

Effect of urinary stone disease and its treatment on renal function

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The epoch of open treatment modalities has passed and currently there are much less invasive treatment approaches, such as percutaneous nephrolithotomy, ureteroscopy, shockwave lithotripsy, and retrograde internal Surgery. Furthermore, advancement in imaging technics ensures substantial knowledge that permit physician to decide the most convenient treatment method for the patient. Thus, effective and rapid treatment of urinary tract stones is substantial for the preservation of the renal function. In this review, the effects of the treatment options for urinary stones on renal function have been reviewed.

Key words: Kidney stones; Chronic kidney disease; Estimated glomerular filtration rate; Renal function; Urinary stone disease

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Core tip: In this article, urinary stone disease, treatment options and its effects on renal function are examined. Moreover, in the light of recent publications, effect of treatment options on functional state of the kidney in patients with renal impairment is investigated.

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Abstract

Urolithiasis is a common disease that affects urinary tract in all age groups. Both in adults and in children, stone size, location, renal anatomy, and other factors, can influence the success of treatment modalities. Recently, there has been a great advancement in technology for minimally invasive management of urinary stones.

INTRODUCTION

Urolithiasis is a widespread disease that affects the urinary system and a considerable, high-priced reason of morbidity. Urinary stone disease influences all age groups. The reported prevalence rate of stone disease is 5%-12% in men, 4%-7% in women^[1]. Stone

formation is affected by gender, age and geography. Men's possibility of forming stones is more than women's. However, the ratio has decreased from a 3:1-male to female predominance to less than 1.3:1^[2]. Recent studies indicate a raise in the prevalence of urinary stones, and this raise comprised in all gender, racial and ethnic ensemble in the United States^[3].

Eating habits and environmental conditions also have a major act in the formation of urinary stones. Diabetes mellitus (DM), gout, and obesity are closely associated with urinary stone formation^[4-6].

Children represent about 1% of all patients with urolithiasis, who have a almost 100% risk for recurrent stone formation. Both in adults and in children, stone size and location, other factors, including stone composition, patient factors, and renal anatomy, can influence the success of specific treatment modalities^[7-9].

Over the years, there has been a great advancement in technology for minimally invasive treatment of urinary stones. The epoch of open pyelolithotomy has supplanted and currently there are much less invasive interventions, for instance, percutaneous nephrolithotomy (PCNL), ureteroscopy, shockwave lithotripsy (SWL), and RIRS (retrograde internal surgery). However, recurrent stone formation is still a major issue among patients with urolithiasis^[10,11].

Chronic kidney disease (CKD) is a significant health issue that affects 13% of the adults in the United States. The potential reasons of renal failure in patients with urolithiasis are multifactorial and enclose hydronephrosis, infection, DM, hypertension (HT), repeated stone surgeries, eating habits, environmental, and genetic factors^[12]. There are many studies that associate stone disease with varying degrees of renal insufficiency, patients with CKD present 0.8% to 17.5% of those presenting with urinary stone disease^[13]. DM and HT, well-defined risk factors, were considerably related with renal impairment in patients with urinary stone^[4,12].

PATHOGENESIS

The pathogenesis of renal calculi is a complicated process and similarly based on stone phenotype. Despite many investigations, the events that lead to kidney stone formation is as yet unknown. Several chemical theory has been proposed to explain the formation of stones^[14]. These theories are supersaturation, nucleation and crystal formation, crystal retention, and effect of inhibitors and promoters on crystal growth.

In respect to the underlying reasons of kidney failure, previous researches have demonstrated that stone formation is related with the sedimentation of fragments in the peritubular field and in the medullary interstitium. A sedimentation like this can create inflammation and aid the advancement of fibrosis, which follows in tubular damage and detriment of kidney function. Moreover, fragment transition itself results in temporary occlusion, and occlusion is a well-

defined risk factor for renal detriment in respect to the effect of fragments on kidney function, minor studies have contrasted the influences of the diverse stone types on kidney function. Two of the most widespread types of non-calcium stones were uric acid and struvite. The existence of struvite stones in some patients can reason the improvement of kidney insufficiency on account of recrudescence urinary tract infection (UTI). Patients with uric acid stone are mostly related with diseases which end up with renal insufficiency such as diabetes and gout^[12].

DIAGNOSIS

Urinary stone formers generally complain with lumbar pain, vomiting, and occasionally fever, however, may not have any symptom as well. Routine assessment consists of an exhaustive history and physical examination. The preliminary diagnosis should be promoted by proper radiological technic. A wide variety of imaging methods are recently present to assist in the detection of urinary stones.

Imaging allows for the rapid and definitive diagnosis of stones, ensures significant knowledge that enables physicians to decide the most proper intervention for the patient. This knowledge contains the location and size of stone, and situation of kidney and collecting system^[15]. Early on, abdominal plain films kidneys-ureters-bladder (KUB) and intravenous urography (IVU) were accepted as gold standards for the diagnosis of urolithiasis. However, with the advent of technologies such as ultrasound (US), noncontrast computed tomography (NCCT), a much larger assortment of imaging studies are now available to physicians appraising patients for stone disease.

Urinary stones can be categorized according to images on radiogram. Stones which contain calcium should be observable on radiogram (radiopaque). However, uric acid, ammonium urate, xanthine, and drug stones are not directly-visible (radiolucent). The declared sensitivity and specificity of radiogram in the determine of stone in patients with renal colic and no history of urolithiasis is limited. Further disadvantages of abdominal plain films in the detection of calculi include impaired image quality in obese patients and difficulty in differentiating pelvic vascular calcifications (phleboliths) from stones in the pelvic ureter. In addition, KUB generally will not generate useful information regarding the presence and/or degree of urinary tract obstruction^[16].

Ultrasound is commonly performed during the evaluation of urolithiasis. The main advantage of ultrasound has over other imaging modalities such as NCCT or IVU is that is implemented without any radiation exposure. US can specify stones placed in the pelvis, calices, and proximal and distal ureter, as well as in patients with hydronephrosis^[17].

Before the improvement of NCCT, IVU was considered the standard imaging technique for the assessment of

Table 1 Effects of shock wave lithotripsy on renal functions and glomerular filtration rate levels

Ref.	No. of patients	Patients' feature	Follow-up	Pre-SWL mean \pm SD GFR (mL/min)	Post-SWL mean \pm SD GFR (mL/min)	P value
Eassa <i>et al.</i> ^[25]	108	Solitary kidney	3.8 \pm 3.5/yr	84.6 \pm 24.7	82.5 \pm 26.5	0.33
Fayad <i>et al.</i> ^[27]	100	Children	6 mo	113.13 \pm 4.51	113.01 \pm 4.27	0.46

Difference is considered statistically significant at $P < 0.05$ and highly significant at $P < 0.01$. SWL: Shock wave lithotripsy; GFR: Glomerular filtration rate.

urinary stones. NCCT has higher sensitivity and specificity for detection of stones in urinary tract than IVU^[18]. Uric acid and xanthine stones (radiolucent) can be determined by NCCT. Nonetheless, indinavir stones (radiolucent) cannot be specified by NCCT^[19]. NCCT can define density and internal formation of the stone and the distance from skin to stone. IVU can provide information about renal function and whether a kidney is obstructed. Delayed images can be useful in evaluating ureteral anatomy for filling defects or strictures. It also provides detailed pelvicalyceal anatomy, which can be useful in planning surgical interventions, especially in those individuals with urinary tract anomalies. Therefore, IVU has largely been replaced by computed tomography (CT) with intravenous contrast or CT urograms. Low-dose NCCT (30 mAs) provides information close to those of standard NCCT (180 mAs) in demonstrating ureteral stone > 3 mm in patients with a BMI < 30 ^[20]. It has been declared that low-dose NCCT provides significant information for the assessment of renal colic in pregnant patients^[21].

TREATMENT OPTIONS AND EFFECTS ON RENAL FUNCTIONS

Extracorporeal SWL

Since its introduction, SWL has been a cornerstone for the management of the stone disease. SWL is the most common first line treatment for the majority of renal stones. Several studies have demonstrated stone-free rates as follows: renal pelvis 76%, upper calyx 69%, middle calyx 68%, and lower calyx 59%. Stone free rates were dependent on stone burden, with stones < 10 mm allowing excellent stone-free rates^[2,22]. SWL success depends on many determinants, such as stone burden, position, composition of the stones, habitus of patient, and the efficacy of the lithotripter. SWL is a non-invasive treatment modality, nevertheless it might be related with some complications, for instance tissue injury, bleeding, adjacent organ injury, urinary tract obstruction, post treatment obstruction, and urinary tract infections, in early period. Clinically significant subcapsular and perirenal hematomas occur infrequently, with reported rates between 0.24% and 4.1%. Comorbidities for instance, HT, DM, obesity, coronary artery disease increase the risk of complication.

Moreover, new onset hypertension or diabetes mellitus after SWL treatment is controversial and

previous studies are incoherent^[23-25]. It has been investigated whether the influence of SWL on kidney function in long-term period. Cass reported that there was an average decline in eGFR of 22% in more than 24 mo of follow up. In contrast, it is stated that serum creatinine levels were not markedly affected after SWL in patients with a solitary kidney in approximately 4 years follow up^[26]. In addition, it is stated that SWL treatment was not associated with a significant impact on kidney function or subsequent renal scarring, regardless of stone size or number of SWL seances in children^[27]. The results of these two studies are shown in (Table 1).

SWL is an influential, proper, and noninvasive intervention in patients with urinary stones. Although the acute effects of SWL are well-known, it is accepted that treatment of renal stones with SWL does not affect kidney functions in the long term.

PERCUTANEOUS NEPHROLITHOTOMY

One of the most important factors in selecting the optimal surgical procedure for the patient with nephrolithiasis is stone burden because it has been shown to strongly influence stone-free rate, need for auxiliary procedures, and complication rate for some treatment modalities^[28]. PCNL is recommended for the treatment of all stones greater than or equal to 2 cm^[29]. Deem *et al.*^[30] randomized 32 patients with moderate sized (1-2 cm) upper or middle calyceal or renal pelvis stones to PCNL or SWL and evaluated them at 3 mo with NCCT. PCNL stone-free rate was superior to SWL (85% vs 33%, respectively) and none of the PCNL patients required a secondary procedure, whereas 77% of the SWL patients required at least one other procedure and 17% required more than one^[30].

The influence of PCNL on kidney function was evaluated in 81 patients with a solitary kidney. Mean eGFR increased from approximately 45 preoperatively to 52, 1 year after intervention^[31]. However, achievement and complication rates of PCNL are different in patient with a solitary kidney. The goal of stone eradication in these patients is aimed at preserving nephrons, preventing stone-related complications, chronic renal failure, and dialysis. A recent global study recommends that the stone-free rate for PCNL in solitary kidneys is lower than in patients with bilateral

Table 2 Effects of percutaneous nephrolithotomy on estimated glomerular filtration rate

Ref.	n	Baseline eGFR (mL/min per 1.73 m ²)	Postoperative eGFR	1 yr eGFR
Ozden <i>et al</i> ^[33]	67	37.9 ± 14.05	45.1 ± 16.8	51.3 ± 19.31
Canes <i>et al</i> ^[31]	81	44.9 ± 19.2	42.7 ± 18.0	51.7 ± 23.1
Bilen <i>et al</i> ^[36]	185	42.4	48.4	-

eGFR: Estimated glomerular filtration rate.

kidneys. Furthermore, it is concluded that kidney function deterioration and transfusion rates are greater in patients with a solitary kidney^[32].

Besides, the existence of urinary stones in patient with CKD necessitates exclusive consideration. Hydro-nephrosis and infection are independent parameters for renal impairment in the patients with urinary stones. The alterations in the renal parenchyma created by infection become more evident with concomitant hydronephrosis. The duration of disease, repeated interventions, and stone recurrence also have unfavorable influences on renal function. Hence, the treatment of urinary stone disease in patients with CKD acts a significant role in improving renal function^[33]. Kukreja *et al*^[34] reviewed the influence of PCNL on renal function in 84 CKD patients with renal stone disease. They stated an overall improvement in renal function in 39%, stable function in 29%, and decreased function in 32% of patients. However, serum creatinine has been used instead of eGFR in this study. Factors predicting impairment in kidney function were proteinuria > 300 mg/d, cortical atrophy, recurrent UTI, stone burden > 1500 mm², time passed after surgical intervention < 15 years, and pediatric age group^[34]. In another study, Kurien *et al*^[35] studied 91 adult patients with serum creatinine level greater than 1.5 mg/dL who performed PCNL. Most patients had stage 3 or 4 CKD and most showed improvement or stabilization in renal function after PCNL. Postoperative complications and peak eGFR were the main factors predicting deterioration of kidney function during follow-up^[35].

In another study, Bilen *et al*^[36] evaluated 185 subjects with eGFR < 60 mL/min per 1.73 m² undergoing PCNL and found the average preoperative eGFR substantially improved from 42.4 to 48.4 at three months follow-up. None of the patients required dialysis during that relatively shorter follow-up. They also found that nearly all stage 5, half of stage 4, and one quarter of stage 3 subjects had some benefit from surgery. Renal function recovery was minimum in stage 2 subjects. They hypothesized that the effect of the calculi itself in a severely affected kidney is greater than the effect of PCNL and the opposite is probably true for moderately affected kidneys in which the detriment of surgery may be more significant, particularly if associated with UTI^[36].

In our study, we analyzed 67 subjects, retrospectively. The eGFR was less than 60 mL/min per 1.73 m². The mean follow up was approximately 46 mo. The mean eGFR before and after PNL was approximately 38 and 46. DM and UTI were independent parameters for renal impairment at 1 year. Of the 67 subjects, 47% had downstaging. On the other hand, 3% of subjects had upstaging at the first year. During the 5-year study period, 1 of the subjects progressed to end-stage CKD. However, 6% of subjects with Stage 5 evolved to Stage 4^[33]. The effects of PCNL on eGFR have shown in (Table 2).

Another important factor that has been proposed to affect renal function is the number of tracts. Animal and human studies have demonstrated that renal damage from nephrostomy tracts is minimal based on nuclear renography and has no effect on systemic renal function^[37,38].

In summary, PCNL remains the primary modality for treatment of complex stones in patients with CKD. Nevertheless, it has important complications which are very important for in patients with CKD. The most common are hypothermia, bleeding, metabolic acidosis, serum electrolytes disturbances, urosepsis, and rarely death^[39]. Anemia and underlying platelet dysfunction in patients with CKD may play important role in the high rate of transfusion^[35,36].

RETROGRADE INTRARENAL SURGERY

Retrograde intrarenal surgery for the treatment of kidney stones has been more preferred approach owing to technological innovation, such as new model flexible ureteroscopies, laser fibers and baskets. The declared stone free rate of RIRS is about 97%, complication rates are lower than in other initiatives^[40]. RIRS can be considered a proper alternative to PCNL in cases with significant comorbidity (anticoagulation, cardiopulmonary disease, advanced age)^[41], and in cases with additional adverse anatomical factors such as obesity and renal malformations^[42].

Giusti *et al*^[43,44] stated that results of RIRS for stones up to 2 cm in diameter in 29 patients with solitary kidney. The primary stone free rate (SFR) was 72.4%, the secondary SFR was 93.1%. The mean number of applications per patient was 1.24. Median follow up time was 35.7 ± 19.3 (12-72) mo. Serum creatinine level, not eGFR, was used to evaluate effect of procedure on renal function and reported that there was no deterioration in kidney function^[43]. Although RIRS has been related with repeated operations for the treatment of renal stones greater than 2 cm in diameter, it contributes to preservation of renal parenchyma, which might be substantial for patient with renal insufficiency^[44,45].

Consequently, more comprehensive studies are needed for evaluating the effect of RIRS on renal function.

CONCLUSION

Urinary stone disease in patients with renal insufficiency can be caused to diverse clinical conditions. Patients with CKD can be a sufferer from other medical comorbidities. Urinary tract stone disease is the direct reason of ESRD in 3.2% of patients on dialysis. Coronary heart disease risk factors, such as obesity, hypertension, hyperuricemia, dyslipidemia and CKD, were related with urinary stone disease. Of these risk factors, hypertension and hyperuricemia demonstrated the most potential relation with urinary stones^[46,47]. Therefore, to prevent morbidity and mortality of CKD, patients with urinary stone disease should be evaluated substantially and treated by an appropriate method.

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