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Nephrolithiasis Associated with Renal Insufficiency: Factors Predicting Outcome

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ABSTRACT

***Background and Purpose*: Renal calculous disease may be associated with various degrees of renal insufficiency secondary to a combination of obstruction, urinary infection, frequent surgical intervention, and coexisting medical disease. Herein, we present our data on the progression of renal function in patients with stones associated with renal insufficiency and assess the significance of various factors that could predict postoperative renal function deterioration.**

***Patients and Methods*: Data were obtained from 4400 patients undergoing treatment for calculous disease at our institute since 1991. Renal insufficiency, defined as a baseline serum creatinine >1.5 mg/dL, was present in 84 (1.9%). Predictive factors evaluated for renal function deterioration were preoperative (age, duration of symptomatology and nephrolithiasis, urinary tract infection, coexistent medical diseases, baseline serum creatinine, and stone burden), intraoperative (number of percutaneous tracts), and postoperative (recurrent infection, proteinuria, cortical atrophy, residual fragments, and stone recurrence).**

***Results*: Over a mean follow-up of 2.2 years (range 6 months–6 years), 33 patients (39.3%) showed improvement, 24 (28.6%) showed stabilization, and 27 (32.1%) showed deterioration in their renal function. Higher baseline serum creatinine, proteinuria >300 mg/day, renal cortical atrophy, stone burden >1500 mm^2, recurrent urinary infection, and age <15 years were significant predictors of subsequent renal function deterioration.**

***Conclusions*: Patients with nephrolithiasis and mild to moderate renal insufficiency warrant aggressive treatment aimed at complete stone clearance and prevention of recurrence of stones and urinary infection. A higher baseline preoperative serum creatinine, proteinuria >300 mg/day on follow-up, renal cortical atrophy, stone burden >1500 mm^2, recurrent urinary infection, and age <15 years are associated with a significantly higher likelihood of renal function deterioration after treatment of the calculous disease.**

INTRODUCTION

RENAL CALCULOUS DISEASE may be associated with various degrees of renal insufficiency.[1,2] The etiology of renal insufficiency in patients with nephrolithiasis is multifactorial and includes renal obstruction, urinary infection, frequent surgical interventions, and coexisting medical disease.[3–5]

In this study, we present our data on patients with nephrolithiasis and renal insufficiency presenting to our institute over the past 10 years with the aim of assessing the long-term renal function and identifying factors that could help predict the likelihood of long-term deterioration in renal function.

PATIENTS AND METHODS

Data were analyzed from 4400 patients with nephrolithiasis presenting to our institute since 1991. Preoperative assessment included a detailed history and physical examination, urine culture and sensitivity, plain radiograph (KUB film), ultrasonography of the kidneys and bladder, and serum creatinine and electrolyte measurements. Calculus size was calculated by millimeter graph tracing in the anteroposterior radiographic projection and is reported in square millimeters.

All patients with renal insufficiency and significant hydronephrosis (dilated calices >1-cm width) had preoperative place-

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ment of a percutaneous nephrostomy tube. Such tubes improve the creatinine value by eliminating the element of acute obstruction and draining the infected urine. They also provide a mature tract for future intervention. To eliminate the influence of reversible acute renal obstruction as a cause of elevated creatinine, the nadir serum creatinine concentration (a minimum of two equal lowest values) after adequate nephrostomy drainage was considered the baseline. The time taken for the serum creatinine to reach nadir ranged from a minimum of 3 days to a maximum of 11 days (mean 6.2 days). Definitive surgical intervention for stone removal was undertaken only after stabilization of the serum creatinine concentration following adequate relief of obstruction.

Renal insufficiency, defined by a baseline nadir serum creatinine of >1.5 mg/dL, was present in 84 patients (1.9%). Demographic and calculus data of these 84 patients are summarized in Table 1. The mean age was 47 ± 14 years (range 10–72 years). Symptoms of renal failure (anorexia, nausea, vomiting, edema, breathlessness) were present in 52 patients (61.9%), and 68 patients (80.9%) were symptomatic for calculous disease (pain, fever, or hematuria). The symptoms of renal failure in 61.9% of the patients were noted when these patients presented to us in the stage of acute-on-chronic failure with significantly elevated creatinine and deranged electrolytes. The mean stone size was 1564.28 mm^2 (range 105–11,036 mm^2); 20 patients had a complete staghorn calculus, while 15 had partial staghorn calculi.

The mean baseline serum creatinine concentration after adequate relief of obstruction was 2.87 mg/dL (range 1.6–6.6 mg/dL). The 84 patients with renal insufficiency were divided into four groups: Group A (serum creatinine <2 mg/dL; N = 13), Group B (serum creatinine 2–2.9 mg/dL; N = 43), Group C (serum creatinine 3–5.9 mg/dL; N = 23), and Group D (serum creatinine >6 mg/dL; N = 5). Twelve patients had bilateral stone disease, while another 12 patients had a solitary functioning kidney.

Table 1. Demographic and Calculus Data of 84 Patients with Nephrolithiasis and Renal Insufficiency

No. of patients	84
No. of involved renal units	96
Mean age (years)	47 ± 14
Sex (% male)	76.2
Side (% right)	53.1
Mean ASA class	2.5
Calculus type (renal units)	
Complete staghorn	20
Partial staghorn	15
Complex	32
Pelvic	22
Caliceal	7
Mean calculus size (mm^2)	1564.28 ± 1567.85
Prior stone treatment	32
Associated hypertension	25
Associated diabetes	12
Associated urinary infection	29
Nephrostomy drainage required	58
Dialysis required	16
Mean preoperative serum creatinine (mg/dL)	2.87 ± 1.19

Table 2. Factors Evaluated for Prediction of Renal Function Deterioration

Preoperative
Age <15 years
Duration of symptoms
Solitary functioning kidney
Coexisting hypertension and diabetes
Stone burden
Atrophic renal cortex (<5-mm parenchymal thickness)
Intraoperative
Number of PCNL tracts
Postoperative
Residual fragments
Recurrent infection
Proteinuria (>300 mg/day)
Recurrence of calculus

Primary surgical treatment of renal calculi in these 84 patients included percutaneous nephrolithotripsy (PCNL) in 87 renal units, nephrolithotomy in 7 renal units, and nephrectomy in 2 renal units. Extracorporeal lithotripsy was reserved for 6 patients with residual calculi. Follow-up included urinalysis and culture for proteinuria and infection, respectively, creatinine estimation, plain radiography of the abdomen, and renal ultrasonography.

Postoperative renal function was defined as improved (>20% fall in serum creatinine), stabilized (<20% rise or fall in serum creatinine), or deteriorated (>20% rise in serum creatinine).

Various factors that were tested for their ability to predict postoperative renal function outcome are enumerated in Table 2. Student's paired *t*-test and chi-square tests were used for statistical analysis of the above-mentioned factors. A P value of ≤ 0.05 was considered statistically significant.

RESULTS

The 87 PCNL procedures required a total of 158 stages (mean 1.9 ± 1.08 per renal unit) and 201 tracts (mean 2.42 ± 1.09 per renal unit; range 1–7). Complete clearance (defined as no visible fragment on KUB films and renal ultrasonography at 1 month follow-up) was achieved in 72 patients (85.7%), while 12 patients (14.28%) had residual fragments.

Over a mean follow-up of 2.2 ± 1.34 years (range 6 months–6 years), 15 patients showed evidence of recurrent calculi, and 24 patients had recurrent urinary tract infection. Overall, 33 patients (39.28%) showed improvement, 24 patients (28.6%) showed stabilization, and 27 patients (32.14%) had deterioration in their renal function. Of the 27 patients with deterioration, 12 went on to end-stage renal disease requiring maintenance dialysis within 2 years. The baseline serum creatinine concentration correlated well with the postoperative renal function (Table 3), which stabilized or improved in nearly all patients in Group A and deteriorated in all patients in Group D. In the entire series, renal function improved in 39.3% and deteriorated in 32.1%.

Table 3. Correlation of Baseline Serum Creatinine with Postoperative Renal Function

	Serum creatinine (mg/dL)		*Renal functional outcome (%)*			
Group	*Range*	*Mean ± SD*	*Improved*	*Stabilized*	*Deteriorated*	*Total*
A	1.6–1.9	1.73 ± 0.11	8 (61.5)	4 (30.7)	1 (7.7)	13
B	2–2.9	2.31 ± 0.29	22 (51.2)	10 (23.3)	11 (25.6)	43
C	3–5.9	3.85 ± 0.49	3 (13)	10 (43.5)	10 (43.5)	23
D	≥6	6.22 ± 0.21	0	0	5 (100)	5
Total	–	–	33 (39.3)	24 (28.6)	27 (32.1)	84

Of the various factors assessed, age <15 years ($P < 0.0001$), atrophic renal parenchyma (cortical thickness of <5 mm on ultrasound) ($P < 0.0001$), stone size >1500 mm^2 ($P = 0.002$), proteinuria >300 mg/day at follow-up ($P < 0.0001$), and recurrent urinary infection ($P < 0.0001$) were found to be significant predictors of postoperative renal deterioration (Tables 4 and 5). In contrast, duration of symptomatology ($P = 0.12$), coexisting hypertension or diabetes ($P = 0.08$ and 0.97), solitary kidney status ($P = 0.27$), number of tracts used for PCNL ($P = 0.35$), presence of residual fragments ($P = 0.6$), and calculus recurrence ($P = 0.68$) were not significant predictors of postoperative renal function deterioration (Table 4).

DISCUSSION

Few studies have addressed the problem of renal insufficiency in patients with nephrolithiasis.[1–4] Marengella and coworkers[4] reported an 18% incidence of renal insufficiency in frequently relapsing idiopathic calcium stone formers. In other unselected series of stone formers, the prevalence has been much lower. In a survey of 2000 patients by Gupta and associates,[3] only 33 patients (1.7%) experienced low to moderate grade renal insufficiency. In this series, 84 patients (1.9%) had variable grades of renal insufficiency after adequate relief of obstruction.

Patients with renal calculous disease, particularly those with struvite staghorn calculi, are prone to renal damage because of various combinations of renal obstruction, infection, and surgical intervention.[1,3–5] Calcium oxalate crystals are known to stimulate the proliferation of renal interstitial cells, thus triggering interstitial scarring.[5] Once chronic renal insufficiency is established, further progression has been attributed to hyperfusion of the remaining functional nephrons.[6] Witherow and Wickham[7] suggested that long-term renal function preservation in patients with complex stone disease depends on adequate blood pressure control, stone size, and stone clearance status. They also reported that renal deterioration occurs more frequently in patients with stone disease in a solitary kidney.[7]

Singh and colleagues in 1973 documented the benefits of treating complex renal calculi.[8] In a retrospective review of 95 consecutive staghorn calculus patients by Rous and Turner,[9] the renal-specific mortality was 30% in the conservatively managed group. In a study of long-term renal function after staghorn calculus management,[10] the renal cause-specific mortality was 0 for patients with complete stone clearance (by PCNL, SWL, or combination therapy) and 67% in patients managed expectantly. Gupta et al[3] have shown improvement in renal function

Table 4. Predicting Postoperative Renal Function Deterioration

	Renal functional outcome			
Factor	*Improved (N = 33)*	*Stabilized (N = 24)*	*Deteriorated (N = 27)*	P *value (predictive of deterioration)*[a]
Duration of symptoms (months)[b]	5.86 ± 10.5	6.7 ± 11.3	6.1 ± 9.1	0.12
Age <15 years (No.)[c]	0	0	4	<0.0001
Stone size (mm^2)[b]	1136.9 ± 1134.4	1300.1 ± 838.9	2292.1 ± 2189.8	0.002
Hypertension (no.)[c]	6	7	12	0.08
Diabetes (no.)[c]	6	5	1	0.97
Solitary kidney status (no.)[c]	2	4	6	0.27
Mean no. of PCNL tracts[b]	2.3 ± 0.98	2.5 ± 1.14	2.5 ± 1.21	0.35
Residual fragments (no.)[c]	1	2	3	0.60
Cortical thickness <5 mm (no.)[c]	4	13	25	<0.0001
Proteinuria >300 mg/day (no.)[c]	1	3	22	<0.0001
Recurrent infection (no.)[c]	4	3	17	<0.0001
Calculus recurrence (no.)[c]	4	5	6	0.68

[a]Improved and stabilized *v* deteriorated.
[b]Student's *t*-test.
[c]Chi-square test.

Table 5. Factors Significant in Predicting Deterioration in Renal Function

	P *value*	*Sensitivity (%)*	*Specificity (%)*	*PPV*[a]	*NPV*
Proteinuria (>300 mg/day)	<0.0001	81.5	92.98	84.6	91.4
Atrophic cortex (<5 mm)	<0.0001	92.6	70.2	59.5	95.2
Recurrent UTI	<0.0001	62.96	87.7	70.8	83.3
Stone bulk (>1500 mm^2)	0.002	62.9	71.9	51.5	80.3
Pediatric age group (<15 yrs)	<0.0001				

[a]PPV = positive predictive value; NPV = negative predictive value.

in 32 of their 33 patients with renal insufficiently with <1-year follow-up. Long-term follow-up data available in 13 of the same patients showed deterioration of renal function in 4 patients, with 3 of these subsequently progressing to end-stage renal disease over a mean follow-up of 4.5 years. Chandhoke and associates[11] found no significant deterioration in renal function in patients with mild or moderate renal insufficiency who underwent treatment for renal calculi with either SWL or PCNL. However, four of the five patients with creatinine values >3 mg/dL showed deterioration.

We undertook this study to evaluate the short-term and long-term renal functional outcome in 70 patients with chronic renal insufficiency who underwent treatment for renal calculous disease. We attempted to eliminate the confounding variable of acute obstruction by using the nadir stabilized preoperative creatinine concentration following placement of a percutaneous nephrostomy tube in all patients with significant hydronephrosis and renal insufficiency.

In our study, the preoperative baseline serum creatinine concentration was an accurate predictor of postoperative renal function deterioration: 92.3% of patients with serum creatinine <2 mg/dL, 74.4% of patients with creatinine between 2 and 3 mg/dL, and 56.5% of patients with serum creatinine between 3 and 6 mg/dL revealed stabilized or improved renal function over a mean follow-up of 2.2 years. The prognosis for patients with a serum creatinine >6 mg/dL was poor, with all five such patients in our series progressing to end-stage renal disease and requiring maintenance dialysis within 6 months.

Our study revealed that age <15 years, atrophic renal parenchyma, large stone burden, proteinuria >300 mg/day at follow-up, and recurrent urinary infection were significant predictors of postoperative renal function deterioration (see Tables 4 and 5). Significant proteinuria and cortical atrophy indicate extensive glomerular and tubular functional loss.[12,13] Increasing functional requirements with increasing body mass in pediatric patients (<15 years) possibly accounts for progressive renal insufficiency postoperatively. Patients with struvite calculi develop renal function impairment because of obstructive or pyelonephritic episodes.[5] Aggressive treatment of obstruction and infection has been known to improve acute renal dysfunction.[5] Large stone burdens may be associated with a greater degree of tubular obstruction, intrarenal interstitial fibrosis, and glomerulosclerosis, which may lead to nephron loss and a reduced glomerular filtration rate.[5]

Teichman and coworkers[10] reported solitary kidneys to be more frequently associated with renal deterioration in patients with staghorn calculi. In our series, of the 12 patients with a solitary kidney, renal function improved postoperatively in two, stabilized in four, and deteriorated in six. The incidence of renal functional deterioration in patients with solitary kidneys (50.0%) was significantly higher than in those with an opposite functioning kidney (29.2%) ($P = 0.04$* using the χ^2-test with Yate's correction).

The safety of PCNL with respect to functional nephron loss is well established.[14,15] The majority of patients in the present series (87 renal units) had a significant calculous burden and were treated by PCNL monotherapy, SWL being reserved for residual calculi. We found PCNL to be safe in patients with renal insufficiency. In fact, our study revealed no correlation between the number of percutaneous tracts required for calculus clearance and renal function ($P = 0.35$), further attesting to the safety and efficacy of aggressive PCNL monotherapy in patients with large-volume complex renal calculi and associated renal insufficiency.

We do agree that serum creatinine alone is not the ideal estimate of renal function. Creatinine clearance and renal scans may be more reliable in this regard.

CONCLUSIONS

Most patients presenting with renal calculous disease and renal insufficiency experience improvement or stabilization of renal function with early aggressive intervention aimed at complete stone clearance and prevention of urinary infection and calculus recurrence. High baseline serum creatinine, age <15 years, significant cortical atrophy, large stone burden, and recurrent or persistent urinary infection are associated with a higher incidence of postoperative renal functional deterioration.

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