]. In our study we divided patients into 2 groups based on

the maximal stone diameter seen on the plain X-ray KUB (<3cm and >3cm). The maximal stone size of the kidney with better parenchymal thickness was taken as the baseline stone burden. There were 44 patients with a stone diameter >3cm in our study. Out of them 24 patients remained symptomatic following surgery. Statistical analysis showed a stone burden > 3cm to be a significant factor in predicting the post-operative outcome. A larger stone burden is associated with significant obstruction, risk of infection and renal parenchymal damage. The stone burden also determines the type of surgical management that the patient will undergo. Larger stones may need PCNL or open surgery for management. PCNL may contribute to the nephron loss and parenchymal damage independently thereby becoming a determining factor in the final outcome.

Patients with a solitary kidney (functional or anatomical) may have a worse outcome compared to patients with B/L functional kidneys [8]. In our study we had 12 patients with solitary kidney (9 anatomical and 3 functional). Functional solitary kidney was diagnosed on the basis of the presence of loss of cortico-medullary and the presence of a shrunken opposite kidney. 9 patients (75%) continued to remain symptomatic following surgery. Statistical analysis showed the presence of a solitary kidney to be a significant factor in determining the post-operative outcome. These findings may be due to the presence significantly lower amount of functional renal parenchyma in a patient with a solitary kidney. Any amount of renal damage in such an individual may present in an exaggerated manner.

Persistent post-operative urinary tract infection may be associated with a poor outcome [9,10]. In our study post-operative urine culture was performed following stent removal. We found 28 patients to be having a positive urine culture post-operatively. Out of them 15 patients (53.5%) were found to be symptomatic post-operatively. Statistical analysis showed this to be statistically significant. The possible reason for this is that persistent infection may cause continuous renal damage and functional deterioration in spite of obstruction relief.

CONCLUSION

The presence of a baseline creatinine >4mg/dl is significant risk factor predicting a poor post-operative outcome. Maximal stone size >3cm is a significant risk factor is significant risk factor predicting a poor post-operative outcome. A renal parenchymal thickness less than 5 mm is a significant risk factor is significant risk factor predicting a poor post-operative outcome. Post-operative urinary tract infection and the presence of a solitary kidney indicate a poor post-operative renal function outcome following surgery. Fall in serum

creatinine by >50% following 1 week of DJS or PCN and the presence of post-obstructive diuresis with urinary acidification indicate a good post-operative outcome. The presence of infective hydronephrosis did not influence outcome in our study.

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