ORIGINAL PAPER

UROLITHIASIS

Successful ureteroscopy for kidney stone disease leads to resolution of urinary tract infections: Prospective outcomes with a 12-month follow-up

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Introduction To investigate the resolution of urinary tract infection (UTI) with the successful treatment of kidney stone disease (KSD).
We reviewed the outcomes of ureteroscopy (URS) and stone treatment for patients with positive urine culture or recurrent UTIs and evaluated whether the infection resolved with the clearance of their urinary stones.
Material and methods Between March 2012 and July 2016, consecutive patients who underwent URS for stone disease with a history of recurrent UTIs or culture proven UTIs were identified from a prospective database. Data was recorded on stone free rate (SFR) and infection free rate (IFR) during the follow-up period at 3, 6 and 12-months.
Results During the study period, 103 consecutive patients with stone disease and associated UTI underwent URS over a 52-month period (mean age: 60 years, Female: Male ratio of 2:1). The mean cumulative stone size was 16 mm (range: 3–107 mm) and a positive pre-operative urine culture was found in 81 (79%) patients. While the overall SFR was 96%, the total complication rate was 12.6% (n = 13) and these were all Clavien I/II complications.
At follow-up, the SFR and IFR was 96% and 88% at 3-months, and 82% and 71% at 12-months, respectively (p <0.001). While almost three-quarters of patients were stone and infection free at 12-months, the majority of those with stones recurrence also had recurrence of their UTI.
Conclusions The majority of patients will remain infection free at the 12-month follow-up if they are stone free after their initial treatment. Stone recurrence, which is more likely in high-risk patients, is also linked to the recurrence of their UTI.

Key Words: urinary tract infection ‹› kidney stone ‹› stone free ‹› ureteroscopy

INTRODUCTION

Urinary tract infection (UTI) is commonly implicated in urolithiasis and recent studies have revealed that 7–28% of patients with kidney stone disease (KSD) have co-existing UTI [1–4]. The risk of females presenting with KSD associated with UTI is 4-fold than that of their male counterparts and is associated with a higher risk of sepsis [5]. Although KSD associated infections were historically associated with urease-producing bacteria leading to struvite stones, recent data suggests that more than a third have calcium stones [6].

Patients who present with KSD associated with urosepsis require immediate surgical decompression followed by an elective planned stone treatment once their infection has resolved [7]. UTI has been implicated in the formation of kidney stones. Patients with KSD associated with recurrent UTIs or positive symptomatic urine culture often need complete

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eradication of their stones for clearance of their UTI [8, 9, 10]. There has been a rising incidence of KSD worldwide with a lifetime prevalence of up to 14% [11]. Consequently, the treatment for KSD has also risen with recent data suggesting that ureteroscopy has significantly risen over the last two decades compared to other treatment modalities [12]. Although large staghorn infective stones usually require a percutaneous nephrolithotomy (PCNL), many smaller stones associated with UTI may be better managed by less invasive techniques, such as ureteroscopy (URS) [13]. Patients with UTIs associated with KSD, including those with a positive urine culture or recurrent infections, warrant treatment of their stones as these form a nidus for infection. We review the outcomes of ureteroscopy and stone treatment for patients with positive urine culture or recurrent UTIs and evaluate whether the infection resolved with the clearance of their stones.

MATERIAL AND METHODS

Between March 2012 and July 2016, all (consecutive) patients who underwent ureteroscopy for stone disease with a history of recurrent UTIs or a positive pre-operative urine culture were identified from a prospective database. Data was also collaborated from electronic notes and results from servers, and recorded on an electronic database. All patients had a pre-operative non-contrast CT scan (NCCT) for the diagnosis of their kidney stones and underwent a urine culture as a part of their pre-operative assessment.

Recurrent UTIs were defined in line with the European Association of Urology (EAU) guidelines on urogenital infections [14].

All active UTIs were treated pre-operatively with antibiotics and in cases of persistent infection, patients were given peri-operative antibiotics in line with local microbiology advice. Data was collected and analyzed with regard to patient demographics, urine cultures, stone parameters, operative factors, length of stay, complications and follow-up with regard to infection and stone-free rates. Patients who were under the age of 16 years, pregnant or with a non-functioning kidney were excluded from the study.

Patients underwent ureteroscopy and stone treatment, either by laser fragmentation or basket extraction. An access sheath was used for larger renal stones where possible and stones were sent for biochemical analysis. Patients did not routinely have a post-operative urethral catheter and were mostly done as a day- case procedure. Most patients had a temporary ureteric stent placed for 1–3 weeks that was subsequently removed via a flexible cystoscopy. A procedural outcome of being endoscopically stone free was recorded. Patients were followed-up at 3-months, 6-months and 12-months with a plain X-ray KUB for radio-opaque stones and ultrasound scan (USS) for radiolucent stones. Patients who were endoscopically stone free or had ≤2 mm fragments were considered stone free. Data was recorded on stone free rate (SFR) and infection free rate (IFR) during the follow-up period at 3, 6 and 12-months. Statistical analysis was calculated using the chi-squared test using SPSS version 24.

RESULTS

A total of 103 consecutive patients with stone disease underwent URS over a 52-month period with a female: male ratio of 2:1 and a mean age of 60 years (range: 21-89 years) (Table 1). The cumulative stone size was 16 mm (range: 3–107 mm) with a mean stone number per patient of 2.2 (range: 1–21/patient).

The location of stones were ureteric (n = 32, 31%), pelvi-ureteric junction (PUJ) (n = 12, 12.5%), renal (n = 40 (39%), three-fifths were in the lower pole), multiple ureteric and renal (n = 17, 16.5%) and in a ureterocoele (n = 1, 1%).

A positive pre-operative urine culture was found in 81 (79%) patients. In the remaining 22 patients (21%) there was a history of recurrent UTIs, but the pre-operative urine culture was negative. While single organisms were present in 67 (82.7%) cases, multiple organisms were seen in 14 (17.3%) (Table 2). These were predominantly Coliforms (n = 51, 63%) either as a single organism (n = 39, 48%) or as part of multiple organisms (n = 12, 15%). Urease-producing bacteria were seen in 26% (n = 21) either as a single organism (n = 11, 14%) or part of mixed organisms (n = 10, 12%).

A total of 115 procedures were performed (1.1 procedure/patient) to achieve a SFR of 96% (Table 3). While the mean operative duration was 51 minutes (range: 10–132 minutes), an access sheath was used for 42 (41%) patients with a post-operative stent insertion rate of 95%. The mean length of stay was 1.4 days and 81% (n = 84) of patients were discharged within 24-hours (60% same day of admission, 21% the following day).

A stone analysis was available for 85 (83%) patients and the ratio of single stone composition: mixed stone composition was 1:3 (Table 4). Of these calcium oxalate stones were seen in 63 (74%) patients and struvite stones in 17 (20%) patients.

The overall complication rate was 12.6% (n = 13) and these were all Clavien-Dindo I/II complications. These were post-operative UTI (n = 3), post-operative sepsis (n = 7) and stent pain or discomfort lead-

Table 1. *Patient demographics, stone size and location*

Patient demographics (N = 103)	n (%) ±SD	
Male: Female (n)	37 (35.9) : 66 (64.1)	
Mean age, years ±SD	60 ±17	
Median age, years	59	
Age range, years	21–89	
Urine growth	**n**	**%**
Positive Pre-op culture	81	78.6
History of recurrent UTIs (negative pre-op culture)	22	21.4
Stone size	**n ± SD**	
Cumulative stone length (range) (mm)	16.4 ±15.1 (3–107)	
Median stone length (mm)	11	
Mean stone number (range)	2.2 ±2.6 (1–21)	
Stone location	**n**	**%**
Ureter	32	31.1
Pelvi-ureteric junction (PUJ)	13	12.6
Renal	40	38.8
in lower pole	*(25)*	*(24.3)*
Multiple locations incl. both ureter & renal	17	16.5
Other (ureterocele)	1	0.97

Table 2. *Urine culture organisms (N = 81)*

Positive urine culture	N = 81	%
Single organism: n = 67 (82.7%)		
Escherichia coli	31	38.3
Enterococcus spp.	10	12.3
Other Coliforms spp.	8	9.88
Yeasts	7	8.64
Proteus spp.	4	4.94
Pseudomonas spp.	3	3.7
Staphylococcus spp.	2	2.47
Klebsiella spp.	2	2.47
Multiple organisms: n = 14 (17.3%)		
Escherichia coli & Proteus spp.	3	3.7
Coliforms & Klebsiella spp.	2	2.47
Escherichia coli & Enterococcus spp.	1	1.23
Escherichia coli & coagulase negative staphylococci	1	1.23
Escherichia coli, Pseudomonas spp., Staphylococcus aureus	1	1.23
Escherichia coli & Pseudomonas spp.	1	1.23
Escherichia coli & Coliforms spp.	1	1.23
Proteus, Enterococcus & Coliforms spp	1	1.23
Staphylococcus epidermis & Pseudomonas spp.	1	1.23
Coliforms & Pseudomonas spp.	1	1.23
Mixed growth	1	1.23

Table 3. *Operative characteristics, length of stay and post-operative complications*

Operative factors N = 103	n ±SD	%
Pre-op stent- No:Yes	56 : 47	54.4 : 45.6
Unilateral URS: Bilateral URS	94 : 9	91.3 : 8.7
Mean op time (mins)	51 ±28	
Median op time (mins)	45	
Range (mins)	10–132	
Type of access sheath – No: Yes: Not recorded	59 : 42 : 2	57 : 41 : 2
9.5F: 12F: 14F: Not recorded	10: 26: 3: 3	
Post-op stent – No:Yes	5 : 98	4.9 : 95.1
2-stage procedure	12	11.7
Stone free – No : Yes	4 : 99	3.9 : 96.1
Length of stay (in days)		
Mean (days) ±SD	1.39 ±3.83	
Median (days)	0	
Range (days)	0 to 29	
Length of stay (in days)	n	%
Day case (same day discharge)	62	60.2
1 day	22	21.4
1–3 days	7	6.8
>3 days	12	11.7
Post-operative complications, n = 13 (12.6%)	n	% of study population
Post-op sepsis	7	6.8
Post-op UTI	3	2.9
Stent pain/symptoms requiring re-admission	3	2.9

ing to delayed discharge or requiring re-admission (n = 3).

At a follow-up of 3-months, the SFR was 96%, and the IFR was 88% (Table 3). At 6-months (n = 90) the SFR and IFR was 90% and 86%, while at 12-months (n=82) the SFR and IFR was 82% and 71%, respectively (p <0.001) (Table 5). While almost three-quarters of patients were stone and infection free at 12-months; in patients with stone recurrence (n = 10), 8 (80%) also had a recurrence of UTI.

In 24 patients who had a recurrence of UTI, risk factors were present in 19 (79%) (Table 6). Of these, 8 had indwelling or intermittent catheterization, 7 had diabetes mellitus and 4 had contralateral stones.

DISCUSSION

Meaning of the study

Our study shows a strong association between KSD and UTIs, whereby clearance of stones leads to resolution

Table 4. *Stone composition*

Stone composition	N = 103
Single composition	n = 22
Calcium oxalate monohydrate	17
Uric acid	2
Cystine	1
Magnesium ammonium phosphate hexahydrate	1
2,8 dihydroxyadenine	1
Mixed composition	n = 63
Calcium oxalate monohydrate & calcium phosphate carbonate	19
Calcium oxalate dehydrate, calcium oxalate monohydrate & calcium phosphate carbonate	14
Calcium phosphate carbonate & magnesium ammonium phosphate hexahydrate	11
Calcium oxalate monohydrate & Calcium oxalate dihydrate	7
Calcium phosphate carbonate & magnesium ammonium phosphate hexahydrate	3
Uric acid + calcium oxalate monohydrate	2
Calcium hydrogen phosphate dihydrate, calcium phosphate carbonate & calcium oxalate monohydrate	1
Calcium oxalate monohydrate & Amorphous calcium phosphate carbonate	1
Calcium phosphate carbonate, beta calcium phosphate & calcium oxalate monohydrate	1
Calcium phosphate carbonate, calcium oxalate monohydrate & magnesium ammonium phosphate hexahydrate	1
Calcium phosphate carbonate, magnesium ammonium phosphate hexahydrate & beta calcium phosphate	1
Uric acid & ammonium urate	1
Not recorded	n = 18

Table 5. *Association of being stone free and UTI free (significant at all time points 3 months, 6 months and 12 months)*

N = 103	Number of patients at follow-up – n (%)		
Follow-up	3 months (n = 103)	6 months (n = 90)	12 months (n = 82)
Stone free	99 (96.1%)	81 (90.0%)	63 (81.8%)
Stones recurred	0	5 (5.5%)	10 (12.1%)
Stones present (includes 4 patients with residual stones)	4 (3.9%)	9 (10.0%)	14 (18.2%)
UTI free	91 (88.3%)	77 (85.6%)	58 (70.7%)
UTI recurred	12 (11.7%)	13 (14.4%)	24 (29.3%)
Both UTI and stone recurrences	–	3	8
	3 months – p (chi-test vs pre- operative data)	*6 months – p (chi-test vs pre- operative data)*	*12 months – p (chi-test vs pre- operative data)*
Concurrent Stone and UTI free (p =)	<0.001	<0.001	<0.001

Table 6. *Other risk factors in patients with UTI recurrences (N = 24)*

	Risk factor	n	Stone recurred
Single	Long term indwelling catheter	6	5
	Diabetes mellitus	5	1
	Contralateral stone	4	2
	Intermittent self- catheterization	2	0
Multiple	Diabetes mellitus and immunosuppression	2	0
	No known risk factors	5	0

of UTI in the majority of cases. Most urinary infections resulted from Coliforms, with the majority of stones composed of calcium oxalate. While the SFR and IFR were 96% and 88% at 3-months, recurrence of stones is associated with a recurrence of UTI in majority of cases noted in our 12-month follow-up. On the same note, once they were made stone free, three-quarters of patients were UTI free at 12-months ($p < 0.001$).

Strengths of the study

This prospective study looks at consecutive KSD patients (>100 patients) with recurrent UTI or a positive urine culture, who underwent ureteroscopic treatment for their stone disease. The data was collected prospectively and patients were followed-up at regular intervals for up to 12-months. Many patients had multiple stones and more-than two-thirds of all stones were renal stones.

Comparison with other studies

The role of KSD treatment in UTI clearance has been previously reported in a retrospective study of 120 patients, however, a third of patients underwent shockwave lithotripsy (SWL) with only 7% undergoing URS and the majority undergoing PCNL [8]. The resolution of UTI in otherwise asymptomatic patients in 12-months was 48%. A proportionately higher percentage of SWL patients had recurrent infections suggesting possible residual fragments or incomplete stone clearance reported with SWL.
The incidence of infected urolithiasis and associated urosepsis has increased in the last two decades highlighting the importance of stone treatment, especially in patients with recurrent UTIs [5]. There is a strong link between KSD and UTIs with up to a third of stones patients having a positive urine culture [15] Trends in the incidence of urolithiasis in the UK have increased in the last decade with a life time risk of 14% (1 in 7), [11] with recent data

suggesting that complications of untreated stone disease is attributable to almost 10 deaths annually [16]. Furthermore, with data suggesting that 1 in 10 cases of urosepsis is complicated by urinary obstruction, [17] it is even more prudent that patients are counselled about the potential for an untreated stone to cause this complication, with nearly half of these asymptomatic stones progressing in size [18].

Strengths, limitations and areas of further research

The strength of our results lies in the prospective nature of our study including consecutive patients who had recurrent urinary tract infections with or without the presence of a positive urine culture. Data was collated and verified independently from trainees and students not directly involved with the original surgery. All patients underwent a standardized ureteroscopy procedure by a single surgeon with a structured 'pre-assessment' and 'post-operative' pathway. While the results of pre-operative urine culture were available on all patients, stone analysis was available for the majority (83%) of patients.

The limitations of the study include incomplete follow-up (at 12-months) for the entire cohort due to patients not attending their follow-up presumably because they remained infection and symptom-free. Similarly, although the diagnosis of KSD was made on a NCCT, the post-operative follow-up relied on plain XR KUB for radio-opaque stones and USS for radiolucent stones to avoid excessive radiation exposure. A post-operative ureteric stent was commonly inserted to ensure adequate drainage and to avoid the potential risk of a UTI or sepsis.

Although the link between kidney stones and urinary tract infections is well established, infection free status on the clearance of KSD has been slightly unclear. Worldwide there is an increasing trend of interventions for stone disease and in the future, larger prospective potentially multi-centric studies are needed for this cohort with standardized reporting on the method of assessing their stone and infection free status [12, 19].

CONCLUSIONS

The majority of patients with kidney stone disease and associated urinary tract infections will remain infection free at 12-month follow-up, if they are stone free after their initial treatment. Stone recurrence, which is more likely in high-risk patients, is also linked with the recurrence of their UTI.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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