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Ureteral stone volume and female gender predicts perioperative complications after complete ipsilateral upper urinary tract stone removal using flexible ureterorenoscopy

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Abstract

Purpose To identify the risk factors for perioperative complications to prevent perioperative complications after complete ipsilateral upper urinary stone removal using flexible ureterorenoscopy.

Materials and methods We retrospectively examined 111 patients who underwent flexible ureterorenoscopy for ipsilateral renal stones with a diameter ≥ 5 mm at the same time as ureterorenoscopy for ureteric stones. The flexible ureterorenoscopy procedures were performed following the fragmentation technique. Patients who experienced (complication group) and did not experience (non-complication group) perioperative complications were compared. The complication group included 33 patients with Clavien–Dindo classification scores of I, II, III, or IV and/or those with a body temperature of > 37.5 ℃ during hospitalization.

Results The overall stone volume, stone-free rate and procedure duration were 1.71 mL, 96.4% and 77 min, respectively. The rate of perioperative complications was 29.7% (grade 1, 2 and 3 was 23.4%, 5.4% and 0.9%, respectively). Severe complications (Clavien–Dindo grade 4) were not observed. Multivariable analysis revealed that ureteral stone volume and female patients were independent predictors of perioperative complications after flexible ureterorenoscopy ($p = 0.015$ and 0.017, respectively).

Conclusions This study showed that ureteral stone volume and female gender have the possibility to increase perioperative complications. These preliminary data help to select for patients who are at low risk of complications. Therefore, in these selected patients, complete ipsilateral upper urinary tract stone removal using flexible ureterorenoscopy may reduce the recurrence of urolithiasis without increasing perioperative complications.

Keywords Ipsilateral · Ureteroscopy · Urinary tract stones · Calculi · Perioperative care · fURS

Abbreviations

fURS	Flexible ureterorenoscopy
MET	Medical expulsive therapy
NCCT	Non-contrast computed tomography
PCNL	Percutaneous nephrolithotomy
PS	Performance status
SFR	Stone-free rate
SWL	Shock wave lithotripsy
URS	Ureterorenoscopy

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Introduction

The prevalence of upper urinary tract stones is gradually increasing each year. Surgical procedures, such as extracorporeal shock wave lithotripsy (SWL), ureterorenoscopy (URS), and percutaneous nephrolithotomy (PCNL), are performed when medical expulsive therapy (MET) is not indicated or effective. URS has a higher lithotripsy effect than SWL and can avoid surgical complications, such as bleeding

requiring blood transfusion and other organ damage due to percutaneous trans-renal puncture. Furthermore, advancements in surgical instruments and techniques have enhanced the efficacy and safety of URS [1–8], endorsing its utilization in the treatment of upper urinary tract stones [9, 10]. Attempts have also been made to broaden the indications of URS for various conditions, including large renal stones and bilateral upper urinary tract stones [10–12].This study aimed to investigate the safety of a single flexible URS (fURS) for the treatment of ipsilateral ureteral and renal stones. Considering that renal stones with diameter > 5 mm are likely to require therapeutic intervention [13–16], simultaneous removal of ipsilateral renal stones with diameter > 5 mm during fURS for ureteric stones is hypothesized to reduce the need for future surgical interventions. However, a decrease in ureteral stone-free rate (SFR) or an increase in complication rate with fURS is undesirable. Therefore, we conducted a retrospective evaluation of SFR and complications in patients undergoing complete ipsilateral upper urinary stone removal. We also identified the predictive factors of perioperative complications.

Materials and methods

Patient data

We retrospectively reviewed the records from 1238 patients who underwent URS for upper urinary tract stones between April 2016 and August 2019 at a single institution. At our facility, following URS for ureteric stones, the renal pelvis and calyxes were observed using a flexible ureteroscope, and renal stones (R2 or R3) were removed if identified. This study specifically focus on patients who underwent fURS for ipsilateral renal stones with diameter ≥ 5 mm at the same time as URS for ureteric stones. A total of 111 patients were divided into two groups: those with perioperative complications (complication group) and those without complications (non-complication group), and were subjected to a comparative analysis. The complication group included patients whose Clavien-Dindo classification score was I, II, III, or IV (Table 1) and/or those whose body temperature during hospitalization was > 37.5 ℃. Informed consent was obtained from all participants included in the study.

Surgical technique

The surgical procedures were performed as described previously [6, 17]. Briefly, the upper urinary tract was viewed using a 6/7.5-Fr semirigid ureteroscope (Wolf™; Richard Wolf GmBH, Knittlingen, Germany) to ascertain the location of the ureteric stones and assess the lumen of the ureter. In the case of stones in the upper ureter (U1) and middle ureter (U2), a ureteric access sheath was placed close to the stones. Stones in lower ureter (U3) were treated without a ureteric access sheath. Lithotripsy of ureteric stones following the fragmentation technique was performed using a 6-Fr flexible ureteroscope (Olympus P-5TM, P-6TM; Olympus, Tokyo, Japan) with a 200-μm holmium:yttrium–aluminum-garnet laser. 1.5-Fr tipless nitinol stone baskets were used for stone removal and clearance of the residual fragments. After the removal of ureteric stones, the ureteral lumen on the renal side and renal stones were observed using a 6-Fr flexible ureteroscope. A ureteric access sheath was then inserted to the renal pelvis: when the surgeon felt resistance during insertion, the access sheath was inserted as close as possible to the renal pelvis. fURS for renal stones was performed as described above. A ureteral access sheath was used in all cases (mainly 11/13 Fr [Boston Scientific, Natick, MA, USA]). The cases using a 9.5 Fr access sheath were defined as a narrow ureter.

After fURS, injury to the upper urinary tract was evaluated using retrograde pyelography and observation of the lumen through endoscopy. In patients with a low risk of perioperative complications, post-stenting was not performed. A conventional ureteric stent was usually removed 3–4 weeks after surgery. Prophylactic antibiotics were administered at the beginning of surgery.

Table 1 Classification and incidence rate of perioperative complications

Clavien–Dindo classification	Number of patients	Complication rate (%)
I	26	23.4
II	6	5.4
III	1	0.9
IV	0	0
Sum of complications	33	29.7

The complication rate refers to the percentage of the 111 analyzed patients who experienced perioperative complications according to each Clavien–Dindo classification level

Preoperative and postoperative evaluation

The preoperative parameters included age, gender, height, body weight, body mass index, side of involvement (right or left), the number of stones, the location of the ureteric stone (U1, U2, U3, multi), sum of the stone volume (mL), the renal stone volume (mL), the ureteric stone volume (mL), the Hounsfield unit of the stone, history of urinary tract infection(UTI), history of SWL pretreatment, preoperative stenting, and narrow ureter. Additionally, the long and short diameters of the largest ureteral and renal stones are also detailed. The side of involvement and the number of stones

were confirmed using preoperative non-contrast computed tomography (NCCT). The volume and Hounsfield unit of the stones were measured using 5-mm axial and 3.5-mm reconstructed coronal NCCT images, as reported previously [18, 19]. The postoperative evaluation consisted of procedure duration, the durations of hospitalization (days), postoperative stenting, SFR, and perioperative complications related to the surgery. The status of the stone was evaluated by performing NCCT within 2 months of surgery. SFR was defined as the complete absence or presence of stones with diameter < 3 mm on NCCT. SFR 1 was defined as stones less than 1 mm or no stones on CT, while SFR 0 was defined as stones not detectable on CT.

Statistical analyses

The continuous variables were compared using the Student's t-test and are expressed as mean ± standard deviation. Non-normally distributed continuous variables were analyzed by the Mann–Whitney U test. The categorical variables were compared using Fisher's exact test. Statistical significance was set at $p < 0.05$; all reported p-values were two-sided. Multivariable logistic regression models were used to assess the perioperative complications. Odds ratios and 95% confidence intervals were calculated. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), JMP Pro version 12.2.0 (SAS Institute Inc., Cary, NC, USA), as well as the R software, version 3.5.3 (R Foundation for Statistical Computing). EZR is a modified version of the R commander, designed to add statistical functions that are frequently used in biostatistics [20].

Results

Patient characteristics and surgical outcomes

The perioperative complications were evaluated using the Clavien-Dindo classification score (Table 1). A febrile complication was defined as a body temperature of ≥ 37.5 ℃. In grade 1 cases, 25 febrile patients were not on antibiotic treatment. One patient had a history of urinary tract injury involving the mucosa and smooth muscle but spared the adventitia. He was conservatively managed without a ureteric stent, and the post-operative CT scan showed no evidence of hydronephrosis. Six febrile UTI patients received antibiotic therapy (Grade 2). One patient with septic shock was treated with antibiotics and fluid management to improve the low blood pressure (Grade 3). Severe complications (Grade 4) were not observed. Postoperative CT 1–2 months after surgery revealed hydronephrosis in five patients.

The characteristics of the two groups of patients are summarized in Table 2. Ureteric stone volume and gender differences between the two groups were significant ($p = 0.02$ and 0.033, respectively). Preoperative UTI tend to be higher in complication groups ($p = 0.065$). Regarding surgical outcomes, the SFR between the two groups was not significantly different (96.2% vs. 97.0%, $p = 1$). No differences were found in SFR1 or SFR0 with an upper limit of 1 mm or 0 mm for residual stones (92.3% vs 87.9%, $p = 0.48$ and 87.2% vs 75.8%, $p = 0.162$, respectively). (Table 3). The procedure duration and the period of postoperative hospitalization in the complicated group were longer than those in the non-complicated group (86.48 ± 21.78 min vs. 73.17 ± 26.53 min, $p = 0.012$ and 3.52 ± 1.35 days vs. 2.99 ± 0.34 days, $p = 0.002$, respectively). The rate of postoperative stenting did not differ between the two groups (46.1% vs. 42.4%, $p = 0.835$, respectively).

Multivariable analysis of the predictors of perioperative complications

Four parameters with a p-value of less than or close to 0.05 in the univariate analysis were used (gender, ureteric stone volume, operating time and history of UTI). A multivariable assessment revealed two independent predictors of perioperative complications after complete ipsilateral upper urinary stone removal using fURS: ureteric stone volume ($p = 0.015$) and gender were ($p = 0.017$) (Table 4).

Discussion

Technological advancements have clarified the advantages of URS, leading to increased utilization. URS for large renal stones with a major axis of ≥ 1 cm and a single URS for bilateral ureteric stones have been reported [10–12]. The recurrence of postoperative urolithiasis is a significant concern, with 21–59% of patients with residual stones requiring treatment within 5 years. Renal stones with a size of size ≥ 5 mm are more prone to require medical intervention compared to smaller stones in the future [13–16]. Stones with a size of ≥ 2 mm are more likely to increase than smaller stones, but there was no increase in the need for intervention. Concurrently removing renal stones measuring 5 mm or larger during URS for ureteric stones may reduce the likelihood of future interventions. The widespread adoption of URS for the simultaneous removal of ipsilateral renal and ureteric stones in a single surgery is anticipated. Therefore, this study analyzed patients who underwent simultaneous fURS for renal stones with diameter ≥ 5 mm following fURS for ureteric stones. To the best of our knowledge, this is the first

Table 2 Comparison of the patient characteristics between the non-complication and complication groups

Variable	Non-complication group	Complication group	*p* value
Number of patients	78	33	
Age (years)	60.60 ± 11.26	56.33 ± 11.87	0.099
Gender			
Female	15	13	0.033
Male	63	20	
Side			
Right	28	16	0.289
Left	50	17	
Height (cm)	164.22 ± 8.41	164.94 ± 8.36	0.682
Body weight (kg)	63.61 ± 10.85	66.75 ± 10.37	0.163
Body mass index (kg/m^2)	23.53 ± 3.23	24.58 ± 3.63	0.135
Number of stone(s)			
Sum of ureteric and renal stones	3.92 ± 2.14	4.19 ± 2.18	0.611
Ureteric stone	1.12 ± 0.51	1.09 ± 0.29	0.822
Renal stone	2.82 ± 2.14	3.03 ± 2.08	0.571
Location of ureteric stone			
U1	52	21	0.56
U2	11	8	
U3	14	4	
Multi	1	0	
Stone volume (mL)			
Sum of ureteric and renal stones	1.56 ± 0.80	1.87 ± 0.93	0.059
Ureteric stones	0.79 ± 0.46	1.05 ± 0.66	0.048
Renal stones	0.77 ± 0.64	0.82 ± 0.59	0.338
Largest ureteric stone diameter (mm)			
Long diameter	10.46 ± 4.22	10.94 ± 3.98	0.295
Short diameter	6.38 ± 2.03	6.82 ± 2.21	0.364
Largest renal stone diameter (mm)			
Long diameter	8.50 ± 3.74	8.09 ± 3.24	0.85
Short diameter	5.92 ± 2.50	6.00 ± 2.36	0.844
Hounsfield units	997 ± 274	983 ± 257	0.804
History of urinary tract infection (yes/no)	17/61	13/20	0.065
History of pretreatment (yes/no)	8/70	4/29	0.748
Preoperative stenting (yes/no)	69/9	28/5	0.755
Preoperative hydronephrosis (yes/no)	54/23	21/8	0.999
Narrow ureter (yes/no)	5/72	1/32	0.666

The values are presented as mean ± standard deviation or number

Table 3 Comparison of surgical outcomes between the non-complication and complication groups

Surgical outcome	Non-complication group	Complication group	*p* value
Operative Time (min)	73.17 ± 26.53	86.48 ± 21.78	0.012
Period of postoperative hospitalization (day)	2.99 ± 0.34	3.52 ± 1.35	0.037
Postoperative stenting (yes/no)	36/42	14/19	0.835
Stone-free rate (%)			
SFR0	87.2	75.8	0.162
SFR1	92.3	87.9	0.48
SFR	96.2	97	1

The values are presented as mean ± standard deviation or as percentage

Table 4 Multivariable logistic regression analysis of perioperative complications

Variable	Odds ratio	95% Confidence interval	*p* value
Gender			
Female/male	3.07	1.21–7.80	0.018
Ureteral stone volume	2.75	1.23–6.14	0.013

report to demonstrate the efficacy and safety of complete ipsilateral upper urinary tract stone removal using fURS.

Ureteral stone volume and female gender were identified as predictive factors for perioperative complications after complete ipsilateral upper urinary tract stone removal using fURS. There were no differences in terms of age and the Hounsfield unit of the stone. Stone volumes including renal or total stone volume did not influenced perioperative complications. The volume of renal stones did not seem to increase perioperative complications, as endoscopic combined intrarenal surgery or PCNL was performed on patients with ureteral and large renal stones. Because we selected only one stone as a representative candidate for stone size, the major and minor diameters of the largest ureteral and renal stones could not accurately reflect stone volume, and no significant differences were observed.

In general, a higher performance status (PS) often correlates with an increased incidence of perioperative complications. Our study could not ascertain the impact of PS on complications since nearly all patients, with the exception of one, had a PS of 0. The effect of the location of the ureteric stones on perioperative complications might not have been fully verified because only a small number of patients had ureteric stones in each location, including U1, U2, U3, and multi-contained. In addition, a different surgical method in which ureteric stones were fragmented and pushed up or removed from the ureter was included. It could not be ruled out that these variations in surgical approaches might have contributed to an inconsistent evaluation. The stone volume was used to precisely evaluate the influence of the stone size instead of stone diameter, stone burden, and gross stone area. The presence of a narrow ureter did not emerge as a significant predictor of perioperative complications. However, the limited number of patients with a narrow ureter included in the study could impact the statistical analysis.

While the addition of fURS for ipsilateral renal stones of size > 5 mm after fURS for ureteric stones might potentially elevate perioperative complications, the incidence of perioperative complications with grade ≥ 2 was found to be 6.3%. This rate is similar to those of previous studies [22, 23]. Only one patient having complications with grade ≥ 3 had septic shock (0.9%). The overall SFR reached 96.4%, a result consistent with previous reports. Even in the case of SFR1 which recognizes only residual stones of less than 1 mm, the rate was 90.9%, and for SFR0, which recognizes no residual stones at all, the rate was 83.8%. It's worth highlighting that the majority of residual stones were situated in the kidney rather than the ureter. While a direct comparison with fURS for ureteric stones or renal stones has not been conducted, it appears that there may not be a significant difference in terms of efficacy and safety. The operation time prolonged due to more surgical steps during URS for ureteric and renal stones; however, this extension did not contribute to an increase in complications. By establishing the criteria for safely performing complete ipsilateral upper urinary tract stone removal, we have provide an index for conducting more detailed studies to evaluate the safety of this procedure. As stone fragments of size > 2 mm are more likely to enlarge [24], planning for complete ipsilateral upper urinary tract stone removal, regardless of the size of renal stones, using URS should be considered in future procedures.

This study has several limitations. Pyuria, urine culture, and diabetes were not included due to a high proportion of missing medical records; therefore, further research including these factors should be conducted to confirm the result that preoperative UTI was not a risk factor of perioperative complications after ipsilateral upper urinary tract stone removal. Complete ipsilateral upper urinary tract stone removal may potentially increase the risk of urinary tract injury. Only one case was managed conservatively without postoperative ureteral stent placemen (0.9%). Further investigation is needed to assess whether this URS procedure increases the risk of ureteral injury in a larger patient population. Late complications, such as ureteric stricture, were not evaluated due to the challenges in the long-term follow-up. To minimize the risk of urinary injury and ureteric stricture, the careful selection of the ureteric access sheath is crucial. In this study, a high SFR of fURS for ureteric stones with simultaneous removal of renal stones with a diameter of ≥ 5 mm was shown; however, it did not establish whether this procedure reduced the long-term recurrence rate. Therefore, further research is needed to assess the impact of ipsilateral upper urinary tract stone removal by fURS on the recurrence rate. It would be beneficial to incorporate parameters such as hypercholesterolemia, estrogen and menopause.

Conclusions

We identified ureteral stone volume and gender as a predictive factor of perioperative complications in patients undergoing ipsilateral upper urinary tract stone removal using fURS. Preoperative UTI also showed a tendency to be a risk factor for complications. Consequently, patients without these characteristics may undergo simultaneous removal

of ipsilateral ureteric and renal stones by fURS without an increased risk of perioperative complications.

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Data availability No additional data are available.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval This study was approved by the institutional ethics committee of Ohguchi East General Hospital.

Research involving human participants and/or animals This study was approved by the Institutional Ethics Committee of Ohguchi East General Hospital.

Informed consent Informed consent was obtained from all participants included in the study.

References

1. Breda A, Ogunyemi O, Leppert JT et al (2009) Flexible ureteroscopy and laser lithotripsy for multiple unilateral intrarenal stones. Eur Urol 55:1190
2. El-Nahas AR, Ibrahim HM, Youssef RF et al (2012) Flexible ureterorenoscopy versus extracorporeal shock wave lithotripsy for treatment of lower pole stones of 10–20 mm. BJU Int 110:898
3. Cohen J, Cohen S, Grasso M (2013) Ureteropyeloscopic treatment of large, complex intrarenal and proximal ureteral calculi. BJU Int 111:E127
4. Breda A, Ogunyemi O, Leppert JT et al (2008) Flexible ureteroscopy and laser lithotripsy for single intrarenal stones 2 cm or greater-is this the new frontier? J Urol 179:981
5. Pearle MS, Lingeman JE, Leveillee R et al (2008) Prospective randomized trial comparing shock wave lithotripsy and ureteroscopy for lower pole caliceal calculi 1 cm or less. J Urol 179:2005
6. Komeya M, Usui K, Asai T et al (2018) Outcome of flexible ureteroscopy for renal stone with overnight ureteral catheterization: a propensity score-matching analysis. World J Urol 36:1871
7. Komeya M, Odaka H, Asano J et al (2019) Development and internal validation of a nomogram to predict perioperative complications after flexible ureteroscopy for renal stones in overnight ureteral catheterization cases. World J Urol 38:2307
8. Komeya M, Odaka H, Watanabe T et al (2020) Gap between UAS and ureteroscope predicts renal stone-free rate after flexible ureteroscopy with the fragmentation technique. World J Urol. https://doi.org/10.1007/s00345-020-03459-7
9. Raheem OA, Khandwala YS, Sur RL et al (2017) Burden of urolithiasis: trends in prevalence, treatments, and costs. Eur Urol Focus 3:18
10. Giusti G, Proietti S, Villa L et al (2016) Current standard technique for modern flexible ureteroscopy: tips and tricks. Eur Urol 70:188
11. Scotland KB, Rudnick B, Healy KA et al (2018) Retrograde ureteroscopic management of large renal calculi: a single institutional experience and concise literature review. J Endourol 32:603
12. Geraghty RM, Rai BP, Jones P et al (2017) Bilateral simultaneous ureteroscopic (BS-URS) approach in the management of bilateral urolithiasis is a safe and effective strategy in the contemporary era—evidence from a systematic review. Curr Urol Rep 18:11
13. Inci K, Sahin A, Islamoglu E et al (2007) Prospective long-term followup of patients with asymptomatic lower pole caliceal stones. J Urol 177:2189
14. Osman MM, Alfano Y, Kamp S et al (2005) 5-Year-follow-up of patients with clinically insignificant residual fragments after extracorporeal shockwave lithotripsy. Eur Urol 47:860
15. El-Nahas AR, El-Assmy AM, Madbouly K et al (2006) Predictors of clinical significance of residual fragments after extracorporeal shockwave lithotripsy for renal stones. J Endourol 20:870
16. Buchholz NP, Meier-Padel S, Rutishauser G (1997) Minor residual fragments after extracorporeal shockwave lithotripsy: spontaneous clearance or risk factor for recurrent stone formation? J Endourol 11:227
17. Ito H, Kawahara T, Terao H et al (2012) The most reliable preoperative assessment of renal stone burden as a predictor of stone-free status after flexible ureteroscopy with holmium laser lithotripsy: a single-center experience. Urology 80:524
18. Rubenstein RA, Zhao LC, Loeb S et al (2007) Presenting improves ureteroscopic stone-free rates. J Endourol 21:1277
19. Shields JM, Bird VG, Graves R et al (2009) Impact of preoperative ureteral stenting on outcome of ureteroscopic treatment for urinary lithiasis. J Urol 182:2768
20. Ahn ST, Kim JH, Park JY et al (2012) Acute postoperative pain after ureteroscopic removal of stone: incidence and risk factors. Korean J Urol 53:34
21. Darrad MP, Yallappa S, Metcalfe J et al (2018) The natural history of asymptomatic calyceal stones. BJU Int 122:263
22. Geavlete P, Georgescu D, Niţă G et al (2006) Complications of 2735 retrograde semirigid ureteroscopy procedures: a single-center experience. J Endourol 20:179
23. Perez Castro E, Osther PJS, Jinga V et al (2014) Differences in ureteroscopic stone treatment and outcomes for distal, mid-, proximal, or multiple ureteral locations: the clinical research office of the endourological society ureteroscopy global study. Eur Urol 66:102
24. Chew BH, Brotherhood HL, Sur RL et al (2016) Natural history, complications and re-intervention rates of asymptomatic residual stone fragments after ureteroscopy: a report from the EDGE Research Consortium. J Urol 195:982