ORIGINAL RESEARCH
Endourology

Doi: 10.4274/jus.galenos.2023.2022.0039
J Urol Surg, 2023;10(2):119-128

The Efficacy and Safety of Retrograde Intrarenal Surgery: A Multi-Center Experience of the RIRSearch Group Study

Murat Akgül[1], Hakan Çakır[2], Önder Çinar[3], Oktay Özman[4], Cem Başataç[5], Duygu Sıddıkoğlu[6], Çağrı Doğan[1], Ali Barbaros Başeskioğlu[7], Cenk Murat Yazıcı[1], Eyüp Sancak[8], Haluk Akpınar[5], Bülent Önal[9]

[1]Tekirdağ Namık Kemal University Faculty of Medicine, Department of Urology, Tekirdağ, Turkiye
[2]Acıbadem Fulya Hospital, Clinic of Urology, İstanbul, Turkiye
[3]Medicana International Samsun Hospital, Clinic of Urology, Samsun, Turkiye
[4]Gaziosmanpaşa Training and Research Hospital, Clinic of Urology, İstanbul, Turkiye
[5]Group Florence Nightingale Hospitals, Clinic of Urology, İstanbul, Turkiye
[6]Çanakkale Onsekiz Mart University Faculty of Medicine, Department of Biostatistics, Çanakkale, Turkiye
[7]Acıbadem Eskişehir Hospital, Clinic of Urology, Eskişehir, Turkiye
[8]Çanakkale Onsekiz Mart University Faculty of Medicine, Department of Urology, Çanakkale, Turkiye
[9]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Urology, İstanbul, Turkiye

What's known on the subject? and What does the study add?

Retrograde intrarenal surgery (RIRS) is a reliable surgical method for the treatment of urinary system stone disease. This study evaluated the effectiveness and safety of RIRS considering more than 1000 cases based on multi-center experience. The size of the stone, stone location and surgical experience could affect the success rate. Although most consequences are mild and rare, there could nevertheless be serious, life-threatening complications.

Abstract

Objective: We reported the results of retrograde intrarenal surgeries (RIRS) according to multi-center experience and to assess the efficacy and safety of this procedure.

Materials and Methods: A total of 1067 patients to whom RIRS operations were performed between 2016 and 2021 were included in the study. The demographic and clinical features of patients, stone properties, per-operative, and post-operative results were analyzed retrospectively. Additionally, the success and complication rates of RIRS according to the clinical and demographic properties of the patients were analyzed.

Results: The mean age, stone volume, operation time, and hospitalization time were 46.8±15.4, 1011 mm^3 (min 19 mm^3- max 12.483 mm^3), 67.4±30.8 min, and 1.83±2.3 days, respectively. The stone-free (success) rate after RIRS was 74.5%. In multivariate analysis, pre-op pyuria, number of stones, and stone volume had a significant effect on success. There were 251 (23.5%) patients with post-operative complications. The most common complications were hematuria, fever, and urinary tract infections; they comprised 86.8% of all complications. The number of stones, pre-op ESL, and absence of pre-operative DJ stent had a significant effect on complications in multivariate analysis.

Conclusion: Retrograde intrarenal surgery is an efficient minimal invasive procedure for treating urinary system stone disease with low morbidity and high success rates. Although the complication rates are mostly insignificant, there may also be severe vital complications.

Keywords: Urinary system stone disease, retrograde intrarenal surgery, success rates, complication

Correspondence: Murat Akgül MD, Tekirdağ Namık Kemal University Faculty of Medicine, Department of Urology, Tekirdağ, Turkiye
Phone: +90 505 339 96 02 **E-mail:** drmuratakgul@gmail.com **ORCID-ID:** orcid.org/0000-0001-6187-1940
Received: 14.04.2022 **Accepted:** 29.01.2023

Cite this article as: Akgül M, Çakır H, Çinar Ö, Özman O, Başataç C, Sıddıkoğlu D, Doğan Ç, Başeskioğlu AB, Yazıcı CM, Sancak E, Akpınar H, Önal B. The Efficacy and Safety of Retrograde Intrarenal Surgery: A Multi-Center Experience of the RIRSearch Group Study. J Urol Surg, 2023;10(2):119-128.

Introduction

Urinary system stone disease (USSD) is one of the most common urological diseases with a worldwide prevalence ranging between 2% and 20% (1-3). It is also a prevalent disease in our country with a reported prevalence rate of 11.1% (4). Extracorporeal shock wave lithotripsy (ESL), percutaneous nephrolithotomy (PNL), mini percutaneous nephrolithotomy, micropercutaneous nephrolithotomy, retrograde intrarenal surgery (RIRS), laparoscopic stone surgery, and open stone surgery are the treatment opportunities for USSD (5,6). With the technological advancements in endoscopic systems, minimally invasive procedures replaced open surgical procedures. A flexible ureteroscope was one of these innovations that enabled the clinician to reach the intrarenal system through the ureters in a retrograde fashion.

During the last 2 decades, RIRS had a significant role for treating USSD with its high efficiency and safety. The urologic guidelines recommended this technique as an alternative to the first-line treatment option for upper urinary tract stones smaller than 2 cm (7,8). Even some studies have showed that this technique might be used effectively in USSD larger than 2 cm (9). Retrograde intrarenal surgery was also shown to be effective and safe in patients with a solitary kidney, pregnant patients, obese patients, and patients with renal anomalies (10,11). However, RIRS is not a complication-free surgery and may also have some significant complications. For this reason, it is important to evaluate the efficiency and safety of RIRS by the data obtained from high-volume centers.

In this study, we aimed to report the multi-center experience of RIRS and evaluate the efficiency and safety of this surgery.

Materials and Methods

The study was designed according to the Declaration of Helsinki principles and was approved by the Tekirdağ Namık Kemal University Ethics Committee (no: 2020.114.05.15). The patients who underwent RIRS for treating USSD between 2017-2021 in 7 referral centers were retrospectively included in the study. Patients younger than 18 years old were excluded from the study. The demographic and clinical characteristics of the patients, including age, gender, body mass index, presence of preoperative DJ stent, anatomic abnormalities, age-adjusted Charlson Comorbidity index (CCI), preoperative serum creatinine level, presence of preoperative hematuria - pyuria, preoperative urine culture, the usage of anticoagulants, preoperative hydronephrosis, operation time, surgical side, stone volume, stone density, stone location, perioperative and postoperative complications, hospitalization time, and stone-free status were noted. All patients had the evaluation of urinalysis, urine culture, serum creatinine level, and non-contrast abdominopelvic tomography before the surgery. The 3-dimensional sizes of the stones were used to determine the stone volume by using the formula: AxBxCx0.524 (12). The sum of each stone volume was used to calculate the total stone volume for the patients with multiple stones. Pre-operative hematuria is defined as the presence of 3 or more erythrocytes (≥3 RBC) per high power field and pre-operative pyuria is defined as >10 white blood cell per high-power field on a urine microscopy evaluation. The patients who had positive urine cultures were treated according to the antibiogram, and the surgery was performed under sterile urine. All patients received second-generation cephalosporins for antibiotic prophylaxis before the surgery. To evaluate the stone-free status of the patients, non-contrast abdominal pelvic tomography was performed in the post-operative 4th week of the surgery. The success of the surgery was defined as the presence of stone-free patients after the surgery, and the patients with residual stone <4 mm were defined as stone-free patients.

The surgical procedure was performed by an experienced surgeon (>50 cases). The surgery started with standard cystoscopy and retrograde pyelography evaluation. Under direct vision and fluoroscopy guidance, a 0.035-inch safety guidewire (Sensor®, Boston Scientific, Marlborough, MA, USA) was introduced to the system. To visualize the ureter and perform active dilatation, a semirigid ureteroscopy was performed. After the semirigid ureteroscopy, a 10-12 Fr. ureteral access sheath (Bi-Flex™, Rocamed, Monaco) was inserted over the guidewire and placed just 1 cm below the ureteropelvic junction or just distal to the upper ureteral stone. For the patients in whom the insertion of the ureteral access sheath (UAS) was impossible, the back-loading technique was used. In this approach, a flexible ureteroscope was directly inserted into the system via the glide wire without UAS. If this was also impossible, the surgery was finished by the insertion of a Double J (DJ) stent and was postponed for 2 weeks. On the other hand, DJ stent insertion was also applied for patients, especially those with colic pain and urinary tract infection in whom diversion was required pre-operatively. In our study design, there is no stone burden limit for the back-loading approach. The bladder was drained by a 10 Fr. feeding tube during the procedure. The flexible ureteroscope (Storz Flex X^2, Germany) was inserted through the UAS and a holmium: YAG laser with a 272 µm laser fiber was used to fragment the stones. Constant gravity-based irrigation was used with a height of 50 cm above the patient, and a hand pumping system was used if necessary. The laser energy and pulse frequency were varied based on the stone burden, stone density, and the surgeon's preference. Stone fragments >2 mm were extracted using a nitinol basket catheter (Dakota®, Boston Scientific, Marlborough, MA, USA). A 4.7Fr DJ stent was inserted into the urinary system and left in place for 2-4 weeks according to the surgeon's preference.

Statistical Analysis

Categorical variables were expressed as frequencies and percentages (%). Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range (IQR). The Shapiro-Wilk test was used to assess the normality assumption for the continuous variables. The differences in proportions between the groups were compared using chi-square or Fisher Exact tests as appropriate. The Student's t-test was used to compare continuous variables in two independent groups. Odds ratios [95% confidence intervals (CI)] of the independent clinical parameters were calculated using univariate and multiple logistic regression models to predict the outcome variables: Success and total complications. A multivariate logistic regression analysis was built by performing a stepwise variable selection on those variables with a univariate p-value <0.25. The Hosmer and Lemeshow test was computed to detect the goodness of fit in the multiple logistic regression models, and a nonsignificant p-value indicated a good fit. All statistical analyses were conducted using SPSS 19.0 for Windows Version 19.0 software (IBM Corp., Armonk, NY, USA). All p-values of less than 0.05 were considered to indicate statistical significance.

Results

A total of 1.067 patients were included in the study. The mean age of the patients was 46.8±15.4 years. There were 429 (40.2%) female and 638 (59.8%) male patients with a female: male ratio of 1:1.48. The clinical and demographic properties of the patients are given in Table 1. There were 509 (47.7%) patients with right-sided, 500 (46.9%) patients with left-sided and 58

Table 1. Demographic and clinical properties of study population

Parameter	Value
Age (years)	46.8±15.4
Gender	
Male (%)	638 (59.8%)
Female (%)	429 (40.2%)
Surgical side	
Right (%)	509 (47.7%)
Left (%)	500 (46.9%)
Bilateral (%)	58 (5.4%)
Body mass index (kg/m²)	26.9±3.5
Preoperative ESL	
No (%)	737 (69.1%)
Yes (%)	330 (30.9%)
Preoperative DJ stent	
No (%)	729 (68.3%)
Yes (%)	338 (31.7%)

Table 1. continued

Parameter	Value
Age adjusted CCI	1.57±1.62
Preoperative creatinine (mg/dL)	0.95±0.37
Preoperative pyuria	
No (%)	449 (42.1%)
Yes (%)	618 (57.9%)
Preoperative hematuria	
No (%)	299 (28.0%)
Yes (%)	768 (72.0%)
Anticoagulant usage	
No (%)	953 (89.3%)
Yes (%)	114 (10.7%)
Preoperative urine culture	
Negative (%)	981 (91.9%)
Positive (%)	86 (8.1%)
Stone location	
Upper calyx	37 (3.5%)
Middle calyx	56 (5.2%)
Lower calyx	120 (11.2%)
Pelvis	237 (22.2%)
Upper ureter	243 (22.8%)
Multicalyx	374 (35.1%)
Stone density (HU)	956±326
Number of stones	1.63±1.20
Stone volume (mm³)	1011.2±1977.7
Multiple stone	
No (%)	624 (58.5%)
Yes (%)	443 (41.5%)
Preoperative hydronephrosis	
No (%)	618 (57.9%)
Yes (%)	449 (42.1%)
Operation time (min)	67.4±30.8
Hospitalisation time (day)	1.83±2.30
Peroperative complication	
No (%)	972 (91.1%)
Yes (%)	95 (8.9%)
Postoperative complication	
No (%)	816 (76.5%)
Yes (%)	252 (23.5%)
Postoperative creatinine (mg/dL)	0.93±0.68
Stone-free status	
No (%)	272 (25.5%)
Yes (%)	795 (74.5%)

ESL: Extracorporeal shock wave lithotripsy, CCI: Charlson Comorbidity index, DJ: Double J, HU: Hounsfield unit

J Urol Surg,
2023;10(2):119-128

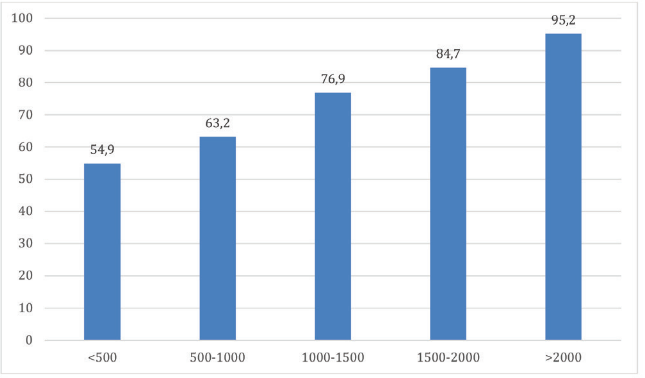

Figure 1. Retrograde intrarenal surgery operation time (minute) according to the stone volume (mm^3)

(5.4%) patients with bilateral RIRS. According to the presence of a kidney anomaly, there were 61(5.7%) patients with a solitary kidney, 25 (2.3%) patients with horseshoe kidney, 7 (0.7%) patients with a double collecting system, and 7 (0.7%) patients with malrotated kidney. In the preoperative evaluation, 981 (91.9%) patients had sterile urine, whereas 86 (8.1%) patients had positive cultures and the most common microorganisms were *E. coli* and *Enterococci*. The mean hospitalization time was 1.83±2.30 days. The mean operation time was 67.4±30.8 min ranging between 20-180 min. The operation times according to the stone volumes are shown in Figure 1. It was observed that the operation time increased significantly as the stone volume increased (p<0.001).

The stone-free rate of the study population was 74.5%. When we evaluated the patients according to surgical succes, the surgical side, age-adjusted CCI, the presence of preoperative pyuria, presence of preoperative hematuria, stone location, Modified Seoul National University Renal Stone Complexity (RESC) score, stone density, the number of stones, stone volume, presence of multiple stones, and operation time were significantly different between the groups (Table 2). The mean age-adjusted CCI was 1.75±1.53 in patients with unsuccessful surgery whereas it was 1.47±1.61 at patients with successful surgery (p=0.003). The presence of preoperative pyuria and hematuria was significantly higher in patients with unsuccessful surgery. The odd's ratios for preoperative pyuria and hematuria were 0.348 (95% CI: 0.252-0.481) and 0.607 (95% CI: 0.422-0.873) respectively. The rate of lower calyx location and the presence of multicalyx stone were significantly higher in patients with unsuccessful surgery (p<0.001). The mean stone density and the mean stone volume were 1067.4±287.5 HU and 1922.4±2781.6 mm^3 in patients with unsuccessful surgery, which were significantly higher than the patients with successful surgery. A total of 338 (31.7%) patients had a DJ stent preoperatively. In this group, the ureteral access sheath was successfully inserted in all cases, except 11 (3.3%). On the other hand, the ureteral access sheath could not be inserted in 55 (7.5%) of 729 patients who did not have a DJ stent preoperatively (p=0.007).

There were 251 (23.5%) patients with postoperative complications. When we compared the study group according to the presence of complications, the surgical side, the presence of preoperative ESL, presence of DJ stent, age-adjusted CCI, preoperative culture, stone location, number of stones, presence of multiple stones, and the presence of preoperative hydronephrosis were significantly different between the groups (Table 3). The rate of the presence of preoperative DJ stent was 17.5% in patients with complications, whereas it was 36.1% in patients without complications (p<0.001). The odd's ratio for the preoperative DJ stent was 0,403 (95% CI: 0.281-0.578). The mean age-adjusted CCI was significantly higher in patients with postoperative complications (p=0.006). The preoperative urine culture was positive at 11.2% and 7.1% of patients with and without postoperative complications, respectively (p=0.039). The odd's ratio for preoperative urine culture was 1.742 (95% CI: 1.056-2.876). The rate of multicalyx stone location and the mean number of stones were significantly higher in patients with postoperative complications (p<0.001 for each). The presence of preoperative hydronephrosis was 47.8% in patients with postoperative complications, whereas it was 40.3% in patients without a complication (p=0.036). The odd's ratio for preoperative hydronephrosis was 1.152 (%95 CI: 0.859-1.546).

The most common complications were hematuria, fever, and urinary tract infection. These three complications compromised 86.8% of all complications (Table 4). When we classified the complications according to Clavien-Dindo classification, 96 (38.2%) patients had Clavien I, 125 (49.8%) patients had Clavien II, 17 (6.8%) patients had Clavien IIIb, 12 (4.8%) patients had Clavien IVa, and 1 (0.4%) patient had Clavien V complications (Table 4). The patient who had a Clavien V complication had a significantly rare complication. This patient had persistent fever, pancytopenia, and hepatosplenomegaly who was diagnosed with hemophagocytic syndrome. The patient died from multiorgan failure during the postoperative third week of the RIRS. The rate of Clavien < III complications was 88.0% and the rate of Clavien ≥ III complication was 12.0%. The main complications in Clavien ≥ III were stent migration and sepsis.

The univariate and multivariate analyzes for the success and complications of RIRS are shown in Table 5. In univariate analysis, bilaterality, age-adjusted CCI, pre-op pyuria, pre-op hematuria, stone location, RESC score, stone density, number of stones, and stone volume had a significant effect on success. In multivariate analysis, pre-op pyuria, number of stones, and stone volume had a significant effect on success. When we examined the univariate and multivariate analyzes for complications; bilaterality, pre-op ESL, absence of pre-op DJ stent, age-adjusted CCI, pre-op pyuria, stone location, RESC score, number of stone and stone

Table 2. Success rates of retrograde intrarenal surgery according to clinical and demographic properties of the patients				
	Success (+) (n=795)	**Success (-) (n=272)**	**Odd's ratio**	**p-value**
Age (years)	46.1±14.8	47.1±13.6		0.348
Gender				
Male (%)	465 (58.4%)	173 (66.6%)		0.078
Female (%)	330 (41.6%)	99 (33.4%)		
Surgical side				
Right (%)	382 (48.0%)	127 (46.7%)		**0.002**
Left (%)	359 (45.2%)	141 (51.8%)		
Bilateral (%)	54 (6.8%)	4 (1.5%)		
Body mass index (kg/m²)	25.8±3.18	27.5±4.38		0.597
Preoperative ESL				
No (%)	548 (68.9%)	189 (69.5%)	1.126 (95% CI: 0.823-1.541)	0.864
Yes (%)	247 (31.1%)	83 (30.5%)		
Preoperative DJ stent				
No (%)	545 (68.6%)	184 (67.6%)	0.948 (95% CI: 0.697-1.288)	0.782
Yes (%)	250 (31.4%)	88 (32.4%)		
Age adjusted CCI	1.47±1.61	1.75±1.53		**0.003**
Preoperative creatinine (mg/dL)	0.94±0.32	0.99±0.51		0.187
Preoperative pyuria				
No (%)	380 (47.8%)	69 (25.4%)	0.348 (95% CI: 0.252-0.481)	**<0.001**
Yes (%)	415 (52.2%)	203 (74.6%)		
Preoperative hematuria				
No (%)	244 (30.7%)	55 (20.2%)	0.607 (95% CI: 0.422-0.873)	**0.007**
Yes (%)	551 (69.3%)	217 (79.8%)		
Anticoagulant usage				
No (%)	715 (89.9%)	238 (87.5%)	0.763 (95% CI: 0.487-1.196)	0.261
Yes (%)	80 (10.1%)	34 (12.5%)		
Preoperative urine culture				
Negative (%)	737 (92.7%)	244 (89.7%)	0.541 (95% CI: 0.316-0.926)	0.117
Positive (%)	58 (7.3%)	28 (10.3%)		
Stone location				
Upper calyx	21 (2.6%)	16 (5.9%)		**<0.001**
Middle calyx	47 (5.9%)	9 (3.3%)		
Lower calyx	76 (9.6%)	44 (16.2%)		
Pelvis	186 (23.9%)	51 (18.8%)		
Upper ureter	212 (26.7%)	31 (11.4%)		
Multicalyx	253 (31.8%)	121 (44.4%)		
RESC score	1.99±1.66	2.32±1.53		**<0.001**
Stone density (HU)	929.2±293.6	1067.4±287.5		**<0.001**
Number of stones	1.51±1.10	1.99±1.36		**<0.001**
Stone volume (mm³)	727.5±1557.8	1922.4±2781.6		**0.011**
Multiple stone				
No (%)	500 (62.9%)	124 (45.6%)	0.423 (95% CI: 0.312-0.524)	**<0.001**
Yes (%)	295 (37.1%)	148 (54.4%)		
Preoperative hydronephrosis				
No (%)	464 (58.4%)	154 (56.6%)	0.993 (95% CI: 0.743-1.328)	
Yes (%)	331 (41.6%)	118 (43.4%)		0.614
Operation time	61.56±27.36	83.68±34.36		**0.001**

ESL: Extracorporeal shock wave lithotripsy, CCI: Charlson Comorbidity index, DJ: Double J, HU: Hounsfield unit, CI: Confidence interval

Table 3. Complication rates of retrograde intrarenal surgery according to clinical and demographic properties of the patients

	Complication (+) (n=251)	Complication (-) (n=816)	Odd's ratio	p-value
Age (years)	45.5±14.7	47.3±15.7		0.043
Gender				
Male (%)	147 (58.6%)	491 (60.2%)	1.074 (95% CI: 0.801-1.440)	0.633
Female (%)	104 (41.4%)	325 (39.8%)		
Surgical side				
Right (%)	114 (45.4%)	395 (48.4%)		**<0.001**
Left (%)	111 (44.2%)	389 (47.7%)		
Bilateral (%)	26 (10.4%)	32 (3.9%)		
Body mass index (kg/m²)	27.2±5.2	26.9±4.1		0.818
Preoperative ESL				
No (%)	200 (79.7%)	537 (65.8%)	0.507 (95% CI: 0.359-0.716)	**<0.001**
Yes (%)	51 (20.3%)	279 (34.2%)		
Preoperative DJ stent				
No (%)	207 (82.5%)	522 (63.9%)	0.403 (95% CI: 0.281-0.578)	**<0.001**
Yes (%)	44 (17.5%)	294 (36.1%)		
Age adjusted CCI	1.65±1.61	1.37±1.61		**0.006**
Preoperative creatinine (mg/dL)	0.95±0.3	0.95±0.4		0.930
Preoperative pyuria				
No (%)	112 (44.6%)	337 (41.3%)	0.628 (95% CI: 0.464-0.848)	0.351
Yes (%)	139 (55.4%)	479 (58.7%)		
Preoperative hematuria				
No (%)	67 (26.7%)	232 (28.4%)	1.021 (95% CI: 0.731-1.426)	0.592
Yes (%)	184 (73.3%)	584 (71.6%)		
Anticoagulant usage				
No (%)	227 (90.4%)	726 (89.0%)	0.828 (95% CI: 0.506-1.356)	0.453
Yes (%)	24 (9.6%)	90 (11.0%)		
Preoperative urine culture				
Negative (%)	223 (88.8%)	758 (92.9%)	1.742 (95% CI: 1.056-2.876)	**0.039**
Positive (%)	28 (11.2%)	58 (7.1%)		
Stone location				
Upper calyx	10 (4.0%)	27 (3.3%)		**<0.001**
Middle calyx	16 (6.4%)	40 (4.9%)		
Lower calyx	40 (15.9%)	80 (9.8%)		
Pelvis	41 (16.3%)	196 (24.0%)		
Upper ureter	36 (14.3%)	207 (25.4%)		
Multicalyx	108 (43.1%)	266 (32.6%)		
Stone density (HU)	1008.1±316.3	953.7±343.7		0.203
Number of stones	2.07±1.42	1.57±1.15		**<0.001**
Stone volume (mm³)	1154.0±1840.7	838.6±1402.6		0.352
Multiple stone				
No (%)	109 (43.4%)	515 (63.1%)	2.118 (95% CI: 1.578-2.842)	**<0.001**
Yes (%)	142 (56.6%)	301 (36.9%)		
Preoperative hydronephrosis				
No (%)	131 (52.2%)	487 (59.7%)	1.152 (95% CI: 0.859-1.546)	**0.036**
Yes (%)	120 (47.8%)	329 (40.3%)		
Operation Time	70.94±36.78	69.22±29.67		0.815

ESL: Extracorporeal shock wave lithotripsy, CCI: Charlson Comorbidity index, DJ: Double J, HU: Hounsfield unit, CI: Confidence interval

Table 4. Complications after retrograde intrarenal surgery according to Clavien-Dindo classification

	Clavien I	Clavien II	Clavien IIIa	Clavien IIIb	Clavien IVa	Clavien IVb	Clavien V	Total (%)
Hematuria (%)	72 (28.7)	20 (8.0)	-		-		-	92 (36.7)
Fever (%)	15 (5.9)	39 (15.5)						54 (21.4)
Urinary tract infection (%)	9 (3.6)	63 (25.1)						72 (28.7)
Stent migration (%)				12 (4.8)				12 (4.8)
Sepsis (%)		3 (1.2)			12 (4.8)			15 (6.0)
Ureteral perforation (%)				3 (1.2)				3 (1.2)
Bladder perforation (%)				2 (0.8)				2 (0.8)
Hemophagocyte syndrome (%)							1 (0.4)	1 (0.4)
Total (%)	96 (38.2)	125 (49.8)	-	17 (6.8)	12 (4.8)	-	1 (0.4)	251 (100)

volume had a significant effect on complications in univariate analysis. Pre-op ESL, absence of pre-op DJ stent, and number of stones had a significant effects on complications in multivariate analysis. When the surgical side was right as a reference side at univariate analysis, there was no difference between the right and left sides on success and complication rates. However, there was a statistical difference between bilateral RIRS both in success and complications (p=0.005 and p=0.003) (Table 5).

Discussion

Urinary System Stone Disease (USSD) is one of the most common diseases in the world. The prevalence rates ranged between 2% and 20% in different parts of the world. It has a significantly high rate of recurrence that has been reported to be 50% (13,14). In terms of prevalence and recurrence rates, USSD is a general health system problem. The success rate of stone surgery depends on many factors; such as stone size, stone localization, stone type, presence of kidney anomaly, presence of obesity, and presence of a skeletal anomaly. For this reason, it may not be easy to choose the most suitable option for treating USSD. In the last three decades, the treatment strategy of USSD significantly changed. With the evolution of new technologic materials, minimally invasive surgical techniques became the pioneer of the USSD treatment. In a recent study, Heers and Turney (15) evaluated the types of procedures that were performed for treating USSD in the United Kingdom between 2009 and 2015. In this study, they documented a decrease in the number of ESLs, while they observed a significant increase in the number of RIRS.

With the worldwide acceptance of RIRS, several studies have evaluated the efficacy and safety of this surgery. Although there are several studies with a high number of patients in the international literature, there are not so many high-volume studies in our country. This kind of study is important for our national data and might be a significant source for international literature. In a national study, Firdolaş et al. (16) reported the result of 598 RIRS and reported a 78% stone-free rate in their series. In another national study, Akcay et al. (17) reported the results of their 290 patients series and reported a stone-free rate as 80%. In our study, the stone-free rate was found to be 74.5%. The stone-free rate of our series was lower than the literature. This difference might be due to the high rate of patients in our series with multicalyx location (35.1%) and lower calyx (11.2%) localization. Additionally, it might be due to the different definitions of "stone-free" status. Another possible reason for this difference may be related to the timing of the control evaluation. The small size of stones may persist just after the surgery that may expulse spontaneously over time. This might lead to lower stone-free rates for the studies, which evaluate their patients just after the surgery. Another factor may be the way of radiological control evaluation. Some studies have evaluated their patients' stone-free status with ultrasonography (USG) or kidney ureter bladder (KUB) X-ray that had lower sensitivity and specificity for evaluating renal stones. Small stones might not be noticed by USG or KUB X-ray and the stone-free rates might be overestimated. The size and localization of the stones could also affect the stone-free rates. Evaluating different high-volume series and performing standardized meta-analyses may overcome these possible biases.

In our study, a multivariate analysis of the demographic and clinical characteristics of the patients documented that the number of stones, preoperative pyuria, and stone volume were the main indicators of RIRS success. In the literature, stone volume was found to be one of the main predictors that may affect the success of the stone-free situation similar to our findings (18-20). Sari et al. (18) observed that stone volume, opacity, and operation time were the main factors that could change considerably the success status of RIRS according to multivariate analysis. Another study showed that (≥15 mm stones), increasing age, presence of a concomitant ureteral stone, and the presence of intraoperative complications were the main predictor factors that may affect the stone-free status (19). We found that preoperative stenting did not affect the

Table 5. Success and complication of retrograde intrarenal surgery according to univariate and multivariate analysis

	Success								Complication							
	Univariate analysis				Multivariate analysis				Univariate analysis				Multivariate analysis			
	p-value	OR	95% CI for OR		p-value	OR	95% CI for OR		p-value	OR	95% CI for OR		p-value	OR	95% CI for OR	
			Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper
Age	0.368	0.995	0.986	1.005					0.119	0.993	0.983	1.002				
Gender (male reference)	0.205	1.210	0.901	1.627					0.633	1.074	0.801	1.440				
Surgical side (right reference)																
Left	0.232	0.837	0.626	1.120					0.757	0.953	0.705	1.290				
Bilateral	0.005	4.487	1.591	12.657					0.003	2.338	1.336	4.091				
Body mass index	0.790	1.016	0.906	1.138					0.576	1.027	0.935	1.128				
Preop ESL	0.458	1.126	0.823	1.541					<0.001	0.507	0.359	0.716	0.001	0.526	0.365	0.756
Preop DJ stent	0.731	0.948	0.697	1.288					<0.001	0.403	0.281	0.578	<0.001	0.417	0.285	0.609
Age adjusted CCI	0.024	0.901	0.822	0.987					0.022	0.895	0.814	0.984				
Preop creatinine	0.063	0.707	0.491	1.019					0.883	0.971	0.660	1.430				
Preop pyuria	<0.001	0.348	0.252	0.481	0.001	0.454	0.290	0.713	0.002	0.628	0.464	0.848				
Preop hematuria	0.007	0.607	0.422	0.873					0.903	1.021	0.731	1.426				
Anticoagulan usage	0.238	0.763	0.487	1.196					0.453	0.828	0.506	1.356				
Stone location (upper calyx reference)																
Middle calyx	0.001	6.576	2.249	19.227					0.113	0.420	0.144	1.228				
Lower calyx	0.012	2.705	1.249	5.858					0.119	0.470	0.182	1.214				
Pelvis	0.014	2.579	1.208	5.505					0.106	0.460	0.179	1.181				
Upper ureter	0.003	3.201	1.490	6.874					0.071	0.420	0.164	1.077				
Multicalyx	<0.001	0.423	0.312	0.574					<0.001	2.118	1.578	2.842				
RESC score	0.010	0.891	0.816	0.973					<0.001	1.222	1.118	1.336				
Stone density (HU)	<0.001	0.998	0.998	0.999					0.124	1.000	1.000	1.001				
Number of stone (1 reference)																
Number of stone (2)	<0.001	0.429	0.297	0.620	0.002	5.925	1.962	17.889	<0.001	2.216	1.531	3.208	<0.001	2.097	1.437	3.060
Number of stone (3)	<0.001	0.240	0.144	0.401	0.016	2.724	1.208	6.142	<0.001	3.264	1.963	5.429	<0.001	3.215	1.906	5.424
Number of stone (4)	0.001	0.324	0.172	0.613	0.002	3.691	1.644	8.287	<0.001	3.726	1.991	6.972	<0.001	3.238	1.704	6.154
Number of stone (≥5)	0.010	0.409	0.196	0.853	0.008	2.940	1.319	6.557	0.012	2.526	1.227	5.199	0.076	1.943	0.932	4.051
Stone volume	<0.001	0.999	0.999	0.999	<0.001	0.999	0.999	1.000	0.045	1.001	1.000	1.000				
Multiple stone	<0.001	0.423	0.312	0.574					<0.001	2.118	1.578	2.842				
Preop hydronephrosis	0.964	0.993	0.743	1.328					0.346	1.152	0.859	1.546				

success rate (p=0.782). The effect of pre-operative stenting on success is controversial in the literature (21). Yuk et al. (22) found that preoperative ureteral stenting did not affect the success rate but it increased the success rate of access sheath placement. Bai et al. (23) also stated that preoperative stenting might not benefit the stone-free rate of the first month after surgery. However, there are also lots of studies in the literature that discuss the positive effect of preoperative stenting in RIRS (24,25). On the other hand, we found that preoperative stenting affects positively on complications.

Clavien and Dindo described a classification to standardize the complications of different surgeries (26). We also used this scale to evaluate the complications of our RIRS. The overall complication rate in our study group was 23.5%, which ranged between 8.3% and 37.5% in the literature (27,28). In a study, Cakici et al. (29) reported that the most frequent complications were fever, urinary system infection, and bleeding in their series. A similar relationship was also observed in our study. The most frequent complications were; bleeding, fever, and urinary tract infection. According to the Clavien classification, 88% of the complications were in the Clavien 1-2 category. These data documented that RIRS is a safe surgical technique. On the other hand, there were 12% of patients who had Clavien-3 or more complications, which documented that RIRS might also have life-threatening complications. We believe that this data also verify the importance of studies with high volume patients. Studies with a limited number of patients may underestimate the rates of Clavien 4 and 5 category complications.

In our study, a multivariate analysis of demographic and clinical characteristics showed that the number of stones, presence of preoperative ESL, and absence of preoperative DJ stent were predictors of postoperative complications. It was shown that different reasons might be related to complications in the literature according to the multivariate analysis (30,31). The study 602 RIRS cases determined that stone size and the mean operation time were the main indicators to predict complication status based on their multivariate analysis results (30). Another study found that urinary tract infections within six months, being female gender, mean operation time, and preoperative urine culture were the main determiners for RIRS related to complications (31).

Retrograde intrarenal surgery may also have mortal complications. The first case of mortality was reported in 1997 with septic shock (32). In the CROES study, it was reported that 5 patients (0.04%) died from various factors such as sepsis, cardiac, and pulmonary embolism (33). We did not have any mortality with sepsis, but one of our patients died due to "hemophagocytic syndrome". This complication was unexpected, but we could diagnose and start the appropriate treatment. Despite the early diagnosis and appropriate treatment, "hemophagocytic syndrome" has high mortality rates. We also observed the progressive deterioration of our patient with a mortal result (34).

Study Limitations

Our study has some limitations. The retrospective nature of our study is a limitation. On the other hand, the data that were used in the study were collected during the surgeries and postoperative time of the patients instantaneously. This may reduce the possible limitation of the retrospective design. The surgeries in this multi-center study were performed by different surgeons, which might lead to interpersonal bias. On the other hand, the surgeons used the same surgical procedures, which might also reduce the multi-surgeon bias.

Conclusion

Retrograde intrarenal surgery is an effective and safe surgical technique for treating USSD. RIRS is on its way to becoming the gold standard for USSD with advances in technology. The success rate of the RIRS depends on the stone size, stone location, and surgical experience. Although the complication rates are mostly low and mostly minor, there may also be severe life-threatening complications.

Ethics

Ethics Committee Approval: The Local Institutional Ethics Committee Tekirdağ Namık Kemal University (no: 2020.114.05.15) approved this study, and all steps were planned and conducted following the Declaration of Helsinki and its later amendments.

Informed Consent: Written informed consent on admittance to the hospital was obtained from all individuals, which permitted the use of respective medical information in clinical studies.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A., H.Ç., Ö.Ç., O.Ö., C.B., D.S., Ç.D., A.B.B., C.M.Y., E.S., H.A., B.Ö., Concept: M.A., C.M.Y., Design: M.A., C.M.Y., Data Collection or Processing: M.A., H.Ç., Ö.Ç., O.Ö., C.B., D.S., Ç.D., A.B.B., C.M.Y., E.S., H.A., B.Ö., Analysis or Interpretation: M.A., D.S., Ç.D., C.M.Y., Literature Search: M.A., Writing: M.A., C.M.Y.

Conflict of Interest: No conflicts of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

J Urol Surg,
2023;10(2):119-128

References

1. Smith LH. The medical aspects of urolithiasis: an overview. J Urol 1989;141:707-710.
2. Trinchieri A. Epidemiology of urolithiasis. Arch It Urol Androl 1996;68:203-249.
3. Curhan GC. Epidemiology of stone disease. Urol Clin N Am 2007;34:287-293.
4. Muslumanoglu AY, Binbay M, Yuruk E, Akman T, Tepeler A, Esen T, Tefekli AH. Updated epidemiologic study of urolithiasis in Turkey. I: Changing characteristics of urolithiasis. Urol Res 2011;39:309-314.
5. Assimos D, Krambeck A, Miller NL, Monga M, Murad MH, Nelson CP, Pace KT, Pais VM, Pearle MS, Preminger GM, Razvi H, Shah O, Matlaga BR. Surgical management of stones: American Urological Association / Endourological Society Guideline, Part I. J Urol 2016;196:1153-1160.
6. Yazıcı C, Akgül M, Arda E, Akpınar H. Can the Urologists Perform Stone Analysis, Metabolic Evaluation and Metaphylaxis at UrinaryTract Stone Disease in Tekirdağ? Dicle Med J 2019;46:405-410.
7. Parikh KP, Jain RJ, Kandarp AP. Is retrograde intrarenal surgery the game changer in the management of upper tract calculi? A single-center single-surgeon experience of 131 cases. Urol Ann 2018;10:29-34.
8. Turk C, Petrik A, Sarica K, Seitz C, Skolarikos A, Straub M, Knoll T. EAU guidelines on interventional treatment for urolithiasis. Eur Urol 2016;69:475-482.
9. Al Busaidy SS, Kurukkal SN, Al Hooti QM, Alsaraf MS, Al Mamari SA, Al Saeedi AK. Is RIRS emerging as the preferred option for the management of 2 cm-4 cm renal stones: our experience. Can J Urol 2016;23:8364-8367.
10. Lavan L, Herrmann T, Netsch C, Becker B, Somani BK. Outcomes of ureteroscopy for stone disease in anomalous kidneys: a systematic review. World J Urol 2020;38:1135-1146.
11. Sanguedolce F, Bozzini G, Chew B, Kallidonis P, de la Rosette J. The Evolving Role of Retrograde Intrarenal Surgery in the Treatment of Urolithiasis. Eur Urol Focus 2017;3:46-55.
12. Sorokin I, Cardona-Grau DK, Rehfuss A, Birney A, Stavrakis C, Leinwand G, Herr A, Feustel PJ, White MD. White. Stone volume is best predictor of operative time required in retrograde intrarenal surgery for renal calculi: implications for surgical planning and quality improvement. Urolithiasis 2016;44:545-550.
13. Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976-1994. Kidney Int 2003;63:1817-1823.
14. Amato M, Lusini ML, Nelli F. Epidemiology of nephrolithiasis today. Urol Int 2004;72:1-5.
15. Heers H, Turney BW. Trends in urological stone disease: a 5-year update of hospital episode statistics. BJU Int 2016;118:785-789.
16. Firdolaş F, Pirinççi N, Ozan T, Karakeçi A, Orhan I. Retrograde intrarenal surgery technique without using fluoroscopy and access sheet in the treatment of kidney Stones. Turk J Med Sci 2019;49:821-825.
17. Akcay M, Tepeler A, Tosun M, Basibüyük İ, Elbir F, Kardaş S, Akman T, Armağan A, Taşçı Aİ. Current Minimal Invasive Surgery Treatment for Kidney Stones: Bezmialem Experience. Bezmialem Science 2016;2:38-42.
18. Sari S, Caniklioglu M, Oztekin Ü, Selmi V, Taspinar MS, Isikay L. Factors Affecting Retrograde Intrarenal Surgery Success: 6 Years Experience of a Clinic in Central Anatolia. Journal of Laparoendoscopic & Advanced Surgical Techniques 2020;30:1340-1343.
19. Goldberg H, Golomb D, Shtabholtz Y, Tapiero S, Creiderman G, Shariv A, Baniel J, Lifhshitz D. The "old" 15 mm renal stone size limit for RIRS remains a clinically significant threshold size. World J Urol 2017;35:1947-1954.
20. Ozbek R, Senocak C, Haberal HB, Damar E, Sadioglu FE, Bozkurt OF. Comparison of scoring systems for predicting stone-free status and complications after retrograde intrarenal surgery. World J Urol 2020;1-6.
21. Law YXT, Teoh JYC, Castellani D, Lim EJ, Chan EOT, Wroclawski M, Pirola GM, Giulioni C, Rubilotta E, Gubbioti M, Scarcella S, Chew BH, Traxer O, Somani BK, Gauhar V. Role of pre-operative ureteral stent on outcomes of retrograde intra-renal surgery (RIRS): systematic review and meta-analysis of 3831 patients and comparison of Asian and non-Asian cohorts. World J Urol 2022;1-13.
22. Yuk HD, Park J, Cho SY, Sung LH, Jeong CW. The effect of preoperative ureteral stenting in retrograde Intrarenal surgery: a multicenter, propensity score-matched study. BMC Urol 2020;20:1-7.
23. Bai PD, Wang T, Huang HC, Wu Z, Wang XG, Qin JX, Wang HQ, Chen B, Hu MB, Xing JC. Effect of Preoperative Double-J Ureteral Stenting before Flexible Ureterorenoscopy on Stone-free Rates and Complications. Curr Med Sci 2021;41:140-144.
24. Assimos D, Crisci A, Culkin D, Xue W, Roelofs A, Duvdevani M, Desai M, de la Rosetta J. Preoperative JJ stent placement in ureteric and renal stone treatment: results from the Clinical Research Office of Endourological Society (CROES) ureteroscopy (URS) Global Study. BJU Int 2016;117:648-654.
25. Chen H, Chen G, Zhu Y, Yang Z, Xiong C, Pan Y. Analysis of Prestenting on Outcomes of Flexible Ureteroscopy for Upper Urinary Urolithiasis: A Historical Control Study. Urol Int 2019;102:175-180.
26. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-213.
27. Fayad AS, Elsheikh MG, Ghoneima W. Tubeless mini-percutaneous nephrolithotomy versus retrograde intrarenal surgery for lower calyceal stones of 2 cm: a prospective randomised controlled study. Arab J Urol 2017;15:36-41.
28. Vilches RM, Aliaga A, Reyes D, Sepulveda F, Mercado A, Moya F, Ledezma R, Hidalgo JP, Olmedo T, Marchan F. Comparison between retrograde intrarenal surgery and extracorporeal shock wave lithotripsy in the treatment of lower pole kidney stones up to 15 mm. Prospective, randomized study. Actas Urol Esp 2015;39:236-242.
29. Cakici M, Sari S, Selmi V, Sandıkçı F, Karakoyunlu N, Ozok U. Is the Efficacy and Safety of Retrograde Flexible Ureteroscopy in the Elderly Population Different from Non-elderly Adults? Cureus 2019;11:e4852.
30. Zhang H, Jiang T, Gao R, Chen Q, Chen W, Liu C, Mao H. Risk factors of infectious complications after retrograde intrarenal surgery: a retrospective clinical analysis. J Int Med Res 2020;48:300060520956833.
31. Baboudjian M, Gondran-Tellier B, Abdallah R, Sichez PC, Akiki A, Gaillet S, Delaporte V, Karsenty G, Lechevallier E, Boissier R. Predictive risk factors of urinary tract infection following flexible ureteroscopy despite preoperative precautions to avoid infectious complications. World J Urol 2020;38:1253-1259.
32. Robert M, Drianno N, Marotta J, Delbos O, Guiter J, Grasset D. The value of retrograde ureterorenoscopy in the treatment of bulky kidney calculi. Prog Urol 1997;7:35-41.
33. Somani BK, Giusti G, Sun Y, Osther PJ, Frank M, Sio MD, Turna B, Rosette JDL. Complications associated with ureterorenoscopy (URS) related to treatment of urolithiasis: the Clinical Research Office of Endourological Society URS Global study. World J Urol 2017;35:675-681.
34. Akgül M, Yazıcı C, Ateş H, Altın E, Turgut B. A Rare Retrograde Intrarenal Surgery Complication: Hemophagocytic Syndrome. J Endourol Case Rep 2020;6:339-342.