Predictive factors for prolonged operative time in ureteroscopic lithotripsy for ureteral stones: A retrospective cohort study

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ABSTRACT

Introduction: A prolonged operative time of lithotripsy with ureteroscopy for urolithiasis increases the risk of infectious complications; however, few reports have investigated the factors prolonging the operative time for ureteral stones. We investigated the factors associated with longer operative time in ureteroscopy for ureteral stones.

KEY MESSAGES

- This study investigates the factors associated with prolonged operative times in ureteroscopic lithotripsy for ureteral stones, comparing patient characteristics and surgical outcomes between groups with operative times exceeding 90 minutes and those under 90 minutes.
- Key findings reveal that larger stone size, presence of ureteral polyps, and mucosa-stone adherence significantly increase operative time.

Methods: This retrospective cohort study analyzed patients who underwent retrograde ureteroscopic lithotripsy for ureteral stones and achieved an endoscopic stone-free status between April 2019 and July 2022. Patients were classified into two groups based on an operative time of ≥90 minutes or <90 minutes. We compared the patient and stone characteristics and surgical outcomes, and investigated the factors associated with a prolonged operative time.

Results: The cohort comprised 519 patients, with 58 patients in the group with an operative time of ≥90 minutes. Compared to the shorter operative time group, the longer operative time group

had a significantly greater proportion of males, stone diameter, stone volume, and Hounsfield units of stone; additionally, the longer operative time group had higher prevalences of endoscopic findings of edema, polyps, and mucosa-stone adherence. Multivariable analysis showed that stone size >10 mm (odds ratio 4.05), polyps (odds ratio 2.40), and mucosal adherence (odds ratio 3.51) were significantly associated with an operative time exceeding 90 minutes. There were no significant differences between the two groups in the incidences of postoperative fever and systemic inflammatory response syndrome.
Conclusions: Stone size, endoscopic findings of polyps, and mucosa-stone adherence were independent factors associated with a longer operative time.

INTRODUCTION

Lithotripsy with ureteroscopy (URS) is a widely used interventional treatment for urolithiasis. With remarkable advancements in URS devices, the number of URS procedures performed has significantly increased in recent years.[1]
One of the complications of URS is infectious complications such as urosepsis. It is well established that a prolonged procedural time is a significant risk factor for infectious complications after URS, similar to older age, diabetes mellitus, ischemic heart disease, preoperative stent placement, and positive urine culture.[2,3] In particular, several studies have reported a higher incidence of infectious complications after URS with an operative time exceeding 90 minutes.[4,5]

Although several reports have investigated the factors that prolong the operative time of lithotripsy with URS for renal stones, few studies have investigated the factors associated with a longer operative time for ureteral stones.[6-8] Therefore, we aimed to identify the predictive factors for a prolonged operative time in lithotripsy with URS for ureteral stones.

METHODS

Study design and patients

This retrospective cohort study analyzed data collected by Hara Genitourinary Hospital and was approved by the institutional review board of Hara Genitourinary Hospital (approval no. 2022-09-27-2).

The study cohort comprised patients who were treated at Hara Genitourinary Hospital for ureteral stones with retrograde ureteroscopic lithotripsy between April 2019 and July 2022. The inclusion criteria were a confirmed diagnosis of ureteral stones, preoperative CT scans, and an endoscopic stone-free status postoperatively. We excluded patients with concomitant renal stones.

We classified the patients into two groups: one group with an operative time of 90 minutes or more and the other with an operative time of less than 90 minutes. We compared the

patient and stone characteristics and surgical outcomes. The endpoint was the identification of predictive factors associated with a prolonged operative time.

Data collection

The data for the characteristics of patients and stones and the surgical outcomes were collected from medical records and imaging study reports. The characteristics of patients included age, sex, body mass index, Eastern Cooperative Oncology Group performance status, hydronephrosis, preoperative stent replacement, preoperative urine culture, preoperative pyelonephritis, and preoperative use of antibiotics. The stone characteristics included laterality, main stone location, number of stones, size, and Hounsfield units. The surgical outcomes included the operative time; type of endoscope; endoscopic findings of edema, polyps, and adherence between mucosa and stones; total laser energy; postoperative complications such as fever, systemic inflammatory response syndrome (SIRS), and intraoperative ureteral injury; and length of stay after surgery.

The decision to proceed with URS was based on a combination of factors, including symptomatic presentation, stone location, failure of conservative treatments such as medical expulsive therapy, and patient preference after discussing the potential risks and benefits. We performed preoperative CT scans on all patients. We assessed the presence of hydronephrosis on CT scans obtained at the initial visit. In patients with hydronephrosis or suspected infection, stent placement was recommended. Additionally, the benefits of stent placement were also discussed with other patients not initially meeting these criteria. On providing a comprehensive overview of both the potential advantages and adverse events associated with stent placement, stents were inserted in those patients who gave their informed consent. When stent placement was accepted, it was performed as soon as possible following the onset of hydronephrosis and was maintained until surgery.

CT scans were performed to measure the stone size along the longest axis and to count the number of stones. The total stone volume was determined by summing the volume of each stone calculated using the ellipsoid formula ($0.167 \times \pi \times$ length $\times$ width $\times$ height). The Hounsfield units of stones were measured as the maximum point value within the circle enclosing the whole stone. Stone locations were classified on radiographic imaging as follows: proximal ureter (from the ureteropelvic junction to the superior border of the iliac crest), middle ureter (area of overlap with the ilium), and distal ureter (from the inferior border of the iliac crest to the ureterovesical junction). Preoperative antibiotics were administered to patients with positive preoperative urine cultures, and to patients for whom the surgeon deemed it appropriate to administer them. The assessment of the stone-free status was based on intraoperative endoscopic findings and on kidney-ureter-bladder radiographs (KUBs) obtained on postoperative day 1. If endoscopic examination of the ureter, renal pelvis, and calyces at the conclusion of the surgery verified the absence of residual stones, except for stone dust, the patient was deemed to have an endoscopic stone-free status. A stone-free status based on KUBs was defined as the absence of residual stones measuring 1 mm or larger.

SIRS was defined as the presence of two or more of the following variables: body

temperature greater than 38°C or less than 36°C; heart rate greater than 90 beats per minute; tachypnea, manifested by a respiratory rate greater than 20 breaths per minute, or hyperventilation, as indicated by a PaCO2 of less than 32 mmHg; alteration in the white blood cell count, namely a count greater than 12,000/cu mm, a count less than 4,000/cu mm, or the presence of more than 10% immature ("band") neutrophils.[9]

Surgical procedure

All surgeries were performed under general anesthesia. The surgical steps of ureteroscopic lithotripsy were as follows. First, we inserted a 6-Fr semi-rigid ureteroscope (8702.534, Richard Wolf, Germany) into the ureter on the diseased side to observe the ureteral lumen; a 4.5-Fr semi-rigid ureteroscope (8701.534, Richard Wolf, Germany) was used if the ureteral passage was narrow. After reaching the stone, we examined the ureteral mucosa to detect the presence of edema, polyps, and adhesion of the stones to the mucosa. If the stones were located in the distal ureter and a clear visual field could be achieved without the use of an access sheath, the fragmentation procedure was started with the semi-rigid ureteroscope. Fragmentation was performed using a holmium-yttrium aluminum garnet laser that was set to 0.6–1.2 J and 6–10 Hz and adjusted at the discretion of the surgeon. A 1.5-Fr nitinol basket (N-circle®, Cook Medical, Japan) was used for stone removal.

In cases where the stones were located in the upper ureter or when an adequate visual field could not be achieved with the semi-rigid ureteroscope, we used a flexible ureteroscope (URF-P7®, Olympus, Japan or FlexX2®, Karl Storz, Germany) after placing an access sheath. The surgeon chose the size of the access sheath that was appropriate for the ureteral diameter (9.5/11.5, 10/12, 10.7/12.7, or 11/13 Fr). After the completion of stone removal, the endoscope was advanced into the renal pelvis to confirm complete clearance of stones. In cases where there was edema or polyps in the ureter, or when the operative time became prolonged, a ureteral stent with string was placed at the end of the surgery.

Statistical analysis

Continuous variables were described as medians and interquartile ranges, while categorical variables were described as numbers with percentages. Clinical variables were compared using the chi-squared test and Mann–Whitney U test. To identify factors associated with a prolonged operative time, we performed univariate and multivariate analyses with logistic regression analysis. Covariates for the multivariable model were selected based on their clinical relevance and statistical significance in univariate analyses. All statistical analyses were performed with EZR for Windows v1.61.[10]

RESULTS

Patient and stone characteristics

The number of patients who underwent lithotripsy with URS for ureteral stones and achieved a stone-free status was 890, of which 371 patients were excluded due to concomitant renal stones. Therefore, the study cohort comprised 519 patients, with 461 patients in the group with an operative time of less than 90 minutes, and 58 patients in the group with an operative time of 90 minutes or more.

The patient and stone characteristics are shown in Table 1. The variables that significantly differed between the two groups were the percentage of males (65.5% versus 81.0%, P=0.02), use of preoperative antibiotics (69.0% versus 86.2%, P<0.01), main stone location (proximal 54.7% versus 55.2%, middle 16.1% versus 29.3%, distal 29.3% versus 15.5%, P=0.01), stone diameter (7.0 mm versus 11.0 mm, P<0.01), stone volume (104.9 mm3 versus 331.4 mm^3, P<0.01), and Hounsfield units of stones (977.0 versus 1267.0, P<0.01).

Surgical outcomes

The surgical outcomes are shown in Table 2. The variables that significantly differed between the two groups were the operative time (39.0 minutes versus 98.0 minutes, P<0.01), endoscopic findings of edema (51.2% versus 87.9%, P<0.01), polyps (18.1% versus 56.9%, P<0.01), and mucosa-stone adherence (23.7% versus 72.4%, P<0.01), and total laser energy (515.0 J versus 1550.0 J, P<0.01). All patients achieved an endoscopic stone-free status; however, in the KUBs obtained on postoperative day 1, the group with the shorter operative time had a higher stone-free rate than the group with the longer operative time (96.7% versus 84.5%, P<0.01). There were no significant differences between the two groups in the incidences of postoperative complications, namely fever exceeding 38°C (6.9% versus 3.4%, P=0.41), SIRS (9.1% versus 10.3%, P=0.81), or ureteral injury (3.5% versus 7.4%, P=0.26), or in the duration of postoperative hospitalization (2.0 days versus 2.0 days, P=0.79).

Multivariate analysis of factors associated with longer operative time

The results of the univariable analysis and multivariable analysis using logistic regression to identify factors associated with an operative time exceeding 90 minutes are shown in Table 3. The significant predictive factors for an operative time exceeding 90 minutes were stone size larger than 10mm (odds ratio, 4.05; 95% confidence interval, 1.81-9.08; P<0.01), polyps (odds ratio, 2.40; 95% confidence interval, 1.18–4.86; P=0.02) and mucosa-stone adherence (odds ratio, 3.51; 95% confidence interval, 1.58–7.78; P<0.01).

DISCUSSION

In the present study, the multivariate analysis found that stone size, ureteral polyps and mucosa-stone adherence were predictive factors for a prolonged operative time of lithotripsy with URS for ureteral stones.

A previous study reported that high-grade edema and mucosa-stone adherence are predictive factors for a prolonged procedural time for the removal of ureteral stones.[6] Our comprehensive study involved a greater number of cases and examined the endoscopic findings, including the presence of polyps. Our findings confirmed that mucosa-stone adherence was a significant contributor to the prolongation of the surgical procedure. Moreover, we identified polyps and stone size larger than 10 mm as significant predictive factors for a prolonged operative time.

Polyps and mucosa-stone adherence were associated with a high risk of a prolonged operative time in the present study. Previous reports have indicated that polyps and mucosa-stone adherence are associated with impacted stones, which may be the reason for the prolonged operative time.[11,12] It is sometimes difficult to obtain a clear endoscopic view of impacted stones, as the mucosa of the ureter just prior to the stone can be draped over the surface of the stone. Additionally, the procedure for removing impacted stones is time-consuming, as the "peeling off and push back" technique is recommended to avoid direct injury to the ureter.[13] Furthermore, the procedural time may be increased by the need for gradual fragmentation of stones in single shots to avoid indirect thermal ureteral injury caused by continuous laser irradiation.[13,14] Additionally, an increase in stone size is recognized as a risk factor for impaction. In the current study, a stone size greater than 10 mm was identified as one of the factors for prolonged operative time, which is likely attributable to the association with impacted stones.[13,15,16]

Some studies have reported that stone volume is a predictor of surgical time for renal stones,[7,8] as well as a predictor of achieving a stone-free status.[17,18] However, in the present study, which focused on ureteral stones, stone volume was not a predictive factor of prolonged operative time. Renal stones are located in the renal pelvis and calyces, which provide a larger space compared with the ureter, and renal stones are usually larger than ureteral stones. In retrograde intrarenal surgery, effective fragmentation and retrieval of these large stones in the large space is a critical step in determining the surgical time. Therefore, it is reasonable that stone size is a predictive factor of operative time. In contrast, when removing ureteral stones, including impacted stones, it is important to break and retrieve the stone carefully without injuring the ureteral wall. Therefore, in surgery for ureteral stones, the condition of the mucous membrane around the stone significantly affects the surgical time. Additionally, as ureteral stones are relatively small and the size range is limited, size may not be a predictive factor of prolonged operative time for ureteral stones.

In the present study, there was no significant difference in the incidence of infectious complications between the group with a prolonged surgical duration and the group without a prolonged surgical duration, although previous reports have suggested that surgeries with a longer duration carry a risk of infectious complications.[2,3] There could be several reasons for this finding. First, preoperative antibiotic administration is known to reduce postoperative infectious complications, and there was a significantly higher prevalence of preoperative antibiotic administration in the group with a prolonged surgical duration in the present study.[19] Second, as

it is known that a high intraoperative intrarenal pressure increases the risk of bacteremia, precautions were taken to ensure that the pressure did not become elevated in the present study.[20,21] We carefully regulated the intrapelvic pressure by maintaining a consistent irrigation pressure using an automatic irrigation system. Additionally, if fluid accumulation was observed in the renal pelvis, appropriate aspiration was performed to prevent an increase in intrapelvic pressure. Therefore, even if the surgical duration was prolonged, the risk of infection decreased. However, there are multiple other factors involved in infectious complications, and our explanations are speculative. Further investigations are necessary to explore these factors in more detail.

The significantly greater proportion of patients receiving preoperative antibiotic administration in the group with an operative time of 90 minutes or more versus the group with an operative time of less than 90 minutes may reflect a more cautious approach in patients anticipated to have longer operative times due to factors such as larger stone size or greater complexity. Preoperative antibiotics are known to reduce the risk of postoperative infections, while prolonged operative times are associated with an increased risk of infectious complications. Therefore, it appears that the clinicians administered preoperative antimicrobial agents to patients anticipated to undergo prolonged surgeries.

The present study has several limitations. First, as a retrospective, single-center study, there may be inherent biases and a potential lack of generalizability to broader populations. Additionally, this retrospective study was conducted based on consecutive data collection without performing power calculations, which means that results not reaching statistical significance may not necessarily indicate a lack of causal relationship but could be due to insufficient statistical power. Second, the evaluation of endoscopic findings was not entirely based on objective criteria and can be challenging in certain instances. However, in the present study, the endoscopic findings were assessed by a limited number of highly skilled operators, which minimized inter-case bias. Third, the study analyzed 519 patients, which may be considered a limited sample size given the variability in patient characteristics and stone complexities. This small sample size might restrict the robustness of our findings and their applicability to a wider patient cohort. Fourth, the exclusion of patients with concomitant renal stones could introduce a selection bias, potentially affecting the complexity of cases and extending operative times, thereby impacting the study outcomes. Future studies should aim to include a broader range of cases across multiple institutions to enhance the representativeness and generalizability of the findings.

CONCLUSIONS

Our study revealed that stone size larger than 10 mm and the presence of ureteral polyps and adherence between the stones and the ureteral mucosa are significant predictive factors for a prolonged operative time during URS for ureteral stones.

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FIGURES AND TABLES

Table 1. Patient and stone characteristics							
Patients (n=519)	**Operative time <90 min (n=461)**		**Operative time >90 min (n=58)**		**p**	**Total (n=519)**	
Age, years, median (IQR)	62.4	(52.2–72.3)	58.1	(48.8–68.1)	0.08	61.8	(51.3–72.2)
Sex, n (%)					0.02		
Male	302	(65.5)	47	(81.0)		349	(67.2)
Female	159	(34.5)	11	(19.0)		170	(32.8)
Body mass index, kg/m^2, median (IQR)	24.0	(21.7–26.6)	24.7	(22.2–27.9)	0.34	24.0	(21.8–26.7)
ECOG performance status, n (%)					0.69		
0	432	(93.7)	55	(94.8)		487	(93.8)
1	15	(3.3)	2	(3.4)		17	(3.3)
2	4	(0.9)	1	(1.7)		5	(1.0)
3	9	(2.0)	0	(0.0)		9	(1.7)
4	1	(0.2)	0	(0.0)		1	(0.2)
Hydronephrosis, n (%)	370	(80.3)	49	(84.5)	0.60	419	(80.7)
Preoperative stent replacement, n (%)	345	(74.8)	49	(84.5)	0.14	394	(75.9)
Preoperative positive urine culture, n (%)	141	(30.6)	14	(24.1)	0.36	155	(29.9)
Preoperative pyelonephritis, n (%)	110	(23.9)	9	(15.5)	0.19	119	(22.9)
Preoperative antibiotics, n (%)	318	(69.0)	50	(86.2)	<0.01	368	(70.9)
Stone laterality, n (%)					0.33		
Right	228	(49.5)	33	(56.9)		261	(50.3)
Left	233	(50.5)	25	(43.1)		258	(49.7)
Main stone location,n (%)					0.01		

Proximal ureter	252	(54.7)	32	(55.2)		284	(54.7)
Middle ureter	74	(16.1)	17	(29.3)		91	(17.5)
Distal ureter	135	(29.3)	9	(15.5)		144	(27.8)
Number of stones, n (%)					0.29		
Simple	405	(87.9)	48	(82.8)		453	(87.3)
Multiple	56	(12.1)	10	(17.2)		66	(12.7)
Stone burden							
Diameter, mm, median (IQR)	7.0	(6.0–10.0)	11.0	(9.0–13.0)	<0.01	8.0	(6.0–10.0)
Volume, mm^3, median (IQR)	104.9	(52.4–220.2)	331.4	(207.7–606.8)	<0.01	125.9	(58.2–256.9)
Hounsfield units of stone, median (IQR)	977.0	(649.0–1236.0)	1267	(1033.0–1383.0)	<0.01	1001.0	(683.5–1270.0)

ECOG: Eastern Cooperative Oncology Group; IQR: interquartile range.

Table 2. Surgical outcomes

Patients (n=519)	**Operative time <90min (n=461)**		**Operative time >90min (n=58)**		**p**	**Total (n=519)**	
Operative time, minutes, median (IQR)	39.0	(28.0–55.0)	98.0	(93.3–110.8)	<0.01	43.0	(29.0–65.0)
Rigid or flexible, n (%)					0.25		
Flexible	196	(42.5)	25	(43.1)		221	(42.6)
Rigid	119	(25.8)	9	(15.5)		128	(24.7)
Flexible + rigid	146	(31.7)	24	(41.4)		170	(32.8)
Endoscopic findings, n (%)							
Edema	235	(51.2)	51	(87.9)	<0.01	286	(55.1)
Polyps	83	(18.1)	33	(56.9)	<0.01	116	(22.4)

Adherence	109	(23.7)	42	(72.4)	<0.01	151	(29.1)
Total laser energy, J, median (IQR)	515.0	(160.0–1237.0)	1550.0	(970.0–3020.0)	<0.01	610.0	(190.0–1550.0)
Stone-free status, n (%)							
Endoscopic stone-free	461	(100.0)	58	(100.0)		519	(100.0)
Based on KUB	446	(96.7)	49	(84.5)	<0.01	495	(95.4)
Length of stay after surgery, days, median,(IQR)	2.0	(2.0–2.0)	2.0	(2.0–2.0)	0.79	2.0	(2.0–2.0)
Postoperative complication, n (%)							
Fever (>38.0 °C)	32	(6.9)	2	(3.4)	0.41	34	(6.6)
SIRS	42	(9.1)	6	(10.3	0.81	48	(9.3)
Ureteral injury	16	(3.5)	4	(7.4)	0.26	20	(3.9)

IQR: interquartile range; KUB: kidney-ureter-bladder radiographs; SIRS: systematic inflammatory response syndrome.

Table 3. Multivariate analysis of factors associated with operative time exceeding 90 minutes

Variables	**Univariable**			**Multivariable**		
	OR	**95% CI**	**p**	**OR**	**95%CI**	**p**
Age						
<60 years	Reference		0.08			
>60 years	0.61	0.35–1.06				
Sex						
Male	Reference		0.02	Reference		0.14
Female	0.45	0.22–0.88		0.56	0.26–1.20	
Hydronephrosis						
Negative	Reference		0.44			

Positive	1.34	0.64–2.83				
Preoperative stent replacement						
Not performed	Reference		0.11			
Performed	1.83	0.87–3.84				
Stone laterality						
Right	Reference		0.29			
Left	1.35	0.78–2.34				
Stone location						
Proximal ureter	Reference					
Middle ureter	1.81	0.95–3.44	0.07			
Distal ureter	0.53	0.24–1.13	0.10			
Stone diameter						
<10.0 mm	Reference		<0.01	Reference		<0.01
>10.0 mm	7.01	3.84–12.80		4.05	1.81–9.08	
Stone volume						
<125 mm^3	Reference		<0.01	Reference		0.45
>125 mm^3	7.21	3.35–15.60		1.49	0.53–4.14	
Hounsfield units of stone						
<1000	Reference		<0.01	Reference		0.33
>1000	4.35	2.24–8.42		1.48	0.67–3.28	
Rigid or flexible						
Flexible	Reference					
Rigid	0.59	0.27–1.31	0.19			

Rigid + flexible	1.28	0.70–2.34	0.42			
Endoscopic findings of edema						
Negative	Reference		<0.01	Reference		0.30
Positive	6.94	3.09–15.60		1.70	0.62–4.71	
Endoscopic findings of polyps						
Negative	Reference		<0.01	Reference		0.02
Positive	5.98	3.38–10.6		2.40	1.18–4.86	
Endoscopic findings of mucosa-stone adherence						
Negative	Reference		<0.01	Reference		<0.01
Positive	8.43	4.56–15.60		3.51	1.58–7.78	

CI: confidence interval; OR: odds ratio.