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Predictive factors for difficult ureter in primary kidney stone patients before retrograde intrarenal surgery

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Introduction Ureter may be resistant to insertion of ureteral access sheath (UAS) and/or semi-rigid ureterorenoscope because of the narrow ureter, 'difficult ureter' especially in primary retrograde intrarenal surgery (RIRS) cases. We aimed to delineate the parameters that affect significantly the accessibility of the ipsilateral ureter of the stone-bearing patient side.

Material and methods The data of age, gender, body mass index, comorbidities, prior urinary tract infection, prior stone passage, stone burden, stone density, number of stones, stone localization, surgery side, the presence of hydronephrosis and need for double J (DJ) stent due to difficult ureter for all patients were reviewed. Difficult ureter was defined as the insertion inability of a semi-rigid ureterorenoscope or UAS into the ureter at the surgery side. All patients were divided into two groups as difficult ureter group and non-difficult ureter group.

Results A total of 454 patients who underwent RIRS for primary kidney stones were included. The incidence of difficult ureter was 7.5% (34/454). The patients in the difficult ureter group were younger. Female gender and prior urinary tract infection rates were higher in the difficult ureter group. Multivariate logistic regression analysis indicated that the factors significantly associated with higher odds of having a difficult ureter in primary RIRS patients were younger age (OR 1.040; 95% CI 1.010–1.070; p = 0.008), female gender (OR 2.859; 95% Cl 1.383–5.908; p = 0.005) and prior urinary tract infection (OR 3.327; 95% CI 1.230–8.999; p = 0.018).

Conclusions Difficult ureter was associated with younger age at the time of RIRS, female gender and the manifestation of urinary infections in the patient's medical history.

Key Words: difficult ureter ‹› RIRS ‹› ureteral access sheath ‹› ureterorenoscope

INTRODUCTION

Kidney stones represent one of the most common urologic diseases, with a prevalence of 7.2–7.7% worldwide. Epidemiological data suggest a continuously increasing rate in the prevalence across the globe, which induces substantial increases in the healthcare burden of the condition. Interestingly, this increasing trend involves mostly the female population, a phenomenon that decreases the prevalence gap between the sexes [1].

The current algorithm for the management of kidney stones includes the options of extracorporeal shockwave lithotripsy (ESWL), retrograde intrarenal surgery (RIRS), percutaneous nephrolithotomy (PCNL), and the various methods of stone retrieval (open surgery, laparoscopy, robotics). The advantages of the RIRS approach over the other methods have contributed to the expansion of the indications of RIRS, which officially is proposed as the first option for stones ≤2 cm, and remains a valid option for stones >2 cm [2, 3].

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Several technological developments and innovative methods have contributed substantially to the configuration of RIRS lithotripsy to its current form. One of the most important developments is the direct access to the renal collecting system through the ureteral access sheath (UAS), which mostly is introduced driven by a guidewire and under fluoroscopic control. The advantages of UAS are underlined both in European and American guidelines and according to the latest data, 93.2% of the RIRS procedures start with the UAS introduction [2, 3, 4]. Additionally, to the intrarenal pressure decrease and the continuous outflow, data from biochemistry measurements suggest that UAS placement plays a protective role for the kidney since the levels of kidney injury biomarkers are lower in patients, who undergo RIRS through UAS [5].

While UAS placement comprises an almost essential step of RIRS, it is considered also a 'double-edged sword' since its introduction seems to be accompanied by an increased risk for ureteral injury. Indeed, in a large patient series, 1.8% of the whole cohort was diagnosed intraoperatively with UAS-related injury [4]. The risk of the above injury is also stated in European guidelines and the International Alliance of Urolithiasis (IAU) guidelines [2, 6]. Nevertheless, the data relating to UAS-related injury are not homogenous. In 2013, a study by Traxer et al. reported a much higher percentage of UAS-related injuries (46.7%) among patients, who underwent RIRS through UAS [7]. On the other side, a more recent report by Bozzini et al. stated that UAS insertion has no impact on ureteral injury risk, but results only in the decrease of postoperative infections [8].

Another condition, that relates to UAS insertion and its risks, is the failure of UAS placement due to difficulty during advancing UAS by the surgeon. According to a study by Mogilevkin et al., this condition is expected in about one-fifth of RIRS patients [9]. There are several reports, which propose the preoperative introduction of a ureteral double J (DJ) stent and the planning of RIRS as a secondary procedure to reduce both the risk of ureteral injury and failure in UAS insertion. Indeed, a study by Sung et al. evaluated the results of primary vs secondary RIRS and concluded that preoperative ureteral stenting can facilitate UAS insertion and reduce total operation time [10]. A meta-analysis by Law et al. pooled the outcomes in prestented vs non-prestented patients and found that the prestented patients had higher success rates of UAS insertion and lower ureteral injury rates [11]. In 2020, Yuk et al. performed the same comparison and reported that preoperative ureteral stenting contributed to an increased success rate in UAS placement, but no difference in terms of stone-free rate (SFR) was found [12]. On the contrary, two recent studies compared the prestented and the non-prestented patients in terms of complication rate and found no difference between the comparing groups [13, 14]. The available guidelines on the above topic recognize the positive effect of prestenting before RIRS on the operative outcomes, yet, they don't recommend routine ureter prestenting in every patient [2, 6].

Ureter prestenting before RIRS can increase the success rate of the latter, but it renders the whole procedure more complicated, less cost-efficient, and more bothersome for the patient due to the stent-related symptoms. In this setting, predicting the patients with difficult ureter would contribute to the individualization of the decision process relating to ureter prestenting. In the current study, we analyzed the data of a patient cohort regarding the factors, which associate with the success of primary RIRS. Our goal was to delineate the parameters that affect significantly the accessibility of the ipsilateral ureter of the stone-bearing patient side.

MATERIAL AND METHODS

This study was prepared in accordance with the principles of the Declaration of Helsinki and was approved by Ankara City Hospital ethics committee (approval number: E2-23-4588). The data of 1116 patients who underwent RIRS between January 2013 and May 2023 were obtained from the hospital information database retrospectively. Cases with prior kidney or ureter stone surgery, concomitant ureteral stone, DJ stent replacement history, kidney anomaly, malignity, radiotherapy history and inadequate data, were excluded from the study. All other patients were included in the study.

The data of age, gender, body mass index (BMI), comorbidities (diabetes mellitus [DM], hypertension [HT]), prior urinary tract infection (urinary tract infection that existed immediately before RIRS and was treated with antibiotics before surgery), prior stone passage (for any side), stone burden, stone density, number of stones (single or multiple), stone localization (pelvis, upper calyx, middle calyx, lower calyx, multiple localization), surgery side, the presence of hydronephrosis and need for DJ stent due to difficult ureter for all patients were reviewed. All patients were diagnosed by non-contrast computed tomoghraphy (CT). Stone burden was defined as longest diameter of the stone and sum of the diamaters of all stones in case of multiple stones.

Difficult ureter was defined as the insertion inability of semi-rigid ureterorenoscope or UAS (even if semi-rigid ureterorenoscopy was successful before UAS) into the ureter at the surgery side. All patients were divided in to two groups as difficult ureter group and non-difficult ureter group. Two groups were compared in terms of demographic, clinical and radiologic parameters.

RIRS procedures were performed under general anaesthesia in the lithotomy position. Ureterorenoscopy was performed with a 9.5 F semi-rigid ureterorenoscope (Karl Storz, Tuttingen, Germany) before RIRS for passive ureteral dilatation. After inserting guidewire by semi-rigid ureterorenoscope, 9.5–11 F ureteral access sheath (Flexor® Ureteral access sheath, Cook Medical, USA) was used and after the access sheath reached the collecting system, the collecting system was reached by entering through the access channel with a 7.5 F flexible ureterorenoscope (Karl Storz, Flex X2, GmbH, Tuttlingen, Germany). If the ureter was resistant to insertion of semi-rigid ureterorenoscope, we did not try to insert UAS and a DJ stent was placed and RIRS was postponed for two weeks for the next RIRS session. If the ureter was resistant to insertion of UAS even if semi-rigid ureterorenoscopy was successful before UAS, a DJ stent was placed and RIRS was postponed for two weeks for the next RIRS session. After two weeks, if the ureter was still resistant to insertion of semi-rigid ureterorenoscope or UAS, we performed a retrograde pyelogram and placed a DJ stent for two more weeks. The stone was fragmented using a holmium-yttrium-aluminum-garnet laser (200–365 μm) sent from the working channel of the flexible ureterorenoscope. All operations were performed by the surgeons with at least 10 years of RIRS experience.

Data coding and statistical analyses were carried out on the computer using the SPSS 22 software (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The conformity of the variables to the normal distribution was analyzed using the Shapiro-Wilk tests. Non-categorical parameters were presented as mean ± standart deviation (SD) or median (interquartile range). Mann–Whitney U test was used to compare non-categorical parameters and Chi-square or Fisher's exact tests were used for categorical variables. The risk factors for difficult ureter were determined by univariate and multivariate logistic regression analysis with Backward LR method. A p value of <0.05 was accepted as statistically significant.

Table 1. *Comparison of demographic, clinical and radiologic characteristics of patients with difficult and non-difficult ureter*

	Total (n = 454)	Non-difficult ureter (n = 420, 92.5%)	Difficult ureter (n = 34, 7.5%)	p
Age (years) (Mean ±SD)	45.6 ±14	46 ±14.1	40.5 ±11.8	**0.016**^{m}
Gender				
Male, n (%)	291 (64.1)	276 (65.7)	15 (44.1)	**0.012**^{c}
Female, n (%)	163 (35.9)	144 (34.3)	19 (55.9)	
BMI (kg/m^2) (Mean ±SD)	27.5 ±4.2	26.4 ±4	28.1 ±4.4	0.136^m
Comorbidities				
DM, n (%)	87 (19.2)	82 (19.5)	5 (14.7)	0.492^c
HT, n (%)	126 (27.8)	117 (27.9)	9 (26.5)	0.862^c
Prior urinary tract infection, n (%)	38 (8.4)	32 (7.6)	6 (17.6)	**0.043**^{f}
Prior stone passage, n (%)	113 (24.9)	9 (26.5)	104 (24.8)	0.825^c
Stone burden (mm^2) (Mean ±SD)	16.5 ±7.5	16.5 ±7.6	17.3 ±6.9	0.34^m
Stone density (HU) (Mean ±SD)	959.6 ±330.8	956.2 ±332.6	1001.9 ±309.6	0.443^m
Number of stones				
Single, n (%)	295 (65)	275 (65.5)	20 (58.8)	0.434^c
Multiple, n (%)	159 (35)	145 (34.5)	14 (41.2)	
Stone localization				
Pelvis, n (%)	197 (43.4)	184 (43.8)	13 (38.2)	
Upper calyx, n (%)	30 (6.6)	28 (6.7)	2 (5.9)	
Middle calyx, n (%)	36 (7.9)	32 (7.6)	4 (11.8)	0.826^f
Lower calyx, n (%)	127 (28)	116 (27.6)	11 (32.4)	
≥2 calyxies, n (%)	64 (14.1)	60 (14.3)	4 (11.7)	
Surgery side				
Right, n (%)	218 (48)	202 (48.1)	16 (47.1)	0.907^c
Left, n (%)	236 (52)	218 (51.9)	18 (52.9)	
Precence of hydronephrosis	265 (58.4)	246 (58.6)	19 (55.9)	0.76^c

SD – standard deviation; BMI – body mass index; DM – diabetes mellitus; HT – hypertension; HU: Houndsfield Unit, n – numer of patients
^{m} Mann Whitney U Test; ^{c} Chi-square Test; ^{f} Fisher's exact test

RESULTS

A total of 454 patients who underwent RIRS for primary kidney stones were included. The mean age of the 454 patients was 45.6 ±14 years and the mean BMI was 27.5 ±4.2 kg/m². 64.1% of the patients were male. The incidence of difficult ureter was 7.5% (34/454). It was not possible to insert semi-rigid ureterorenoscope into the ureter in 23 patients and access sheath in 11 patients. The patients in difficult ureter group were younger (mean age 40.5 years vs 46 years, p = 0.016). In addition, female gender and prior urinary tract infection rates were higher in difficult ureter group (55.9% vs 34.3%, p = 0.012 and 17.6% vs 7.6%, p = 0.043, respectively). There were no significant differences between two groups in terms of BMI, presence of comorbidities, prior stone passage, surgery side, presence of hydronephrosis and radiologic characteristics of stones. Demographic, clinical and radiologic characteristics of patients were summarized in Table 1.

Multivariate logistic regression analysis indicated that the factors significantly associated with higher odds of having a difficult ureter in primary RIRS patients were younger age (OR 1.040; 95% CI 1.010–1.070; p = 0.008), female gender (OR 2.859; 95% Cl = 1.383–5.908; p = 0.005) and prior urinary tract infection (OR 3.327; 95% CI 1.230–8.999; p = 0.018) (Table 2).

DISCUSSION

Primary RIRS represents an effective approach for the clearance of stone burden from the cavities of the pelvicalyceal system in one step, but the existing data demonstrate that this scenario is not always feasible. Patients with younger age, female gender and prior urinary tract infection should be informed that they have a higher risk of failed semi-rigid ureterorenoscope or UAS insertion.

In our patient cohort, there was one case of ureter access failure for every 13 patients, and this failure manifested mostly at the initial step of ureter dilatation by semi-rigid ureteroscope insertion. The data analysis showed that the characteristics of the stone disease (stone burden, laterality, localization into the pelvicalyceal system, density, hydronephrosis) were not different among patients with and without successful ureteral access. On the contrary, the possibility of achieving ureteral access was significantly higher among males, older patients, or patients without prior urinary tract infections. The above results are in part anticipated since the tension of ureteral wall musculature is expected to be higher in younger patients, which comprises an unfavorable parameter for UAS insertion. Moreover, the manifestation of symptomatic urinary infection episodes in the patient's medical history suggests a narrower ureter and a subsequent higher resistance in urine transport. Interestingly, the UAS insertion was easier in male patients, despite the more complex anatomy of the lower urinary system.

During our literature search on the accessibility of the ureter during retrograde endoscopic surgery, we found several studies relating to significant parameters and predictive factors. The role of patient age was already demonstrated in 2014 by Mogilevkin et al., with older patients being more amenable

Table 2. *Determination of independent risk factors for difficult ureter by logistic regression analysis*

Parameters	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Younger age (per 1 year)	1.030 (1.003–1.059)	**0.03**	1.040 (1.010–1.070)	**0.008**
Female gender	2.428 (1.198–4.92)	**0.014**	2.859 (1.383–5.908)	**0.005**
BMI (per 1 kg/m²)	1.008 (0.911–1.116)	0.872		
Precence of DM	0.711 (0.267–1.892)	0.494		
Precence of HT	0.932 (0.423–2.057)	0.862		
Prior urinary tract infection	2.598 (1.002–6.735)	**0.049**	3.327 (1.230–8.999)	**0.018**
Prior stone passage	1.094 (0.495–2.419)	0.825		
Stone burden (per 1 mm)	1.014 (0.971–1.059)	0.538		
Stone density (per 1 HU)	1 (0.999–1.001)	0.438		
Presence of multiple stones	1.328 (0.651–2.706)	0.435		
Surgery side (left)	0.959 (0.476–1.932)	0.907		
Precence of hydronephrosis	0.896 (0.443–1.812)	0.76		

SD – standard deviation; BMI – body mass index; DM – diabetes mellitus; HT – hypertension; HU: Houndsfield Unit, n – numer of patients to UAS insertion [9]. As expected, the anatomic characteristics of the ureter and the adjacent structures seem to play a significant role in ureter accessibility. In 2020, Cho et al. studied the anatomic course of the ureter in male patients with and without failure during ureteral access and found that patients with a difficult ureter had a significantly more lateral course of the lower ureter [15]. More recently, Azhar et al. studied the effect of ureteral orifice configuration on ureter accessibility and found that a tent-shaped ureteral orifice was the significant factor in the multivariate analysis [16]. In 2022, Hu et al. investigated the factors contributing to the failure of UAS insertion and reported that a short diameter of the ipsilateral common iliac artery was unfavorable for advancing the UAS in the ureter [17]. Not only the anatomic parameters but also the dynamic characteristics of the ureteral wall seem to affect the ureteral accessibility. According to a study by Viers et al., the reduced (<50%) opacification of the ureter during the excretory phase of contrast-enhanced CT, a finding suggesting narrowed ureteral lumen or increased ureteral wall tension, increased the possibility for ureteral access failure by 4.4 times [18]. Similarly, Imano et al. compared the patients with ureteral access success and failure, and reported that negative traceability of the ureter (failure to detect the ureter in every slice of the non-enhanced CT) was the most significant independent factor, which predicted the need for prestenting [19]. In 2022, Mao et al. investigated the effect of bladder filling status on the UAS insertion resistance and the risk of distal ureteral injury during RIRS [20]. The study concluded that bladder filling was a significant and independent factor of the above outcomes. Recently, Hu et al. pooled the results of the studies on the effect of a1-blockers on the success rate of UAS insertion and found that preoperative a1-blockers can increase the above rate and contribute to the decrease of complications [21].

This study has some limitations. This study was designed retrospectively, and all data are from single center. In addition, the data on preoperative alpha-blocker use by patients which is known to aid in UAS insertion was not available.

The results of our study can be considered complementary to the already existing data on the prediction of UAS insertion success. The sum of the evidence on the above topic shows that a wide variety of parameters affect ureteral accessibility. Additionally, to this multifactorial effect, the continuous technological advancements and the miniaturization of the endourological equipment are expected to complicate further the prediction of the eligible patients for primary RIRS. Lastly, the results of the available studies are operator-dependent, which renders the pooling of these results not feasible. More studies, prospectively conducted and adequately powered, are needed to construct a reliable predicting system for the difficult ureter in patients planned for RIRS.

CONCLUSIONS

In the current study, we reported one case of failed ureteral access for every 13 RIRS procedures, and we found that these cases of difficult ureter were associated with younger age at the time of RIRS, the female sex and the manifestation of urinary infections in the patient medical history. The above factors affected the ureteral accessibility significantly and independently, and they can contribute to the construction of a predictive system for patients, who are not eligible for primary RIRS and must undergo preoperative ureteral stenting.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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