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Predictors of renal recovery in renal failure secondary to bilateral obstructive urolithiasis

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KEYWORDS

Calculus anuria;
Obstructive urolithiasis;
Renal failure

ABBREVIATIONS

AUC, area under the ROC curve;
CKD, chronic kidney disease;
HR, hazard ratio;
KUB, kidney, ureter,

Abstract ***Objectives:*** To identify factors predicting renal recovery in patients presenting with renal failure secondary to bilateral obstructing urolithiasis.

Patients and methods: Data from electronic records of consecutive adult patients presenting with bilateral obstructing urolithiasis between January 2007 and April 2011 were retrieved. Ultrasonography of the abdomen, and kidney, ureter, bladder (KUB study) X-ray or abdominal non-contrast computed tomography confirmed the diagnosis. Interventional radiologists placed bilateral nephrostomies. Definitive intervention was planned after reaching nadir creatinine. Renal recovery was defined as nadir creatinine of $\leqslant 2$ mg/dL.

Results: In all, 53 patients were assessed, 50 (94.3%) were male, and 18 (33.9%) were aged $\leqslant$40 years. Renal recovery was achieved in 20 patients (37.7%). A symptom duration of $\leqslant$25 days ($P < 0.01$), absence of hypertension ($P = 0.018$), maximum renal parenchymal thickness of >16.5 mm ($P = 0.001$), and haemoglobin >9.85 g/dL ($P < 0.01$) were significant on unadjusted analysis. Symptom duration

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bladder;
PCN, percutaneous nephrostomy;
ROC, receiver operating characteristic;
US, ultrasonography

of ⩽25 days alone remained significant after adjusted analysis. Symptom duration of ⩽25 days (hazard ratio (HR) 13.83, 95% confidence interval (CI) 4.52–42.26; $P < 0.01$), parenchymal thickness of ⩾16.5 mm (HR 5.91, 95% CI 1.94–17.99; $P = 0.002$), and absence of hypertension (HR 9.99, CI 95% 1.32–75.37; $P = 0.026$) were significantly related to time to nadir creatinine. Symptom duration of ⩽25 days (HR 17.44, 95% CI 2.48–122.79; $P = 0.004$) alone remained significant after adjusted analysis. A symptom duration of ⩽25 days ($P = 0.007$) was 22-times more likely to indicate renal recovery.

Conclusions: Shorter symptom duration (⩽25 days) is predictive of renal recovery in renal failure secondary to bilateral obstructive urolithiasis.

Introduction

Renal failure secondary to bilateral obstructive urolithiasis has variable clinical outcomes, which are often dependent on the timing and nature of surgical intervention. The prevalence rate for urinary stones ranges from 1% to 20% and the incidence of hospitalisation for calculus disease ranges from 0.03% to 0.1% [1]. The estimated lifetime risk for urolithiasis is 11% in men and 7% in women with recurrence rates for renal stones reported as 14%, 35%, 52% at 1, 5 and 10 years, respectively [2]. The incidence of bilateral calculus disease varies between 6% and 20% amongst those presenting with urolithiasis [3]. Ureterolithiasis is the most common cause of obstructive uropathy, presenting with urosepsis [4]. Obstructing urinary calculus with urosepsis is an emergency and surgical decompression in the form of percutaneous nephrostomy (PCN) or ureteric stenting has been shown to reduce mortality from 19.2% to 8.8% [5].

Obstructive uropathy accounts for 10% of community acquired acute kidney injury [6] and urolithiasis is responsible for 10–20% of obstructive uropathy. Delay in relieving ureteric obstruction has been shown to worsen renal function and hypertension [7]. There are published studies on predictors of renal recovery in the subset of patients with renal insufficiency undergoing treatment for nephrolithiasis and in the subgroup of patients with bilateral obstructive urolithiasis and chronic kidney disease (CKD) [8,9]. There is a need for studies, which look at factors predicting renal recovery as well as investigate the pattern of renal recovery. Thus in the present study, we investigated the factors associated with renal recovery in bilateral obstructive urolithiasis and the pattern of renal recovery.

Patients and methods

Electronic medical records at the Department of Urology, Christian Medical College, Vellore, India, was retrieved from January 2007 to April 2011. Consecutive adult patients presenting with bilateral obstructing urolithiasis were included in the analysis. Institutional Review Board clearance was obtained. The clinical presentation comprised decreased urine output associated with flank pain, vomiting, fever, or pedal oedema.

Ultrasonography (US) of the abdomen with kidney, ureter, bladder (KUB study) X-ray or non-contrast CT scan was used to confirm the diagnosis. The interventional radiologists placed bilateral PCNs under US guidance; fluoroscopy was used to confirm the location. Local anaesthesia and sedation were used to perform the procedure under aseptic conditions. Broad-spectrum antibiotics were administered, which was later modified based on the urine culture report.

Patients who presented with severe metabolic acidosis, persistent hyperkalemia, or fluid overload underwent emergency haemodialysis before PCN placement. A urine sample obtained at initial puncture was sent for culture. Patients were admitted for at least 48–72 h, to monitor post-obstructive diuresis, and correct fluid and electrolyte imbalance. Serum electrolytes and renal function tests were monitored on a regular basis. Maximum renal parenchymal thickness was noted on US. Maximum parenchymal thickness refers to the parenchymal thickness on the healthier kidney. The time taken to reach nadir creatinine was documented. Nadir creatinine was defined as the lowest serum creatinine recorded during the recovery period. Patients were educated on the importance of PCN care, close medical supervision until nadir creatinine and definitive management of obstructing urolithiasis.

The variables studied included age, gender, duration of presenting symptoms, stone location and number and size, infection, maximum renal parenchymal thickness, time to nadir creatinine, and presence of co-morbid factors. Renal recovery was defined as nadir creatinine of ⩽2 mg/dL. Several studies in the past have defined renal recovery as serum creatinine of < 2 mg/dL or within 20% of the baseline value, partial renal

Table 1 Social demographic characteristics and clinical features at presentation.

Variable		N (%)	Median (IQR)
Age at presentation, years			48 (18–69)
Sex – male		50 (94.3)	
Duration of symptoms, days			45 (1–730)
Haemoglobin, g/dL			9.4 (5.1–15.3)
Symptoms at presentation	Flank pain	18 (33.9)	
	Vomiting	13 (24.5)	
	Fever	8 (15.1)	
	Fatigue	5 (9.4)	
	Gross haematuria	4 (7.5)	
	Pedal oedema	4 (7.5)	
	Calculuria	2 (3.8)	
Co-morbid illness	Hypertension	14 (26.4)	
	Diabetes mellitus	5 (9.4)	
	Hyperuricaemia	5 (9.4)	
Stone location	Bilateral ureteric	26 (49.1)	
	Ureteric + renal pelvis	17 (32.1)	
	Bilateral renal pelvis	10 (18.8)	
Stone number and size, mm	Pelvis	28	25 (6–68)
	Staghorn	4	49 (46–56)
	Upper ureter	42	12 (5–28)
	Mid ureter	10	8 (6–20)
	Lower ureter	21	10 (5–19)
Creatinine at presentation, mg/dL			5.7 (2.0–24.7)
Serum creatinine after PCN, mg/dL			2.5 (1.0–7.5)
Renal recovery, creatinine $\leqslant$2 mg/dL		20 (37.7)	
Poor recovery, creatinine $>$2 mg/dL		33 (62.3)	

IQR, interquartile range.

recovery as $>20\%$ from baseline value, and dialysis dependence as no recovery [10].

Statistical analysis

The mean and standard deviation (SD) were used to describe continuous variables, frequency, and percentages to depict categorical data. The variables were examined for the normality of their distribution using Kolmogorov–Smirnov and Shapiro–Wilk tests and we documented median and interquartile range values. The Student's *t*-test and chi-squared test were used to assess statistical significance for continuous and categorical variables, respectively. Receiver operating characteristic (ROC) curves were used to obtain optimal threshold duration of illness, maximum renal parenchymal thickness, and time to nadir creatinine for predicting renal recovery.

Multivariable logistic regression analysis was carried out using factors significant on bivariate analysis, to assess the statistical significance of factors associated with recovery. We estimated the regression coefficients, calculated the odds ratios and 95% CIs. Survival analysis was used to assess the time taken to nadir creatinine. Survival curves were obtained using Kaplan–Meier estimates for the absence of hypertension, symptom duration, and maximum renal parenchymal thickness. Log-rank statistics was used, with 5% level to evaluate significance. We also used the Cox proportional hazard model to assess the hazard ratios (HRs) for risk factors for time to nadir creatinine. The statistical software SPSS (version 16.0 for Windows) was used to analyse the data.

Results

In all, 53 patients were evaluated; their social demographics and clinical features at presentation are described in Table 1. Most of the patients were middle-aged men, with bilateral ureteric calculi and 20 (37.7%) patients had renal recovery. Five patients underwent a PCN change for blocked PCNs; two of them had good renal recovery. Three patients were treated for febrile UTI; one patient had good renal recovery. Two patients required long-term renal replacement therapy. There was no mortality noted in the study group. A small minority of patients had complications; hence, it was not possible to do a subgroup analysis. One patient, who presented with a creatinine of 2 mg/dL, reached a nadir creatinine of 1 mg/dL.

Factors associated with recovery

ROC curves were constructed with the outcome variable being good renal recovery vs poor renal recovery. They were used to obtain optimal thresholds for the variables, duration of symptoms, haemoglobin at presentation, and maximum renal parenchymal thickness, which were

Table 2 Factors predicting renal recovery on unadjusted analysis.

Risk factor	Good renal recovery, n (%) $N = 20$	Bad renal recovery, n (%) $N = 34$	Unadjusted analysis	
			OR (95%CI)	P
Symptoms duration ⩽25 days	15 (78.9)	3 (11.1)	30.0 (5.9–153.1)	< 0.01*
Haemoglobin > 9.85 g/dL	15 (78.9)	8 (25.0)	11.25 (2.88–43.94)	< 0.01*
Hypertension not present	1 (5.6)	14 (43.8)	13.22 (1.6–111.7)	0.018*
Parenchyma thickness > 16.5 mm	14 (77.8)	9 (26.5)	9.72 (2.53–37.40)	0.001*

* $P < 0.05$. The following variables were not statistically related to good renal recovery: age, presence of diabetes, stone location, pre-PCN creatinine, and positive urine culture.

⩽25 days, > 9.85 g/dL, and > 16.5 mm, respectively. For duration of symptoms of ⩽25 days, the area under the ROC curve AUC was 0.881 (95% CI 0.774–0.998; $P < 0.01$). For haemoglobin > 9.85 g/dL, the AUC was 0.825 (95% CI 0.701–0.948; $P < 0.01$). For maximum renal parenchymal thickness > 16.5 mm, the AUC was 0.828 (95% CI 0.714–0.942; $P < 0.01$). Table 2 shows the factors associated with renal recovery. Good recovery, on bivariate analysis, was associated with a symptom duration of ⩽25 days, absence of hypertension, parenchymal thickness of > 16.5 mm, and haemoglobin of < 9.85 g/dL. The following variables were not significantly related to outcome on bivariate analysis: age, presence of diabetes, stone location, pre-PCN creatinine, and positive urine culture.

On multivariable analysis, using logistic regression and including all statistically significant variables on bivariate analysis in the model, only symptom duration remained significant suggesting its crucial role in renal recovery (Table 3). Absence of hypertension, maximum renal parenchymal thickness, and anaemia lost their statistical significance after multivariate modelling. Adjusted analysis showed that a symptom duration of ⩽25 days made renal recovery 22-times more likely.

Time taken to nadir creatinine

Survival curves were obtained using Kaplan–Meier estimate for duration of symptoms, absence of hypertension, and parenchymal thickness and compared using Log-rank statistics. Significance was considered at 5% level. Duration of symptoms (HR 13.83, 95% CI 4.52–42.26; $P < 0.01$), maximum renal parenchymal thickness (HR 5.91, 95% CI 1.94–17.99; $P = 0.002$), and absence of hypertension (HR 9.99; 95% CI 1.32–75.37; $P = 0.026$) were statistically significantly related to time to nadir creatinine on univariate analysis. Only duration of symptoms (HR 17.44; 95% CI 2.48, 122.79; $P = 0.004$) remained significant in the adjusted analysis using the Cox proportional hazard model (Fig. 1).

In the good renal recovery group, 17 of 20 (85%) patients reached nadir creatinine in 22.5 days. There was no further decline in serum creatinine after 42 days and 53 days in the good and bad recovery groups, respectively.

Discussion

The present study examined factors associated with renal recovery and factors linked to the speed of recovering renal function. It employed a retrospective cohort design and used multivariable statistics to adjust for confounding.

Many of the clinical characteristics of the sample are similar to those reported in the literature. Male predominance and delayed help seeking in patients presenting with bilateral obstructing urolithiasis have been reported by similar studies [8]. Whilst many variables were related to good renal outcome on bivariate analysis (e.g. duration of symptoms, absence of hypertension, parenchymal thickness, creatinine at presentation, and time to reach nadir creatinine), only the duration of symptoms remained statistically significant after adjusting for confounders. Similarly, multivariable analysis supported that the duration of the symptoms also seemed to determine time to reach nadir creatinine, arguing that early intervention is the key to a good outcome.

Table 3 Factors predicting renal recovery on adjusted analysis.

Risk factor	Good renal recovery, n (%) $N = 20$	Bad renal recovery, n (%) $N = 33$	Adjusted analysis	
			OR (95%CI)	P
Symptoms duration ⩽25 days	15 (78.9)	3 (11.1)	21.49 (2.27–202.76)	0.007*
Haemoglobin > 9.85 g/dL	15 (78.9)	8 (25.0)	9.25 (0.83–102.86)	0.07
Hypertension not present	1 (5.6)	14 (43.8)	5.154 (0.26–102.84)	0.283
Parenchyma thickness > 16.5 mm	14 (77.8)	9 (26.5)	1.288 (0.12–14.37)	0.837

* $P < 0.05$.

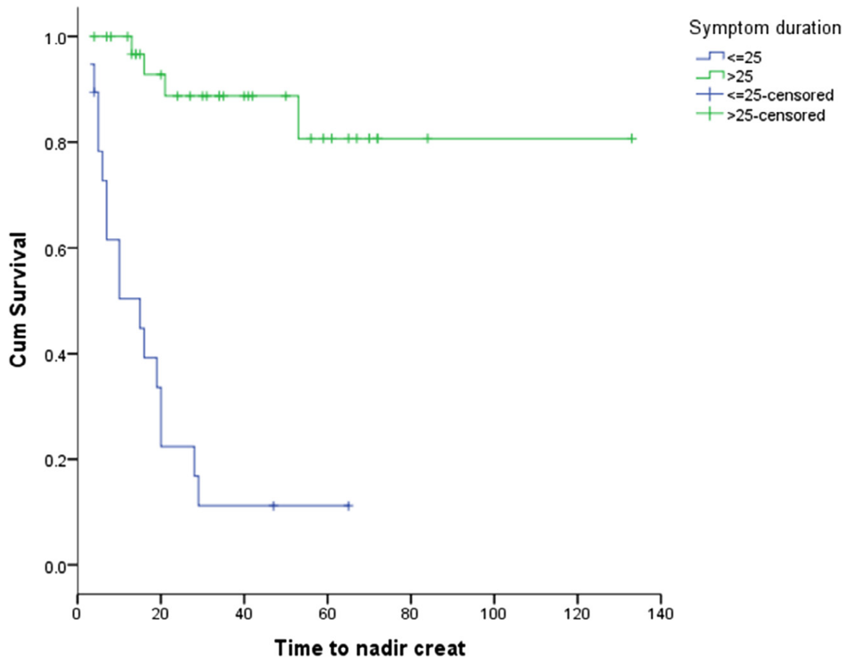

Figure 1 Survival curves were obtained using Kaplan–Meier estimate for duration of symptoms compared using Log-rank statistics. Significance was considered at 5% level.

The symptom duration refers to the duration of patient's presenting complaints, which could be flank pain, vomiting, fever, fatigue, pedal oedema, calculuria or decreased urine output. This does not strictly represent the duration of bilateral obstruction. Two patients had intermittent flank pain over a period of 2 years with no definite point of worsening of symptoms. The long duration of symptoms could represent the chronic nature of patient's condition, with multiple insults to the renal parenchyma. As expected most patients with symptom duration of >60 days had poor renal recovery.

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 centre, and financial constraints.

Emergency decompression of the collecting system with PCN or ureteric stenting in obstructing urolithiasis with sepsis is the standard of care [11]. Placing a PCN in an obstructed, infected hydronephrotic kidney has many advantages. In addition to monitoring output, it avoids ureteric instrumentation that can worsen urosepsis or result in ureteric perforation [12]. It avoids general anaesthesia in a sick patient. The disadvantages of PCN include a longer procedure, patient discomfort, and morbidity. Whilst clinical outcome with both ureteric catheterisation and PCN for obstructive urolithiasis has been essentially similar [13], PCN placement has been found to be less expensive [14]. Availability of an interventional radiologist and longer waiting time for operating room favour PCN placement [15]. Considering these facts, emergency PCNs were placed by interventional radiologists in our institution for almost all the patients presenting with obstructive urolithiasis. Delaying relief of obstruction of iatrogenic ureteric obstruction beyond 2 weeks has been shown to cause long-term renal damage and hypertension [7]. There should be no delay in placing PCNs to expedite renal recovery. In patients presenting with obstructive uropathy and urosepsis, urological source control in the form of immediate low-level invasive treatment (PCN or ureteric stenting) should be done in the first 6 h [4].

The criteria to assess renal recovery can be based on serum creatinine, creatinine clearance, or urine output. We decided to use serum creatinine to define renal recovery in the present study, based on the availability of data. Renal recovery could be defined on the rate of decline in serum creatinine. In the present study, we aimed to study the factors, which predict renal recovery and the pattern of renal recovery. In order to have two groups for comparison, we decided to use a nadir creatinine of 2 mg/dL to define renal recovery based on previous studies [10]. Many factors have been implicated to affect renal recovery after relief of obstruction. These include the age of the patient, duration and degree of obstruction, presence of pyelolymphatic backflow, compliance of collecting system, presence of infection, and concomitant use of nephrotoxic agents, like contrast material [16]. Long-term follow-up of patients with complete and partial renal recovery after acute renal failure showed age and absence of co-morbid illness as factors associated with better prognosis [17]. In a large retrospective review of patients with renal insufficiency undergoing treatment for nephrolithiasis, higher preoperative creatinine, proteinuria of > 300 mg/day, renal cortical atrophy, stone burden of $> 1500\ mm^2$, and recurrent UTI were associated with renal deterioration [9]. Stone-forming patients have reduced creatinine clearance when compared with non-stone formers [18]. Age-related decline in creatinine clearance was at a higher rate in stone formers when compared to normal individuals [19]. A case-control study in Olmsted County showed that hypertension and diabetes in patients with kidney stones significantly increase the risk of CKD [20]. In our present study, absence of hypertension was a significant factor on unadjusted analysis.

A prognostic model for renal recovery has been reported in patients with bilateral obstructive urolithiasis and CKD (nadir creatinine was > 1.5 mg/dL within 5 days of urinary diversion) [8]. The following factors were found significant on adjusted analysis: combined renal cortical thickness, presence of proteinuria, positive urine culture, and nadir creatinine.

Striking inequalities and glaring gaps in health persist in the 21st century both within and between countries. It is important to educate health workers at primary and secondary level hospitals on the importance of early diagnosis and urgent referral to tertiary care for emergency decompression of the collecting system.

Limitations of the present study include the small sample size and the retrospective nature of the study. The findings of the present study give direction for future research. Prospective studies are required to validate this predictive scoring.

Conclusions

Renal recovery in bilateral obstructive urolithiasis with renal failure is facilitated by timely urological intervention. A symptom duration of $\leqslant 25$ days made renal recovery 22-times more likely.

Conflicts of interest

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.aju.2016.08.001.

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