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

Rachel Oliver, Anngona Ghosh, Robert Geraghty, Sacha Moore, Bhaskar K. Somani

University Hospital Southampton NHS Trust, Southampton, United Kingdom

Article history
Submitted: Sept. 3, 2017
Accepted: Oct. 29, 2017
Published online: Nov. 7, 2017

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
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 urological 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 cystoscope. 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 (US) 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-
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
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.

**References**

1. Holmgren K, Danielson BG, Fellström B, Ljunghall S, Niklasson F, Wikström B. The relation between urinary tract infections and stone composition in renal stone formers. Scand J Urol Nephrol. 1989; 23: 131-136.

2. Huang WY, Chen YF, Chen SC, Lee YJ, Lan CF, Huang KH. Pediatric urolithiasis in Taiwan: a nationwide study, 1997-2006. Urology. 2012; 79: 1355-1359.

3. Borghi L, Nouvenne A, Meschi T. Nephrolithiasis and urinary tract infections: ‘the chicken or the egg’ dilemma? Nephrol Dial Transplant. 2012; 27: 3982-3684.

4. Hugosson J, Grenabo L, Hedelin H, Lincolen K, Pettersson S. Chronic urinary tract infection and renal stones. Scand J Urol Nephrol. 1989; 23: 61-66.

5. Sammon JD, Ghani KR, Karakiewicz PI, et al. Temporal trends, practice patterns, and treatment outcomes for infected upper urinary tract stones in the United States. Eur Urol. 2013; 64: 85-92.

6. Ohkawa M, Tokunaga S, Nakashima T, Yamaguchi K, Orito M, Hisazumi H. Composition of urinary calculi related to urinary tract infection. J Urol. 1992; 148: 995-997.

7. Borofsky MS1, Walter D, Shah O, et al. Surgical decompression is associated with decreased mortality in patients with sepsis and ureteral calculi. J Urol. 2013; 189: 946-951.

8. Omar M, Abdulwahab-Ahmed A, Chaparala H, et al. Does stone removal help patients with recurrent urinary tract infections? J Urol. 2015; 194: 997-1001.

9. Brown PD. Management of urinary tract infections associated with nephrolithiasis. Curr Infec Dis Rep. 2010; 12: 450-454.

10. Jan H, Akbar I, Kamran H, et al. Frequency of renal stone disease in patients with urinary tract infection. J Ayub Med Coll Abbottabad. 2008; 20: 60-62.

11. Rukin NJ, Sidiqui Z, Chedgy ECP, et al. Trends in upper tract stone disease in england: evidence from the hospital episodes statistics database. Urol Int. 2017; 98: 395-396.

12. Geraghty, Jones P, Somani BK. Worldwide trends of urinary stone disease treatment over the last two decades: a systematic review. J Endourol. 2017; 31: 547-556.

13. Geraghty R, Abourmarzouk O, Rai B, Biyani CS, Rukin NJ, Somani BK. Evidence for ureterorenoscopy and laser fragmentation (URSL) for large renal stones in the modern era. Curr Urol Rep. 2015; 16: 54.

14. Grabe M, Bartoletti R, Johansen TE, et al. EAU guidelines on Urogenital infections, 2015. https://uroweb.org/wp-content/uploads/19-Urological-infections_LR2.pdf (Accessed March 2017).

15. Schwaderer AL, Wolfe AJ. The association between bacteria and urinary stones. Ann Transl Med. 2017; 5: 32.

16. Kum F, Mahmalji W, Hale J, Thomas K, Bulttide M, Glass J. Do stones still kill?
An analysis of death from stone disease 1999-2013 in England and Wales. BJU Int. 2016; 118: 140-144.

17. Reyner K, Heffner AC, Karvetski CH. Urinary obstruction is an important complicating factor in patients with septic shock due to urinary infection. Am J Emerg Med. 2016; 34: 694-696.

18. Koh LT, Ng FC, Ng KK. Outcomes of long-term follow-up of patients with asymptomatic renal calculi. BJU Int. 2012; 109: 622-625.

19. Somani BK, Desai M, Traxer O, Lahme S. Stone free rate (SFR): A new proposal for defining levels of SFR. Urolithiasis. 2014; 42: 95.