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ORIGINAL PAPER

Factors affecting infectious complications following flexible ureterorenoscopy

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Abstract

In the present study, we aimed to clarify predictive factors that may cause postoperative infectious complications after flexible ureterorenoscopy (f-URS). In a 4-year prospective study, charts of patients who underwent f-URS between January 2014 and January 2018 for renal stone(s) in a tertiary academic center were reviewed. A standardized f-URS procedure was performed for all patients. Post-operative infectious complications including fever, sepsis and septic shock were categorized into same group. Patients with and without infectious complications were compared in the terms of preoperative, operative and post operative characteristics. In total, 463 patients who did not face infectious complications and 31 patients who faced infectious complications were enrolled into the study. The mean age was significantly lower in patients who did face infectious complications (34.8 vs 44.7 years old, $p < 0.001$). On the other hand, presence of renal abnormality was significantly more common in patients with infectious complications (12.3% vs 35.5%, $p < 0.001$). The mean operation time was 65.3 min in patients with infectious complications and significantly longer when compared with patients who did not face infectious complication (47.8 min, $p < 0.001$). Stone-free rate was significantly higher in patients without infectious complications (85.3% vs 77.5, $p = 0.009$). Multivariate regression analysis revealed that longer operation time ≥ 60 min, presence of renal abnormality and age ≤ 40 years were predictive factors for infectious complications following f-URS. The present study has demonstrated that operation time ≥ 60 min, presence of renal abnormality and patients with ≤ 40 years were significantly associated with infectious complications following f-URS.

Keywords Complication · Fever · Flexible ureterorenoscopy · Infectious · Sepsis

Abbreviations

f-URS	Flexible ureterorenoscopy
SWL	Shock wave lithotripsy
PNL	Percutaneous nephrolithotomy
CT	Computerized tomography
BMI	Body mass index
ASA score	American Society of Anaesthesiologists Score

Introduction

The management of kidney stone(s) has changed dramatically in the last three decades and minimal invasive techniques including flexible ureterorenoscopy (f-URS), shock wave lithotripsy (SWL) and percutaneous nephrolithotomy (PNL) have gained popularity in urology practice [1]. Flexible ureterorenoscopes are a state-of-the-art methodology that can access all parts of pelvicalyceal system and provide excellent stone fragmentation with holmium laser. Recently, f-URS has been accepted as the first-line alternative treatment choice for renal stones under 20 mm with better stone-free rates over SWL and less complication rates over PNL [2]. Although the reliability of f-URS has been proved, the procedure itself has some potential risks including infectious complications.

Infectious complications including fever, sepsis and septic shock have been reported in a wide range up to 37% during renal stone treatment [3]. Predictive factors that may be associated with infectious complications in PNL and SWL have been evaluated intensively, however, only a limited number of studies have tried to identify predictive factors to infectious complications following f-URS, yet [4]. Cindolo et al. have reviewed the f-URS series of 11 experienced surgeons and death was observed in six patients. Authors

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have stated that four of six cases were lost due to infectious complications, however, they did not focus on predictive factors for infectious complications [5]. In another study, Berardinelli et al. have found 7.7% infectious complication rate after f-URS in 403 patients, but they did not find any predictive factor for infectious complications [6].

Although previous studies have discussed f-URS' complications in the literature, there is no consensus on predictive factors that may lead infectious complications following f-URS. In the present study, we aim to clarify predictive factors that may cause postoperative infectious complication after f-URS.

Materials and methods

In a 4-year prospective study, charts of patients who underwent f-URS between January 2014 and January 2018 for renal stone(s) in a tertiary academic center were reviewed. Patients who were older than 18 years old, were accepted as a participant of the study. Patients with a bleeding diathesis, neurogenic bladder, immunosuppressive disease and concomitant ureter stone(s) were excluded. Other exclusion criteria were; procedures with digital f-URS, pregnancy, presence of nephrostomy tube during procedure and presence of bladder stone(s). The patients who underwent f-URS under antibiotic therapy due to positive urine culture, were also excluded from the study. Patients were divided into two groups according to development of infectious complications following f-URS. Patients with and without infectious complications were compared in the terms of preoperative, operative and postoperative characteristics.

In all patients, an elaborated medical history was achieved and a detailed physical examination was performed. Characteristics of stone(s) and renal anatomy were evaluated using intravenous pyelography and/or non-contrast abdominal computerized tomography (CT). None of the patients had bacteriuria ($< 10^3$ cfu/ml) before the surgery. Finally, all patients signed an informed consent prior to the surgery.

f-URS technique

A standardized f-URS procedure was performed for all patients by four experienced endourologists. Antibiotic prophylaxis was given half an hour before induction of general anesthesia. Semi-rigid ureteroscopy was done for visual evaluation of the ureter and to facilitate placement of ureteral access sheath with 11/13 Fr in size. A 7.5 Fr fiber-optic flexible ureterorenoscope (Storz FLEX-X 2, Tuttlingen, Germany) was inserted into the kidney. To obtain lower pelvic pressure, we did not hang the irrigation fluid higher than a meter and did not use manual hand pump to increase pressure irrigation fluid. Stone fragmentation was done using 200 or 273 µm laser fiber with an energy of 0.8–1.5 J and a rate of 5–10 Hz. Stone fragments > 2 mm were extracted with stone retrieval basket and stone fragments < 2 mm were left for spontaneous passage. A 4.8 Fr JJ stent insertion was routinely performed at the end of the operation. Operation time was accepted as the time between the f-URS insertion into the kidney to the completion of JJ stent placement. The JJ stent was removed using cystoscope 2 weeks after the f-URS procedure.

Definition

Postoperative infectious complications including fever, sepsis and septic shock were categorized as within the same group in the present study. The fever was defined as an increase in body temperature > 38 °C, which remained for more than 48 h or any fever > 39 °C in the first postoperative day. Sepsis was accepted with the existence of an infection source and the presence of SIRS criteria (two or more of the following four criteria: white cell count > 12,000 or < 4000/mm^3; temperature < 36 °C or > 38 °C; heart rate > 90/min; respiratory rate > 12/min or $PaCO_2$ < 32 mmHg). Septic shock was defined as acute circulatory failure and persistent hypotension requiring vasopressors to obtain adequate mean arterial pressure of ≥ 65 mmHg [3, 7].

Success of procedure was evaluated with a kidney–ureter–bladder (KUB) radiogram and/or an urinary ultrasound at hospital discharge. In follow-up, stone-free status was reevaluated with abdominal CT between 1 and 3 months postoperatively. The procedure was accepted to be successful if complete stone clearance was determined without any residual fragments.

Statistical analysis

The Statistical Package of Social Sciences for Windows (SPSS) version 20 was used for statistical analysis. Patients were divided into two groups based on postoperative stone-free status. Categorical variables were presented as numbers and percentages and compared with Chi square test. Continuous variables were presented as means and standard deviations and were compared with independent sample *t* test. Correlation analyses were evaluated using Pearson's correlation coefficient. Multivariate analysis (logistic regression) was performed with significant parameters in univariate analysis. Statistical significance was considered when two-tailed p value < 0.05.

Results

In the study period, 787 patients' charts were evaluated and 293 patients were excluded from the study due to strict exclusion criteria. In total, 463 patients who did not face

infectious complications and 31 patients who faced infectious complications were enrolled into the study. The infection rates following f-URS, did not differ according to surgeons ($p=0.544$). Gender, body mass index, ASA score and presence of diabetes mellitus were similar between the groups ($p=0.435$, $p=0.968$, $p=0.538$ and $p=0.644$, respectively). Also, stone size, stone location and presence of solitary kidney were comparable ($p=0.458$, $p=0.460$ and $p=0.792$, respectively). However, the mean age was significantly higher in patients who did not face infectious complications (44.7 vs 34.8 years old, $p<0.001$). On the other hand, presence of renal abnormality was significantly more common in patients who faced infectious complications (12.3% vs 35.5%, $p<0.001$). Preoperative parameters are listed in Table 1.

The mean operation time was 65.3 min in patients with infectious complications and significantly longer when compared with patients who did not face infectious complication (47.8 min, $p<0.001$). Similarly, the mean hospitalization time was significantly longer in patients who faced infectious complications (61.3 h vs 24.1 h, $p=0.001$). Groups were comparable in terms of fluoroscopy time, balloon

Table 1 Comparison of preoperative demographics of patients

	Groups		*p* value
	Non-infectious group	Infectious group	
Number	463	31	
Gender (male/female)	257/206	16/15	0.435
Age (years)[a]	44.7 ± 15.2	34.8 ± 14.3	< 0.001
BMI (kg/m^2)[a]	26.9 ± 14.9	25.9 ± 5.0	0.968
The ASA score[a]	1.3 ± 0.5	1.4 ± 0.6	0.538
DM	58 (12.5%)	3 (9.7%)	0.644
Hydronephrosis grade (mild/severe)	80/41	7/5	0.534
Renal abnormality	57 (12.3%)	11 (35.5%)	
Malrotation abnormality	24	4	
Pelvic kidney	14	2	< 0.001
Horseshoe kidney	17	4	
Cross ectopic kidney	2	1	
Solitary kidney	36 (7.8%)	2 (6.5%)	0.792
Stone size (mm)[a]	182.4 ± 152.0	161.3 ± 96.6	0.458
Stone location			0.460
Upper pole	29	1	
Middle pole	29	7	
Lower pole	172	9	
Pelvis	79	5	
Proximal ureter	13	0	
Multiple	142	9	
Stone opacity (opaque/non-opaque)	431/33	29/2	0.890
Number of infectious stones (315 stone analysis, available)	11	6	0.119
Magnesium ammonium phosphate	7	3	
Apatite	2	0	
Ammonium urate			
Pre op JJ stent	90 (19.4%)	9 (29.0%)	0.195
Previous stone treatment			0.829
SWL	45	3	
PNL	59	5	
URS/f-URS	46/12	2/0	
Open surgery	5	1	
Multiple surgery	71	5	

BMI body mass index, *DM* diabetes mellitus, *ASA score* American Society of Anaesthesiologists Score, *f-URS* flexible ureterorenoscopy, *SWL* shock wave lithotripsy, *PNL* percutaneous nephrolithotomy

[a]Mean

dilatation rate and complication rate ($p=0.204$, $p=0.236$ and $p=0.143$, respectively). Stone-free rate was significantly higher in patients without infectious complication (85.3% vs 77.5, $p=0.009$) (Table 2).

Multivariate regression analysis revealed that operation time ≥ 60 min, increased the development of infectious complications 2.36-fold ($p=0.04$). Moreover, presence of renal abnormality and age ≤ 40 years were predictive factors for infectious complications following f-URS. On the other hand, multivariate regression analysis showed that stone-free status was not a predictive factor for infectious complications after f-URS ($p=0.76$) (Table 3).

Table 3 Multivariate analysis

	Odds ratio[a]	*p* value
Operation time[b]	2.36 (1.13–3.07)	0.04
Age[c]	2.69 (1.24–5.81)	0.01
Renal abnormality	3.60 (1.59–8.15)	0.01
Stone-free status	0.86 (0.33–2.21)	0.76

Logistic regression analysis

[a]95% confidence interval

[b]< 60 min vs ≥ 60 min

[c]≤ 40 years vs > 40 years

Discussion

Infective complication rates following f-URS were reported to be in a wide range due to the under-reporting or non-reporting in literature. Moreover, while reporting infectious complications, severity of infectious disease was not classified according to a standardized classification system. Hyams et al. have faced two infectious complications (fever in one patient and pyelonephritis in one patient) after 120 f-URS cases (1.67%) [7]. In another study, Pan et al. have managed fever in four patients and urosepsis in three patients following f-URS in 56 cases (12.5%) [8]. Moreover, Mariani et al. have found 18.7% infectious complication rate after 16 cases, but the stone volume for each patient was > 40 mm in their study [9]. In this present study, we have determined 31 infectious complications in 494 f-URS cases and the infectious complication rate was 6.3%, in accordance with literature.

The presence of a foreign body such as stone in the urinary system may increase infectious complications following f-URS. However, Fan et al. did not find a significant relationship between infectious complications following f-URS and residual stone ($p=0.110$) [10]. In another study, Berardinelli et al. achieved stone-free status in 271 of 372 patients (72.8%) without infectious complications and 16 out of 31 patients (51.6%) had infectious complications ($p=0.02$). Although authors found a significant difference in univariate analysis, multivariate regression analysis revealed that a unsuccessful f-URS procedure was not associated with postoperative infectious complications ($p>0.005$) [6]. Similarly, we obtained a higher stone-free rate in patients without infectious complications ($p=0.009$), however, we did not demonstrate a significant association between stone-free status and infectious complications following f-URS in multivariate regression analysis ($p=0.76$).

Age is an important parameter for both anesthetic evaluation and surgical decision. Also, older people require more attention during surgical procedures due to the higher incidence of diabetes mellitus, hypertension, chronic kidney disease, heart failure and are expected to be more prone to anesthetic and surgical complications. However, many reports have stated that endourological stone surgeries were as safe for elderly patients as they were for the young patients [11, 12]. In this study, surprisingly, patients with infectious complications were significantly younger (34.8 vs 44.7, $p=0<0.001$). Moreover, being ≤ 40 years old was found as a predictive factor for post f-URS infectious complications in

Table 2 Comparison of perioperative parameters and outcomes

	Groups		*p* value
	Non-infectious group	Infectious group	
Number	463	31	
Operation time (min)[a]	47.8 ± 21.2	65.3 ± 20.9	< 0.001
Fluoroscopy time (min)[a]	2.1 ± 1.6	2.4 ± 1.4	0.204
Hospitalization time (h)[a]	24.1 ± 15.1	61.3 ± 65.4	0.001
Balloon dilatation	33 (7.1%)	4 (12.9%)	0.236
Per-op complications			0.143
Hemorrhage	10 (2.2%)	0	0.623
Termal injury	4 (0.9%)	1 (3.2%)	0.562
Perforation	1 (0.4%)	0	0.795
Stone-free status	396 (85.3%)	24 (77.5%)	0.009

[a]Mean

multivariate regression analysis ($p = 0.01$). We do not know for sure why younger age was significantly associated with infectious complications. We believe that future studies will clarify this issue.

Previous reports had stated that prolonged operation time was associated with infectious complications in PNL due to the increased pressure in pelvicalyceal system, pyelovenous and pyelolymphatic circulation. Zhong et al. had demonstrated that intrapelvic pressure more than 30 mmHg was more likely to result in postoperative fever following PNL [13]. There is no reason to believe the effect of these parameters during f-URS will have different influences during PNL. In accordance with that knowledge, Fan et al. found a significant correlation between prolonged operation time during f-URS and postoperative infectious complications [10]. Also, the present study revealed that operation time ≥ 60 min increased the development of infectious complications 2.36-fold ($p = 0.04$).

Management of renal stone in anomalous kidney is a challenging issue for a urologist, however, previous reports have demonstrated that f-URS was a safe and effective treatment option for renal stones in an anomalous kidney. Ugurlu et al. obtained 88% stone-free rate in 26 patients with anomalous kidney and detected only one urosepsis after f-URS [14]. Bozkurt et al. achieved 84.6% success rates in 26 pelvic kidneys and faced with one infectious complication [15]. In another study, Atıs et al. have seen three infectious complications after f-URS in 20 patients with horseshoe kidney [16]. In the present study, the presence of anomalous kidney was found as a predictive factor of infectious complication. In our cases, we placed ureteral access sheath 2–3 cm below the ureteropelvic junction. On the other side, presence of partial obstruction in ureteropelvic junction is common in anomalous kidneys. We believe that partial obstruction prevents the return of irrigation fluid which may increase the pressure in pelvicalyceal system, pyelovenous and pyelolymphatic circulation. However, our hypothesis must be supported by further studies.

Ureteral access sheath (UAS) is used during f-URS to protect flexible ureteroscopes, facilitate stone fragment extraction and decrease intrapelvic pressure. Intrarenal pressure increased up to 328 mmHg if force irrigation was applied to obtain better vision, however, physical intrarenal pressure was 4–7 mmHg [17]. Rehman et al. have demonstrated that intrapelvic pressure decreased under 15 mmHg and 22 mmHg, if 12/14 Fr and 10/12 Fr UASs are used, respectively [18]. Similarly, Schwalb et al. suggested the use of UAS to prevent complications such as bleeding, urinoma, sepsis and postoperative pain [19]. In accordance with these knowledge, we routinely use UAS during f-URS procedures.

The present study has some limitations. First of all, we categorized all infectious complications including fever, sepsis and septic shock into the same group. Second, our study had included a relatively small number of patients with infectious complications. However, infectious complications following f-URS are rare and we achieved that patient number after analyzing 494 f-URS procedures. Also, we were not able to achieve optimal evaluation to understand the effect of stone type on infectious complications after f-URS due to insufficient data. We suggested all patients to undergo infrared spectroscopy or X-ray diffraction, however, due to the Turkish health system which does not pay for these procedures, some of our patients did not prefer to perform stone analysis. To avoid misinterpretation, we did not examine the relationship between stone type and infectious complications.

In conclusion, our study has demonstrated that operation time ≥ 60 min, presence of renal abnormality and patients with ≤ 40 years were significantly associated with infectious complications following f-URS. The outcomes of the present study must be supported by further prospective randomized studies with larger patient volumes.

Author contributions OF: project development, manuscript writing. AA: data analyzing. CA: manuscript editing. SO, OM: data collection. SM: manuscript editing, data collection. OM: data collection, data management.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical standards Informed consent was obtained pre-operatively from all of the patients who were included in our study.

Ethical compliance All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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