

Factors Predicting Febrile Urinary Tract Infection After Ureterorenoscopic Lithotripsy in Pediatric Patients

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ABSTRACT

Objective: To our knowledge, there is no study investigating the factors predicting postoperative febrile urinary tract infection (UTI) in pediatric patients. We aimed to determine the factors predicting postoperative febrile UTI in pediatric patients who underwent ureterorenoscopic lithotripsy (URS-L).

Methods: Pediatric patients who underwent URS-L due to ureter or kidney stones in our tertiary center between 2012 and 2019 were analyzed retrospectively. The demographic data, stone characteristics, and intraoperative and postoperative data of those with and without postoperative febrile UTI were compared. Multivariable binary logistic regression analysis was performed to determine predictors of postoperative febrile UTI.

Results: A total of 136 patients were included in the study. The mean age of the patients was 10 ± 5.4 years and 78 patients (57.4%) were male, and 58 patients (42.6%) were female. Semirigid URS-L was applied to 72 (52.9%), and flexible URS-L to 64 (47.1%) patients. The mean operation time was 45.5 ± 15.4 minutes. In the postoperative 1st month, 104 (76.5%) patients were found to be stone-free. Postoperative febrile UTI developed in 17 patients (12.5%). History of stone surgery, history of UTI, presence of nephrostomy / D-J stent, type of surgery, operation time, length of stay, and presence of complication except febrile UTI were found to be significantly different in patients with postoperative febrile UTI compared to those without. In multivariate analysis, only the history of UTI was identified as an independent predictive factor.

Conclusion: In pediatric patients, infectious complications constitute the majority of complications after URS-L. History of UTI is the only independent factor that predicts postoperative febrile UTI after URS-L.

Keywords: Pediatric urolithiasis, ureterorenoscopic lithotripsy, complication, urinary tract infection

INTRODUCTION

Globally urolithiasis is a very common disease and its incidence is increasing worldwide (1). Studies have shown that the incidence of pediatric urolithiasis has also increased in recent years (2–4). Pediatric urolithiasis has a high risk of relapse, and the primary goals in its treatment are ensuring the stone-free status and minimizing the risk of recurrence (5). In the past, while extracorporeal shock wave lithotripsy (ESWL) was the preferred treatment method in pediatric patients, thanks to technological advances ureterorenoscopic lithotripsy (URS-L) has been used more often in the treatment of ureter and kidney stones in recent years (6). In pediatric patients, semirigid and flexible URS can be successfully applied with stone-free and complication rates similar to adults (7). Most of the postoperative complications are high fever and urinary tract infection (UTI) (8). In the literature, there are studies investigating the factors predicting postoperative febrile

UTI in the adults (9–11). Although febrile UTI is the most common postoperative complication in pediatric patients (12, 13), as far as we know, there is no study investigating the factors predicting this complication. Only Doğan et al. investigated the factors predicting the overall complication rate, and in their multicentric study, operation time was indicated as the only independent predictor affecting the complication rate (14). In this study, we aimed to determine the factors predicting postoperative febrile UTI in pediatric patients who underwent URS-L.

METHODS

After obtaining the local ethics committee approval (Approval Number: 2021/165), the data of 140 pediatric patients aged 0-18 years who underwent URS-L due to ureteral or kidney stones in our tertiary center between 2012 and 2019 were obtained from our prospective URS-L database and were analyzed retrospectively.

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tively. Age, gender, medical history, stone characteristics, presence of preoperative UTI, presence of D-J stent/nephrostomy, type of operation, degree of hydronephrosis, operation time, postoperative D-J stenting, stone-free status, complications, and follow-up data were investigated. Exclusion criteria were: patients with anatomical abnormality, patients with comorbidities that predispose to infection, such as diabetes mellitus or immunodeficiency, patients undergoing URS-L for residual stone, and patients with missing follow-up data. ESWL was not applied to any patient before surgery. As a result, a total of 136 patients were included in the study. The demographic data, stone characteristics, and intraoperative and postoperative data of those with and without postoperative febrile UTI were compared.

Urine culture was obtained in all patients preoperatively. All urine cultures were evaluated in a single laboratory, and less than 10³ CFU was considered negative. Patients with positive urine culture were treated with antibiotics for at least 1 week according to the culture antibiogram results and a sterile urine culture was obtained before surgery. Abdominal low-dose computed to-

mography (CT) without contrast was performed in accordance with ALARA (As Low As Reasonably Achievable) principles for each patient to be operated on. Stone features and degree of hydronephrosis were determined preoperatively by CT. Stone size was calculated based on the longest dimension of the stone on CT. The journal article by Cietak and Newton was used as a reference to classify hydronephrosis (15). Simultaneous and moderate expansion of the pelvis and calyces (Grade 3 hydronephrosis) and simultaneous and severe expansion of the pelvis and calyces (Grade 4 hydronephrosis) were defined as the presence of high-grade hydronephrosis.

All operations were performed under general anesthesia with the lithotomy or frog-leg position. As antibiotic prophylaxis, second-generation cephalosporin was administered intravenously during anesthesia induction. Semirigid URS-L was performed using 4.5-6 Fr ultra-thin semirigid pediatric ureterorenoscope (Richard Wolf, Knittlingen, Germany) and flexible URS-L was applied with 7.5 Fr flexible ureterorenoscope (Flex-X2, Karl Storz, Tuttlingen, Germany). We applied semi-rigid URS-L to lower

Table 1. Comparison of patients with and without postoperative febrile UTI

Variables	Total (n=136)	Febrile UTI+ (n=17)	Febrile UTI- (n=119)	p
Age (Years) -Mean ± SD	10 ± 5.4	10.7 ± 4	9.99 ± 5.6	0.651
Gender (female) -n (%)	58 (42.6)	10 (58.8)	48 (40.3)	0.238
Stone Diameter (mm) -Mean ± SD	13.2 ± 4.8	15.0 ± 3.4	12.9 ± 5	0.108
Stone Number -n (%)	1.35 ± 0.5	1.24 ± 0.4	1.37 ± 0.5	0.280
Stone Density (HU) -Mean ± SD	1067 ± 421	993 ± 133	1077 ± 446	0.500
High-grade Hydronephrosis -n (%)	51 (37.5)	7 (41.2)	44 (37.0)	0.948
History of Stone Surgery -n (%)	35 (25.7)	8 (47.1)	27 (22.7)	0.041
History of UTI -n (%)	8 (5.9)	4 (23.5)	4 (3.4)	0.009
Presence of Nephrostomy/D-J Stent -n (%)	21 (15.4)	6 (35.3)	15 (12.6)	0.026
Type of Surgery -n (%)				0.019
Semi-rigid URS-L	72 (52.9)	4 (23.5)	68 (57.1)	
Flexible URS-L	64 (47.1)	13 (76.5)	51 (42.9)	
Flexible URS-L with UAS -n (%)	51 (79.7)	10 (76.9)	41 (80.4)	0.717
Operation Time (min) -Mean ± SD	45.5 ± 15.4	55.2 ± 8	44.2 ± 15.7	<0.001
Postoperative D-J Stenting -n (%)	119 (87.5)	13 (76.5)	106 (89.1)	0.229
Length of Stay (days) -Mean ± SD	2.6 ± 2.7	8.7 ± 3.4	1.8 ± 0.7	<0.001
Complications* -n (%)	12 (8.8)	4 (23.5)	8 (6.7)	0.045
Stone-free Rate -n (%)	104 (76.5)	11 (64.7)	93 (78.2)	0.231
D-J Stent Removal Time (days) -Mean ± SD	26.8 ± 8	30.4 ± 8.4	26.4 ± 7.8	0.085

SD: Standard deviation HU: Hounsfield Unite UTI: Urinary tract infection URS-L: Ureterorenoscopic lithotripsy *except febrile UTI

Table 2. Multivariate binary logistic regression analysis results for prediction postoperative febrile UTI

Variables	Multivariate		
	OR	95% CI	P value
History of Stone Surgery	0.699	0.196-2.496	0.581
History of UTI	0.152	0.029-0.809	0.027
Presence of Nephrostomy/D-J Stent	1.875	0.499-7.042	0.352
Type of Surgery (Flexible URS-L)	0.513	0.119-2.210	0.371
Operation Time	1.028	0.987-1.071	0.185
Complications*	0.630	0.132-3.010	0.562

HU: Hounsfield Unit, UTI: urinary tract infection, URS-L: ureteroscopic lithotripsy, *except febrile UTI

and middle ureteral stones and flexible URS-L to upper ureteral stones and kidney stones. In patients who underwent flexible URS-L, a 9.5/11.5 Fr ureteral access sheath (UAS) was advanced over hydrophilic guidewires under the guidance of fluoroscopy. In patients whose UAS could not be placed, a flexible ureterorenoscope was advanced over a hydrophilic guidewire. If this procedure was also unsuccessful, a D-J stent was placed, and a second session was performed 2-4 weeks later. Active orifice dilatation was not applied to any patient. The stones were fragmented with the holmium:yttrium-aluminum-garnet (Ho:YAG) laser. Postoperatively, a D-J stent was placed in case of need, according to the surgeon's preference.

During the hospitalization, the patients were given second-generation cephalosporin prophylaxis. The patients without complications were discharged with oral second-generation cephalosporin prophylaxis on the first or second postoperative day. One month after the operation, ultrasonography (US) was used to evaluate the stone-free status, and kidney-ureter-bladder radiography (KUB) was used in cases with opaque stones that could not be determined clearly by US. CT was used only in selected cases with high suspicion for residual stones. The absence of any stone or presence of a stone smaller than 2 mm in KUB or US was defined as stone-free status. Postoperative febrile UTI was defined as a fever above 38 °C within 1 month after surgery if symptoms related to fever were caused only by urinary tract abnormalities and the presence of UTI was confirmed in urine culture.

Statistical Analysis

Categorical data were presented as numbers and percentages. Data for continuous variables were presented as mean and standard deviation. The Shapiro-Wilk test was used to determine whether the distributions of continuous variables were normal. Mean differences between two related groups of normally distributed data were compared with the independent T-test, while the Mann-Whitney U test was used to compare non-normally distributed data. The frequencies of categorical variables were compared using Pearson's Chi-Square, Yates' Chi-Square, or Fisher's exact test, when appropriate. Statistical significance was considered when p value was <0.05. Multivariable binary logistic

regression analysis was performed to determine predictors of febrile UTI. Statistical analysis was performed using Statistical Package of Social Sciences version 21 (IBM SPSS Statistics; IBM Corp., Armonk, NY).

RESULTS

A total of 136 patients were included in the study. The mean age of the patients was 10±5.4 years and 78 patients (57.4%) were male, and 58 patients (42.6%) were female. Of the patients, 45 had lower ureteral stones, 27 had middle ureteral stones, 22 had upper ureteral stones and 42 had kidney stones. Thirty-five patients (25.7%) had a history of stone surgery. Twenty-seven of them were semirigid URS-L and 8 were flexible URS-L. Before the operation, 20 patients had a D-J stent and 1 patient had a nephrostomy. Eight patients (5.9%) had a history of UTI (E. coli in six patients, K. pneumoniae in one patient, and P. mirabilis in one patient). Postoperative febrile UTI developed in 17 patients (12.5%) (E. coli in fourteen patients, P. aeruginosa in two patients, and P. mirabilis in one patient). The same microorganism was grown in 3 of 4 patients with a history of UTI with febrile UTI (E. coli in two patients and P. mirabilis in one patient) before and after the surgery. Semirigid URS-L was applied to 72 (52.9%), and flexible URS-L to 64 (47.1%) patients. UAS was used in 51 of 64 patients (79.7%) who underwent flexible URS-L. UAS could be placed in 46 (71.9%) of 64 patients who underwent flexible URS-L in the first session. In 13 patients (20.3%), the flexible ureterorenoscope could be advanced over the guidewire. In the remaining 5 patients (7.8%), the second session was performed by inserting a D-J stent. UAS was easily placed in all patients after passive dilatation. The mean operation time was 45.5±15.4 minutes. In the postoperative 1st month, 104 (76.5%) patients were found to be stone-free. The demographic data, stone characteristics, and perioperative data of the patients are shown in Table 1.

The rate of developing postoperative febrile UTI was significantly higher in patients with a history of stone surgery, history of UTI, presence of nephrostomy / D-J stent, and presence of complication except febrile UTI (p=.041, p=.009, p=.026 and p=.045, respectively). The application rate of flexible URS-L was significantly higher in patients with postoperative febrile UTI compared to those without (76.5% vs 42.9%, p=.019, respectively). The operation time was significantly longer in patients with postoperative

febrile UTI compared to those without (55.2 ± 8 min vs 44.2 ± 15.7 min, $p < .001$, respectively). The length of stay was significantly longer in patients with postoperative febrile UTI compared to those without (8.7 ± 3.4 days vs 1.8 ± 0.7 days, $p < .001$, respectively). Although stone-free rate (SFR) was lower in patients with postoperative febrile UTI, there was no significant difference in SFR between patients with and without postoperative febrile UTI (64.7% vs 78.2%, $p = 0.231$, respectively). A comparison of patients with and without postoperative febrile UTI is shown in Table 1. In multivariate analysis, only a history of UTI was identified as an independent predictive factor. Multivariate regression analysis results of factors predicting postoperative febrile UTI are shown in Table 2.

Twelve (12.2%) complications developed apart from postoperative febrile UTI, including hematuria (Clavien I), which did not require additional treatment in 6 patients, and nausea and vomiting (Clavien I) in 4 patients which improved with the use of anti-emetics. Two Clavien III complications requiring additional intervention were observed. The first was ureteral wall damage due to impacted stone which was successfully managed by inserting a D-J stent. Secondly, on the first postoperative day, the D-J stent was seen to be migrated to the distal of the residual fragments in the proximal ureter, so the D-J stent was replaced.

DISCUSSION

The efficacy of ESWL in pediatric patients is well known. The fact that the ureter is both more elastic and flexible in children allows the passage of stone fragments and prevents impaction. Also, the small size of the child's body transmits most of the ESWL energy. However, there are concerns about the harmful effects of shock waves on the growing kidney and surrounding tissues, and the results are controversial (16). Advances in endoscopic equipment and laser technology have led to the increase in popularity of URS in the treatment of pediatric urolithiasis and consequently URS has been accepted as first-line treatment by many clinicians (17, 18). De Dominicis et al. found that URS in pediatric patients was more effective than ESWL in distal ureteral stones (SFR: 94% with URS, 64% with 2 sessions of ESWL) (19). In addition, in a meta-analysis, He et al. investigated treatment modalities used in the management of pediatric upper urinary tract stones and determined that retrograde intrarenal surgery (RIRS) had higher single session-SFR and lower retreatment rates compared to ESWL (5). In our clinic, we apply URS-L as the first-line treatment in pediatric patients due to the possibility of stone removal in one session, in addition to higher SFR and reasonable complication rates of URS. We prefer ESWL especially, in adolescents that do not require anesthesia.

Studies have shown that URS has high efficacy in the treatment of both ureteral and kidney stones in pediatric patients. In the literature, SFRs have been reported to range between 88–100% with semirigid URS in pediatric patients (14). In the systematic review, Ishii et al. evaluated flexible URS in pediatric patients and found an overall mean SFR of 85.5% (12). In our study, the number of patients treated with semi-rigid and flexible URS-L was almost half and half, and SFR was determined as 76.5%, similar to the literature.

Although URS is a minimally invasive procedure with a high success rate, it is not without complications. Most of the early postoperative complications in pediatric patients, as in adults, are infectious complications. In the study conducted by Doğan et al. with 642 children who underwent semirigid URS, the overall complication rate was found to be 8.4%, and the febrile UTI rate was 3% (14). A higher complication rate with RIRS relative to the semirigid URS is an expected condition, which is also supported by various studies. In the study conducted by Erkurt et al. with 65 patients of preschool age who underwent RIRS, the overall complication rate was 27.7% and the rate of febrile UTI was 15.4% (20). In our series, the overall complication rate was 18.4% and the rate of febrile UTI was 12.5%, in line with existing studies. In addition, the application rate of flexible URS-L was higher in patients who developed febrile UTI than those who did not (76.5% vs 42.9%, respectively, $p = .009$). However, flexible URS-L was not a predictor of febrile UTI in multivariate analysis.

Although the pediatric literature on infectious complications after URS is insufficient, studies in adults can guide. Sohn et al. determined that preoperative bacteriuria, hydronephrosis, and the presence of a catheter (urethral catheter, ureteral stent, or nephrostomy tube) predicted infectious complications after URS (9). Mitsuzaka et al. determined that the presence of preoperative pyuria and pyelonephritis were factors predicting infectious complications after URS (10). In the present study, according to our knowledge, for the first time in the literature, we investigated the factors predicting febrile UTI in pediatric patients who underwent URS-L. We also determined that the history of UTI is the only independent predictor for febrile UTI. The findings of our study are partially consistent with existing studies. Differences may have resulted from factors such as inclusion criteria, patient population, variety of procedures performed, antibiotic prophylaxis policy, and local resistance profile. Additionally, in this study, we determined that postoperative complications except febrile UTI were much more frequent in patients with febrile UTI (23.5% vs 6.7%, $p = 0.045$). We believe this is due to the longer operative time in more complex cases, and therefore the higher likelihood of developing febrile UTI and other complications.

It has been shown that the use of UAS enables repetitive access, decreases intrarenal pressures, and operation time, and improves SFR in the adult population (21). However, there are concerns regarding the use of UAS due to the potential risk of ureteral injury and vesicoureteral reflux in pediatric patients. Although there are studies showing that UAS is safe for use in children, the literature on this subject is insufficient (20, 22, 23). In addition, the advancement of the UAS or flexible ureterorenoscope over the hydrophilic guidewire may be more difficult in pediatric patients with a smaller ureter. In the study of Erkurt et al., 61.5% of the patients could have UAS placed and in 30.8% of their patients, a flexible URS could be advanced over the guidewire. In 7.7% of the patients, the procedure was left for the second session by placing a D-J stent (20). In our study, UAS could be placed in 71.9% of the patients. Compared to the study of Erkurt et al., the reason for our high rate of success may be that our patient population consists of older children, including adolescents (mean age 4.31 vs 10 years).

Postoperative D-J stenting is important in terms of allowing the recovery of local edema and preventing postoperative pain and possible infectious complications secondary to obstruction. However, requiring additional anesthesia limits its use in pediatric patients (14). Studies have shown that the postoperative stenting rate is between 61.7-92.3%. The postoperative stenting rate is higher in patients undergoing RIRS (7, 14, 18, 20). Doğan et al. stated that the rate of complications was higher in patients who underwent postoperative stenting compared to those who did not (14). This may be due to more frequent stenting in complicated cases. Sohn et al. found that postoperative placement of ureteral stent decreased the incidence of infectious complications in adults (9). In our study, the postoperative stenting was 87.5%, and D-J stents were placed routinely in patients using UAS. However, postoperative stenting was not one of the factors affecting febrile UTI positively or negatively in our study.

Our study has some limitations. Its retrospective design is the most important limitation. Another important limitation is that we evaluate stone-free status with US and/or KUB instead of CT to avoid radiation exposure one month after the surgery. Therefore, the actual stone-free rate is likely to be lower than reported. However, we believe this difference is negligible. Also, we cannot comment on the reliability of the use of UAS since patients had no long-term follow-up data. The etiology of patients who had a history of UTI has not been evaluated. The stone analysis results (especially infection stones) of the patients were not recorded. However, we believe that our study will be a guide for prospective multicentric studies to be performed on this subject.

CONCLUSION

In the pediatric patients, infectious complications constitute the majority of complications after URS-L. History of UTI is the only independent factor that predicts postoperative febrile UTI after URS-L. Appropriate antibiotic prophylaxis based on previous antibiotic susceptibility tests and closer follow-up of patients with a history of UTI may be an appropriate approach to prevent postoperative febrile UTI. There is a need for prospective, randomized studies with larger populations to reach more definitive conclusions.

Ethics Committee Approval: Ethics committee approval was received for this study from the Bakirkoy Dr. Sadi Konuk Training and Research Hospital Ethical Committee (Decision number: 2021/165, Date: 15.03.2021).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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