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ORIGINAL PAPER

Efficacy of Flexible ureterorenoscopy in treating multiple renal stones: A cohort study

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Summary ***Introduction:*** *While the efficacy of flexible ureterorenoscopy (URS) in managing solitary kidney stones (KSs) is widely acknowledged, its effectiveness in treating multiple stones has scarcely been investigated. This study aims to assess the effectiveness and safety of retrograde intrarenal surgery (RIRS) utilizing flexible URS and laser lithotripsy in the management of multiple KSs.*

Methods: *This study was a single-group cohort study conducted on patients with multiple KSs who underwent treatment with RIRS using flexible URS and laser lithotripsy. Stone-free status was considered as the lack of residual stone fragments or any residual stone of any size. The first follow-up appointment was arranged 3-4 weeks following the procedure. If significant residual stones were present, patients underwent reintervention within 2-4 weeks.*

Results: *A total of 110 patients with multiple KSs were included. The mean stone burden was 27.5 ± 7.9 mm, and the mean duration of the operation was 54.9 ± 19.7 minutes. Seven cases (6.3%) experienced intraoperative complications, while postoperative complications were found in eight cases (7.3%). After four weeks, a stone-free rate (SFR) was documented in 80.9% of the cases, and this rate increased to 93.6% after three months. The SFR after three months was significant with Guy's stone score ($p < 0.001$); however, it did not reach a significant level with any other parameters.*

Conclusions: *The RIRS with flexible URS may be an effective and potentially safe procedure for treating multiple KSs. It may yield a favorable SFR with an acceptable complication rate.*

KEY WORDS: *Kidney stone; Urinary tract; Retrograde intrarenal surgery; Ureterorenoscopy; Nephrolithiasis.*

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INTRODUCTION

Nephrolithiasis, also known as *kidney stone* (KS), is a common condition with a global concern (1). Following urinary tract infections and prostate diseases, KS is the most presented urinary tract disease. Regarding epidemiology, KSs affect about 5% of females and 12% of males over their lifetimes (2, 3). Variations in risk factors for KSs can be observed among different population groups (4). The incidence of KSs is influenced by multiple factors, including environmental factors, gender, race, geographical location, occupation, exposure to hot climates, family history, unhealthy diet, obesity, smoking, alcohol consumption, and low fluid intake (5). Additionally, comorbid metabolic disorders, such as hypertension, diabetes mellitus, cardiovascular disease, and chronic kidney disease can be associated with an elevated risk (3, 4, 6, 7). The symptoms of KSs exhibit variability based on their location—whether within the kidney, ureter, or urinary bladder (8). Common sites for stone dislodgement include the vesicoureteric junction, mid-ureter, and pelvoureteric junction (9). Clinical presentations encompass renal colic and flank pain, often accompanied by gross hematuria, a burning sensation during urination, nausea, vomiting, and fever (9-11). Over the last three decades, there have been notable advancements in KS treatment. Currently, treatment options include minimally invasive methods such as *extracorporeal shock wave lithotripsy* (ESWL), *percutaneous nephrolithotomy* (PCNL), and *retrograde intrarenal surgery* (RIRS), as opposed to conventional open surgery (12). The applications of RIRS in treating KSs have expanded significantly due to recent advances in endoscopic technology (13). Although the efficacy of flexible *ureterorenoscopy* (URS) in managing solitary KS is widely acknowledged in the literature, its effectiveness in treating multiple stones has scarcely been investigated (14). The present study aims to assess the effectiveness and safety of RIRS utilizing flexible URS and laser lithotripsy in the management of multiple KSs.

METHODS

Setting and design

This single-group cohort study was carried out on patients with multiple KSs who underwent treatment with RIRS with flexible URS and laser lithotripsy at a single center between September 2020 and July 2023. The *Iraqi Council for Medical Specializations* granted ethical approval for the study. Patients underwent comprehensive counseling concerning various treatment approaches, the risk of complications, and the potential necessity for a staged or auxiliary procedure to ensure an optimal stone-free rate.

Eligibility criteria

The inclusion criteria comprised the following: 1) Patients aged ≥ 18, presenting with multiple KSs sized between 11 and 30 mm. 2) Stones distributed anywhere within the pelvicalyceal system. 3) Conducting RIRS was based on patient preference and several characteristics, such as morbid obesity, congenital renal anomalies, coagulopathy, and treatment failure with PCNL or ESWL. Patients with calyceal diverticular stones, ipsilateral ureteric stones or strictures, staghorn stones, pelvic-ureteric junction obstruction, or a medullary sponge kidney were excluded.

Patient examination and data collection

Patients underwent preoperative assessment through non-contrast *computed tomography* (CT). Stone sizes were determined by calculating the sum of the greatest dimensions of each stone observed on non-contrast CT scans. The collected data encompassed patients' demography, family history for KS, history of KS intervention, comorbidities, renal *ultrasonography* (U/S), non-contrast CT *Kidney-Ureter-Bladder* (KUB), the indication of RIRS, stone parameters (laterality, number, size), operation time, complications, and stone-free status. Complications were classified based on the *Modified Clavien Classification System* (MCCS) (15). Stone-free status was considered as the lack of residual stone fragments or any residual stone of any size, as determined by U/S and KUB imaging. The outcomes of interest encompassed *stone-free rate* (SFR) and complication rates.
Stones exceeding the 400-600 HU threshold were more likely classified as radiopaque, whereas those falling below were considered radiolucent, although assessment based solely on HU values may have limitations and clinical correlation with additional imaging modalities or stone analysis was often necessary for accurate characterization.

Intervention

Under either general or spinal anesthesia and with patients positioned in lithotomy, a semi-rigid ureteroscope (*8-9.5F, Karl Storz Endoscopy, Tuttlingen, Germany*) was utilized for all procedures. This facilitated the passive dilation of the ureter, enabling the evaluation of the presence of concurrent ureteral stones or strictures. A Zebra nitinol guidewire (0.032/0.035 inches) (*Boston Scientific, USA*) was threaded into the pelvicalyceal system through the ureteroscope. Following this, a 7.5 Fr flexible URS (*Storz Flex-X2S, Tuttlingen, Germany*), or a digital single-use ureteroscope (*HU32, Shenzhen Huge Med Medical Technical Development, China*), was advanced along the guidewire in a monorail manner. In patients pre-stented, a *ureteral access sheath* (UAS) was placed over the guidewire, followed by the advancement of the flexible URS through the UAS. Stone fragmentation was achieved using either the Holmium: YAG laser (*Cyber-Ho 60 Holmium laser system, Quanta System, Milan, Italy*) or the Calculase III (*Storz, Tuttlingen, Germany*). This involved applying 0.5-0.8 J power at a frequency of 15-30 Hz through a 200 µm fiber. To obviate the necessity for stone retrieval, a stone dusting technique was utilized, fragmenting the stones into minuscule pieces or fine powder. Following the completion of lithotripsy, a visual assessment of the pelvicalyceal system was conducted to detect any residual stone fragments. To prevent overlooking substantial pieces or fragments, fluoroscopy was utilized. Under direct endoscopic vision, the guidewire was carefully inserted into the renal pelvis or collecting system. Following this, the flexible ureteroscope was gradually retracted, allowing for a thorough examination of the entire ureter to identify larger calculi, fragments, and any instances of significant ureteral damage. Subsequent to the procedure, a *double-J* (DJ) stent with dimensions 5-6 F and a length of 26 cm was inserted in all cases. Additionally, an indwelling Foley catheter was left in place for approximately 6-12 hours. If the postoperative course was uncomplicated, patients were discharged on the postoperative day with prescribed oral antibiotics.

Follow-up

The first follow-up appointment was arranged 3-4 weeks after the procedure. The KUB examination was conducted, and the DJ stent was removed in the absence of any complications. In the presence of significant residual stones and substantial complications, patients underwent reintervention within 2-4 weeks. Conversely, patients without complications but with residual stones remained under observation for three months. Subsequent evaluations, utilizing renal U/S and KUB X-ray, took place three months after the intervention. CT scans were excluded from the diagnostic protocol to minimize expenses and reduce radiation exposure. At the three-month mark following the intervention, the SFR was determined. This categorization included either complete stone-free status, indicating the lack of residual stone fragments, or the presence of residual stones, identified through U/S and KUB X-rays.

Statistical analysis

The data were organized in *Microsoft Excel* (2019). Subsequently, they were analyzed using the *Statistical Package for the Social Sciences* (SPSS) (*Version 22, IBM SPSS Statistics Inc., USA*). The data are presented as frequency, percentage, range, mean, and standard deviation. The chi-square test and independent samples T-test were employed to identify significant relationships between the SFR and other variables. Statistical significance was defined as p-values less than 0.05.

Results

A total of 110 patients with multiple KSs were included, with a mean age of 45 ± 13.82 years and a mean BMI of 25 ± 3.39 kg/m^2. The majority of the cases (66.4%) were male. A positive history of KS intervention was found in 26.4% of cases. Hypertension was the most common comorbidity (74.5%). Ten patients (9.1%) had a history of ischemic heart disease, and nine of them were receiving anticoagulant medications. The degree of hydronephrosis was commonly distributed between mild (39.1%) and moderate (31.8%). Renal malformation was present in 18.2% of the patients, while renal malfunction was observed in 20%. The indication for RIRS was predominantly primary (80.9%). Half of the cases (50%) presented with two stones, 38 (34.5%) with three stones, and 17 cases (15.5%) had more than three stones. The mean stone burden was 27.5 ± 7.9 mm and the majority of them were unilateral (91.8%). Radiopaque was the prevalent radiologic characteristic of the stones (74.5%). According to *Guy's stone score* (GSS), the majority of the stones were categorized as grade 2 (87.3%). Intraoperative fluoroscopy was utilized in 52 (47.3%) patients. The mean duration of the operation and laser operating time were 54.9 ± 19.7 minutes and 31.8 ± 15.8 minutes, respectively. Seven cases (6.3%) experienced intraoperative complications, including bleeding in four cases (3.6%) and ureteral injury in three cases (2.7%). Postoperative complications were urinary tract infection (5.5%) and hematuria (1.8%), of which seven cases (6.4%) were re-admitted to the hospital and managed conservatively. Five cases (4.5%) needed the second stage of RIRS due to residual stones. After four weeks, stone free status was achieved in 80.9% of the cases, and this increased to 93.6% after three months (Table 1). The SFR after three months was significant with GSS; however, it did not reach a significant level with any other parameters (Tables 2 and 3).

Discussion

Renal stones have several treatment options, each with its advantages and drawbacks. PCNL is a method known for effectively treating large KSs (16). However, it involves accessing the kidney through the renal parenchyma. Furthermore, the widely used prone position during the procedure may increase the risks associated with anesthesia and result in a decline in oxygen saturation levels, especially in patients who are obese or elderly and already have respiratory disorders (17). Complications, including hemorrhage, hydrothorax, septicemia, bowel and major vessel injuries, and renal collecting system perforation, pose significant risks during and after this procedure. This has driven heightened interest in alternative treatment modalities (18, 19). Recently, there has been a growing discussion about using RIRS for multiple KSs. Several studies have investigated the feasibility and effectiveness of RIRS in treating the issue (20, 21). *Çakıcı et al.* compared the efficacy of RIRS and PCNL in treating multicalyceal stones. PCNL was the preferred treatment modality unless patients had comorbidities such as anesthesia risk, bleeding diathesis, or anatomical issues where PCNL was unsuitable (20). *Alazaby et al.* assessed RIRS for the treatment of multiple KSs and reached a positive conclusion regarding its efficacy. They recommended the utilization of RIRS for patients with multiple KSs, especially in cases where prior treatments such as ESWL and PCNL have been unsuccessful (21). In the present study, the results indicated a favorable outcome, with the SFR reaching 93.6% at 3 months postoperatively. The mean operation time was 54.9 ± 19.7 minutes. No significant correlations were identified between the mean operation time and the SFR at both 4 weeks and 3 months postoperatively. *Ozgor et al.* reported a mean operation time of 47.8 ± 22.2 minutes. Also, they reported no significant correlation between it and SFR (22). In contrast, Demirbas et al. reported a mean operative time of 62.8 ±

Table 1.
Baseline characteristics of the patients.

Variables Demographics	Frequency/Percentage
Mean Age, year ± SD	45 ± 13.82
Mean BMI, kg/m^2 ± SD	25 ± 3.39
Gender	
Male	73 (66.4%)
Female	37 (33.6%)
Family history for KS	
Yes	8 (7.3%)
No	102 (92.7%)
History of KS intervention	
Yes	29 (26.4%)
No	81 (73.6%)
Comorbidities	
Diabetes mellitus	15 (13.6%)
Hypertension	82 (74.5%)
Ischemic heart disease	10 (9.1%)
Degree of hydronephrosis	
None	28 (25.5%)
Mild	43 (39.1%)
Moderate	35 (31.8%)
Severe	4 (3.6%)
Renal malformation	
Yes	20 (18.2%)
No	90 (81.8%)
Renal malfunction	
Yes	22 (20%)
No	88 (80%)
Indication of RIRS *	
Primary	89 (80.9%)
Secondary	21 (19.1%)
Number of stones	
Two	55 (50%)
Three	38 (34.5%)
More than three	17 (15.5%)
Stone burden, mm (Mean ± SD)	27.5 ± 7.9
Stone laterality	
Right side	46 (41.8%)
Left side	55 (50%)
Bilateral	9 (8.2%)
X-ray characteristics of stone	50 (21.9%)
Radiopaque	82 (74.5%)
Radiolucent	28 (25.5%)
Guy's stone score	
Grade 2	96 (87.3%)
Grade 3	14 (12.7%)
Use of fluoroscopy	
Yes	52 (47.3%)
No	58 (52.7%)
Operation time, min (Mean ± SD)	54.9 ± 19.7
Laser operating time, min (Mean ± SD)	31.8 ± 15.8
Intraoperative complication	
Bleeding #	4 (3.6%)
Ureteral injury #	3 (2.7%)
Postoperative complication	
Urinary tract infection #	6 (5.5%)
Hematuria#	2 (1.8%)
Re-admission to hospital	7 (6.4%)
Re-intervention (second stage RIRS)	5 (4.5%)
Stone free after 4 weeks	89 (80.9%)
Stone free after 3 months	103 (93.6%)

SD: Standard deviation; KS: Kidney stone; Min: minute.
** A primary indication means that the patient underwent RIRS for the first time, while a secondary indication means the patient had a positive history of RIRS.*
 # Grade II according to Modified Clavien Classification System.

Variable		No.	Stone free after 4 weeks	P-value *	Stone free after 3 months	P-value *
IIndication of RIRS	Primary	89	72 (80.9%)	0.63	84 (94.4%)	0.40
	Secondary	21	17 (81%)		19 (90.5%)	
Number of stones	2	55	48 (87.3%)	0.14	54 (98.2%)	0.08
	3	38	27 (71.1%)		33 (86.8%)	
	> 3	17	14 (82.4%)		16 (94.1%)	
Pre-operative stent placement	Yes	23	18 (78.3%)	0.46	21 (91.3%)	0.45
	No	87	71 (81.6%)		82 (94.3%)	
X-ray characteristics	Radio-opaque	82	67 (81.7%)	0.45	77 (93.9%)	0.57
	Radiolucent	28	22 (78.6%)		26 (92.9%)	
Use of ureteric access sheath	Yes	80	66 (82.5%)	0.33	75 (93.8%)	0.61
	No	30	23 (76.7%)		28 (93.3%)	
Guy's Stone Score	G2	96	77 (80.2%)	0.068	90 (93.8%)	< 0.001
	G3	14	13 (92.9%)		14 (100%)	

* *Chi-square test.*
SFR: Stone-free rate; RIRS: Retrograde intrarenal surgery.

Table 2.
Correlation of SFR with RIRS indication, stone characteristics, stent placement, and ureteric access sheath.

Variable	SFR after 4 weeks		P-value **	SFR after 3 months		P-value **
	Yes (89)	No (21)		Yes (103)	No (7)	
Mean stone burden (mm)	27.10 ± 8.44	29.09 ± 4.97	0.15	27.40 ± 8.0	29.30 ± 4.85	0.26
Mean operation time (min)	54.40 ± 20.36	57.14 ± 16.77	0.39	54.94 ± 19.70	55 ± 21	0.82

** *Independent t-test.*

Table 3.
Correlation of stone burden and operation time with SFR.

17.57 minutes and identified a highly significant correlation between the procedure time and SFR (23). A mean operation time of 51.97 ± 20.18 minutes has also been reported (24). Variations in the duration of procedures among different studies may reflect the overall proficiency and the inherent complexities of the surgical tasks. It is crucial to recognize that these differences may also arise from varying methodologies used to estimate operative time. Notably, some practitioners begin their time assessment with the initiation of cystoscopy, while others commence the measurement at the start of URS.
The SFR in the current study was similar to that Alazaby et al. reported (92.8%) (21). The similarity may be attributed to the close resemblance in mean stone burden. Our reported stone burden was 27.5 mm, and *Alazaby et al.* reported a mean stone burden of 25.7 mm (21). In the present study, although SFR was higher with fewer stones per renal unit, the difference was not statistically significant when comparing two stones with three or more at three months post-procedure. This contrasts with Alazaby et al., who reported significant differences: 100% SFR for two stones, 77.7% for three, and 50% for four stones. In our cohort, SFR was 98.2% for two stones, 86.8% for three stones, and 94.1% for more than three stones. This discrepancy may be attributed to the larger sample size in this study and differences in the definition of SFR. The current study considered patients as stone-free when no stone fragments were detected by US and KUB, while *Alazaby et al.* considered SFR when fragments of 3 mm or less detected in CT-KUB (21).
The current study unveiled a significant correlation between the SFR observed three months post-operation and the GSS. This may suggest that as the complexity of stones increases, the probability of achieving stone-free status diminishes within the three months following the operation. This aligns with the conclusions drawn by Karsiyakali et al., who also found a significant correlation between SFR and GSS grade 3 (25). Notably, their study questioned the GSS scoring system's effectiveness in predicting SFR after RIRS. This is due to the reduced utility for GSS grade 1 and grade 4 stones, making the system less effective across the entire stone complexity spectrum. As a result, their findings highlight the necessity for a nuanced approach to predict SFR post-RIRS (25). In this study, the assessment of radiopacity in stones showed no significant correlation with SFR at four weeks and three months post-operation. This aligns with *Lim et al.*'s findings on the relationship between stone radiopacity and SFR after RIRS procedures (26). *Ozgor et al.* similarly concluded that there was no significant correlation between these parameters (22). These outcomes emphasize the need for a nuanced consideration of factors influencing SFR beyond focusing solely on stone radiopacity in the postoperative context.
With decreased instrument size, potential complications like ureteral avulsion are now extremely rare. Our study found no major complications, but 15 patients (13.6%) experienced manageable minor complications—seven intraoperative and eight postoperative. This aligns with Alazaby et al., reporting 16.6% minor complications (21). In contrast, Atis et al. documented 3.4% minor complications in their RIRS group; this variance may be due to varying sample sizes, and notably, our cohort included intraoperative complications (27). This research is subject to several limitations, including the study's small sample size, which limits its generalizability. The definition of stone burden varies, introducing potential inconsistencies. Additionally, the absence of a comparison with alternative stone treatment methods hinders a comprehensive assessment. The study's short follow-up duration restricts the evaluation of long-term outcomes. To avoid citing non-peer-reviewed data, the authors ensured the credibility of the referenced studies (28).

In conclusion, RIRS with flexible URS may be an effective and potentially safe procedure for treating multiple KSs. It may yield an excellent SFR with an acceptable complication rate.

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