Flexible ureteroscopy for large renal stones: Are we pushing the limits: A multi-center retrospective analysis

Original Article

Hani Nour[a,b], Hazem Elmansy[c], Ayman Ali[a,d], Younis Alshamsi[b], Amr Hodhod[c], Afaf Mogharbel[b], Amin Fraij[b], Mohamed Gadelmoula[b,e], Ahlam Busaber[b], Ahmad Ismail[a]

Department of Urology, [a]Theodor Bilharz Research Institute, Giza, [b]AlQassimi Hospital, EHS, Sharjah, United Arab Emirates, [c]Thundar Bay Regional Health Science Center, Northern Ontario School of Medicine, Ontario, Canada, [d]Royal United Hospitals, NHS, England, United Kingdom, [e]Assiut University, Assiut, Egypt.

ABSTRACT

Background: Managing large renal stones presents challenges. While percutaneous nephrolithotripsy (PCNL) is the gold standard, flexible ureteroscopy (f-URS) with laser technology has emerged as a minimally invasive alternative.

Objective: To evaluate the outcomes of f-URS for renal stones larger than 20 mm in three centers and identify factors that influence stone-free rates (SFR).

Patients and Methods: A retrospective analysis of 423 patients who underwent f-URS with holmium laser lithotripsy for renal stones greater than or equal to 20 mm between January 2021 and October 2023 was conducted. Data from three centers in UAE, Canada, and Egypt were analyzed. Stone size, site, density, preoperative stenting, operative time, postoperative complications, and SFR at 30 days were assessed. Univariate and multivariate analyses were performed to identify factors influencing SFR.

Results: A total of 103 patients met the inclusion criteria. The median stone size was 25 mm. Preoperative stents were inserted in around half of the cohort. Disposable f-URS and ureteral access sheath were used in the majority of patients. Median operative time was 94 min. Postoperative complications occurred in 21%. Significant residual fragments were assessed 30 days postoperatively, around 50% of the study cohort required auxiliary procedures. Univariate analysis revealed no significant associations between SFR and stone size, location, number, density, or preoperative stenting.

Conclusion: In this multi-center study, f-URS with holmium laser lithotripsy could not achieve decent early stone-free rates for large renal stones, further research is needed to optimize treatment strategies for large renal stones.

Key Words: Flexible ureteroscopy, laser, renal, stones.

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Corresponding Author: Hani Nour, MD, Department of Urology, Theodor Bilharz Research Institute, Korniche ElNile, Alwarak, Giza, Egypt. **Tel.:** +971544308284, **E-mail:** Hani_nour@hotmail.com

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INTRODUCTION

The primary objective of every urologist is to achieve optimal stone clearance with minimal morbidities[1]. Managing large renal stones (>20 mm) presents a considerable challenge, with factors including but not limited to stone composition, density, location, shape, patient anatomy, comorbidities, and availability of suitable armamentarium, guiding the choice of treatment modality[2].

For many years, percutaneous nephrolithotripsy (PCNL) has been considered the gold standard for managing large upper urinary tract stones due to its reliability, effectiveness, and favorable safety profile, with stone-free rates (SFR) exceeding 88%[3]. Recent advancements, including changes in patient positioning from prone to supine, instruments miniaturization, and innovations in lithotripsy energy sources have further improved the safety profile of PCNL while maintaining excellent SFR. However, PCNL still has its challenges including bleeding, infection, organ injury, and relatively long hospital stay[4].

Flexible ureteroscopy (f-URS), along with high-power laser technology, has revolutionized the management of upper urinary tract stones as a minimally invasive technique[5]. Initially, retrograde intrarenal surgery (RIRS) has been utilized for small to medium-sized stones (<20 mm), but recent technological advancements and increased experience have encouraged urologists to offer it for larger stones (≥20 mm), yet with nonuniform results[3].

Compared with PCNL, RIRS is less invasive and, when combined with laser technology, allows for precise

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fragmentation of stones of almost any composition with minimal damage to surrounding tissues[6]. This was the rationale that prompted urologists to consider it as a viable option for managing stones larger than 20 mm[7]. Several studies have reported SRF ranging from 60 to 90% for stones up to 4 cm after one or more sessions[8]. However, f-URS for large renal stones does have its limitations, including longer operative time, higher cost, limited availability, and technical complexity[7,8].

In a recent real-world practice study evaluating the outcomes of f-URS for renal stones, stone-free rates were significantly lower than those reported in earlier studies even with a median stone size lower than 20 mm[8,9].

Our study aims to evaluate the results of f-URS for renal stones larger than 20 mm in three different centers and identify factors that may enhance SRF.

PATIENTS AND METHODS:

A multicenter retrospective outcome analysis was conducted in 3 different centers in United Arab Emirates (UAE), Canada, and Egypt between January 2021 and October 2023.

Our retrospective analysis focused on patients with renal stones (≥20 mm) who underwent flexible ureteroscopy and Holmium laser lithotripsy. The study received institutional review board approval for the conduction of clinical research and adhered to the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments.

Data from three participating centers were evaluated for this study. Inclusion criteria comprised patients over 18 years old with stone sizes greater than or equal to 20 mm who underwent flexible ureteroscopy with holmium laser lithotripsy as the primary treatment. Patients with associated active urinary tract infections, associated ureteral stones, renal and/or musculoskeletal abnormalities, and patients undergoing bilateral simultaneous procedures were excluded. Patients with prior stenting were not excluded.

Stone size was determined by measuring the largest anteroposterior diameter (AP). In cases of multiple stones, the sum of their largest AP diameters was calculated. Alongside routine demographic information and preoperative tests, all patients underwent noncontrast-enhanced computerized tomography of the urinary tract (noncontrast CT-UT) to register stone size, site, number, and density. The presence of a preoperative stent was also recorded.

Flexible ureteroscopy with holmium laser lithotripsy was performed on all patients using high-power machines (>80W), following the standard of care and surgical practices of each institute. All three centers used both disposable and reusable f-URS as outlined in the results section, laser power, and frequency were adjusted according to the surgeon's preference, but all surgeons utilized combined dusting/fragmentation techniques, and stone retrieval was performed when deemed necessary by the surgeon.

Operative time, the need for postoperative stenting, and intraoperative complications were documented, with postoperative complications graded using the modified Clavien–Dindo classification[10]. Operative time was defined as the time from the cystoscope introduction to stent insertion. The primary endpoint of our study was the SFR at 30 days postoperative. To determine SFR, fragments smaller than 4 mm were considered insignificant residual, and due to the retrospective nature of the study, residual fragments were assessed using combined renal ultrasound with plain films of the urinary tract or noncontrast CT-UT.

Secondary endpoints included evaluating perioperative factors that affect SFR.

Statistical analysis

We used IBM SPSS Software version 26 for our statistical analysis. We described continuous variables using medians and ranges, while categorical variables were expressed as numbers and percentages. To examine the connection between SFR and potential influencing factors, we employed a binary logistic regression model. These influencing factors encompassed age, sex, stone characteristics (side, size, density), as well as the number and location of stones. All parameters with a P less than 0.1 would enter a multivariate analysis. A *P value* of less than 0.05 was considered statistically significant.

RESULTS:

A total of 423 adult patient files were included in this study, focusing on f-URS with holmium laser lithotripsy for treating stones larger than 20 mm.

Among the initial patient files, 320 patients were excluded for various reasons: 93 patients had a preoperative planned staged f-URS, 17 had associated ureteral stones, and 81 had bilateral stones. In addition, 11 patients had their procedure changed to PCNL, 58 patients did not reach 30 days postoperatively, 42 patients did not have a postoperative imaging study, and 18 patients were lost to follow-up.

A total of 103 patients remained for evaluation, and their baseline characteristics are presented in (Table 1). The cohort consisted of 61.2% male patients, with a median age of 52 years. The median stone size was 25 mm, with a

density ranging from 353 to 1384 Hounsfield Units (HU). Fifty-four patients presented with a single stone, while multiple stones were found in 49 patients. Renal pelvic stones were found in 50 patients, and calyceal stones, including staghorn stones, were found in 52 patients. Preoperative stents were inserted in 49 patients (47.6%) either to relieve an obstruction or as a preliminary step before f-URS.

Intraoperative characteristics are shown in (Table 2). Disposable f-URS was used in 78 patients, and a ureteral access sheath was inserted in 80% of the cases, even in the presence of preoperative stents. The median operative time was 94 min. All patients had a postprocedure ureteral stent inserted, and the median hospital stay was 1 day. Postoperative complications developed in 34% of the patients, as recorded using the modified Clavien–Dindo classification[10].

Postoperative results are presented in (Table 3). Evaluation of residual fragments was performed using either a CT-UT or a combined radiography KUB and renal ultrasound protocol at least 30 days postoperatively. Fifty-three patients showed significant residual fragments greater than or equal to 4 mm, and auxiliary procedures were required in 52 of these cases. A second session of f-URS was performed in 35 patients, 13 patients underwent shock wave lithotripsy (SWL), and four patients had semirigid ureteroscopy with stent exchange for persistent ureteral fragments.

In an attempt to evaluate factors that affect the SFR univariate analysis was conducted (Table 4). However, we found that factors like stone size, location, number, density, and whether a preoperative stent did not show any significant association to the SFR. Therefore, the multivariate analysis was not carried out.

Table 1: Baseline characteristics

Parameter	Values
Total number of participants *n* (%)	103 (100)
Sex	
Male *n* (%)	63 (61.2)
Female *n* (%)	40 (38.8)
Age median (range)	52 (19–81)
Stone diameter (mm) median (range)	25 (20–40)
Stone density (HU) median (range)	824 (353–1384)
Laterality	
Left *n*(%)	53 (51.5)
Right *n*(%)	50 (48.5)
Stone number	
One *n*(%)	54 (52.4)
Two *n*(%)	30 (29.1)
Three *n*(%)	12 (11.7)
Four or more *n*(%)	7 (6.8)
Stone site	
Upper pole *n*(%)	2 (1.9)
Middle pole *n*(%)	8 (7.8)
Lower pole *n*(%)	26 (25.2)
Pelvis *n*(%)	50 (48.5)
Staghorn *n*(%)	17 (16.5)
Presence of ureteral stent preop *n*(%)	49 (47.6)

Table 2: Intraoperative parameters

Type of ureteroscope *n* (%)	
Disposable	78 (75.7)
Reusable	25 (24.3)
Access sheath insertion *n*(%)	82 (79.6)
OR time (min) median (range)	94 (35–140)

Postop ureteral stent *n*(%)	103 (100)
Complications n (%)	
None	68 (66)
Clavien I	27 (26.2)
Clavien II	8 (7.8)
Hospital stay (days) median (range)	1 (0.5–8)

Table 3: Postoperative results

Residual ≥4 mm after 30 days n (%)	53 (51.5)
Axillary procedure *n* (%)	52 (50.5)
2nd session f-URS *n*(%)	35(33)
SWL *n*(%)	13 (12.6)
Semirigid URS *n*(%)	4 (3.8)

Table 4: Univariate analysis

	Univariate analysis		
Parameters	OR	CI (95%)	*P* value
Age	1.014	0.99–1.042	0.29
Side	1.474	0.675–3.219	0.33
Sex	1.707	0.763–3.82	0.2
Stone size	1.043	0.967–1.126	0.272
Stone number	1.147	0.563–2.335	0.706
Preopertative stent	1.089	0.491–2.419	0.833
Stone density HU	1	0.998–1.002	0.914
Stone location	1.052	0.673–1.645	0.823

DISCUSSION

The management of large renal stones presents a significant challenge for urologists, and the choice of treatment modality is influenced by various factors[1,3]. PCNL has long been considered the gold standard for treating large upper urinary tract stones due to its high SFR[11]. However, PCNL is not without limitations, including bleeding, infection, organ injury, and prolonged hospitalization[12]. In recent years, RIRS has emerged as a minimally invasive alternative for managing upper urinary tract stones, including larger stones. While f-URS offers advantages such as precision and minimal damage to surrounding tissues, its efficacy for stones larger than 20 mm remains uncertain[13].

Our retrospective analysis included 103 patients from three different centers who underwent f-URS with holmium laser lithotripsy. The baseline characteristics of the cohort revealed a median stone size of 25 mm, with a density ranging from 353 to 1384 Hounsfield Units. The majority of patients had a single stone, although 48% of the cohort presented with multiple stones

Although several research studies have favored the use of RIRS over PCNL for stones greater than 20 mm; in a real-world setting, recent large-scale retrospective and prospective studies failed to support this practice. In a retrospective analysis of more than 2000 f-URS for renal stones in both general and specialized urology centers, Ghani *et al*.[9] reported a median stone size of 9 mm, multiple stones present in 22% of patients and 25% of the study cohort were stented preoperatively; even with this relatively small stone size and number, UAS was used in around 60% of the cases.

These results surprisingly showed the same trend in a prospective pattern when the global Flexible Ureteroscopy Outcomes Registry (FLEXOR)[14] reported their results including more than 6000 patients with renal stones of any size who underwent RIRS as a primary treatment or after failure of other modalities. The mean stone size of 10.4 mm, yet multiple stone, and preoperative stenting were present in 41 and 47% of the study cohort, respectively, with UAS used in 93% of procedures. We believe that the use of UAS even in presented patient have to be the standard practice in larger stones, although does not affect SFR, use of UAS helps to reduce intrarenal pressure during prolonged procedures[5].

In our study, the median operative time was 94 min. Operative duration was previously proven directly related to stone burden[15]. In an evaluation of f-URS in patients with large renal stones, Huang JS *et al*.[16] reported 126 min as the mean operative time per procedure. However, it is important to note that the stone size can not be an independent predictor for an operative time as many various factors, including stone composition, density, location, surgeon experience, and the need for additional procedures such as stone extraction or stent placement usually play roles.

Disposable f-URS are gaining territories against reusable ones, according to a market projection study, the market share of disposable f-URS will reach 80% by 2025[17]. This was reflected in recent studies, which showed a shift from reusable to disposable f-URS, especially for large stone burdens[5,17].

Large stone size and the possible need for an auxiliary procedure was the main reason for insertion of ureteral stent post any type of stone management procedure[18] including our study, the same rationale was adopted by Huang JS *et al*.[16] who stented all cohort of their study; even for small stones, postprocedure stents were inserted in more than 90% of the patients the FLEXOR study[14].

The median hospital stay was 1 day, confirming the minimally invasive nature of the procedure, and the possibility to perform f-URS for larger stones in a daycare setting. Postoperative complications were observed in 34% of patients but were mostly of low severity (Clavien I or II)[10].

Evaluation of postoperative results revealed that 51.5% of patients had residual fragments larger than 4 mm, requiring auxiliary procedures. The most common auxiliary procedure was a second session of f-URS, followed by SWL and semirigid ureteroscopy with stent exchange. These findings are aligned with previous reports that have demonstrated variable SFR for f-URS in larger renal stones. Huang JS *et al*.[16] reported a 61% SFR after the first procedure, using a 3 mm cutoff for residual fragments, in their analysis of their cohort.

Even with smaller stones, SFRs was frustrating, in their study that included more than 2000 patients, Gandi *et al*.[9] reported a 50% SFR at a follow-up of 60 days using a zero fragment policy yet with a median stone size of 9 mm, the same as reported in the FLEXOR study[14] which reported a 71%SFR using a 2 mm cutoff residual, and a mean stone size of 10.4 mm

In our analysis we used a 30 days postoperative to assess residual fragments, this may explain the relatively lower SFR. We opted for this relatively short time frame to assess the results of a single-session f-URS and to avoid delaying auxiliary procedures.

In an attempt to identify factors influencing the stone-free rate, univariate regression analyses failed to identify significant correlations between stone size, site, number, density, location, or the presence of a pre/postoperative stent to stone-free rate. We believe that SFR would not be associated with the size of the stone if it goes beyond a certain limit. In another way, this research focused only on stones larger than 2 cm, and it is not surprising that SFR was not influenced by this factor for stones above this size.

It is important to note that our study has certain limitations. First, it is a retrospective analysis, which may introduce bias in patient selection and data collection. We only used high power holmium laser machines, the presence of Thulium Laser Fiber was not tested. Additionally, the study was conducted across three different centers, which may introduce variability in surgical techniques and outcomes. New forms of UAS including suction and bendable types were also not used, theoretically, they may positively affect SFR but further independent studies are needed to confirm. Furthermore, the study only evaluated the stone-free rate at 30 days postoperative, this may be a relatively short time for analysis, the effect of a longer time for residual fragment follow-up may be needed.

CONCLUSION

Our study assessed the outcomes of f-URS with holmium laser lithotripsy for renal stones larger than 20 mm and identified factors that may enhance SFR. It seems that up till this moment, RIRS for stones larger than 20 mm presents a step beyond the limits, and can not be presented as primary treatment option for standard patients.

ABBREVIATION LIST

AP, antroposterior; CT-UT, computarized tomography of the urinary tract; f-URS, flexible ureteroscop; HU, hounsfield unit; KUB, kidney, ureter, bladder; PCNL, percutaneous nephrolithotomy; RIRS, retrograde intrarenal surgery; SFR, stone free rate; SWL, shock wave lithotripsy; UAE, United Arab Emirates; UAS, ureteral access sheath.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Hiller SC, Ghani KR Frontiers of stone management. Curr Opin Urol 2020; 30:17–23.

2. chlomer BJ. Urologic treatment of nephrolithiasis. Curr Opin Pediatr 2020; 32:288–294.

3. Awedew AF, Alemu CT, Yalew DZ. Efficacy and safety of various endosurgical procedures for management of large renal stone: a systemic review and network meta-analysis of randomised control trials. Urolithiasis 2023; 51:87.

4. Shabana W, Oquendo F, Hodhod A, Ahmad A, Alaref A, Trigo S, *et al*. Miniaturized ambulatory percutaneous nephrolithotomy versus flexible ureteroscopy in the management of lower calyceal renal stones 10-20 mm: a propensity score matching analysis. Urology 2021; 156:65–70.

5. Geraghty RM, Davis NF, Tzelves L, Lombardo R, Yuan C, Thomas K, *et al*. Best Practice in Interventional Management of Urolithiasis: An Update from the European Association of Urology Guidelines Panel for Urolithiasis 2022. Eur Urol Focus 2023; 9:199–208.

6. De Coninck V, Keller EX, Somani B, *et al*. Complications of ureteroscopy: a complete overview. World J Urol 2020; 38:2147–2166.

7. Bagley DH, Healy KA, Kleinmann N. Ureteroscopic treatment of larger renal calculi (>2 cm). Arab J Urol 2012; 10:296–300.

8. Cosmin C, Georgescu DA, Geavlete P, Popescu RI, Geavlete B. Comparison between retrograde flexible ureteroscopy and percutaneous nephrolithotomy for the treatment of renal stones of 2-4 cm. Medicina (Kaunas) 2023; 59:124.

9. Kim HJ, Daignault-Newton S, DiBianco JM, Conrado B, Mohammad Jafri S, Ghani KR; Michigan Urological Surgery Improvement Collaborative. Real-world practice stone-free rates after ureteroscopy: variation and outcomes in a surgical collaborative. Eur Urol Focus 2023; 9:773–780.

10. Öğreden E, Oğuz U, Demirelli E, Benli E, Sancak EB, Gülpinar MT, *et al*. Categorization of ureteroscopy complications and investigation of associated factors by using the modified Clavien classification system. Turk J Med Sci 2016; 46:686–694.

11. Khadgi S, El-Nahas AR, El-Shazly M, Al-Terki A. Comparison of standard- and mini-percutaneous nephrolithotomy for staghorn stones. Arab J Urol 2021; 19:147–151.

12. Grosso AA, Sessa F, Campi R, Viola L, Polverino P, Crisci A, *et al*. Intraoperative and postoperative surgical complications after ureteroscopy, retrograde intrarenal surgery, and percutaneous nephrolithotomy: a systematic review. Minerva Urol Nephrol. 2021; 73:309–332.

13. Tonyali S, Haberal HB, Esperto F, Hamid Z, Tzelves L, Pietropaolo A, Emiliani E. The prime time for flexible ureteroscopy for large renal stones is coming: is percutaneous nephrolithotomy no longer needed? Urol Res Pract 2023; 49:280–284.

14. Gauhar V, Chew BH, Traxer O, Tailly T, Emiliani E, Inoue T, *et al*. Indications, preferences, global practice patterns and outcomes in retrograde intrarenal surgery (RIRS) for renal stones in adults: results from a multicenter database of 6669 patients of the global FLEXible ureteroscopy Outcomes Registry (FLEXOR). World J Urol 2023; 41:567–574.

15. Skolarikos A, Gross AJ, Krebs A, Unal D, Bercowsky E, Eltahawy E, *et al*. Outcomes of flexible ureterorenoscopy for solitary renal stones in the CROES URS global study. J Urol 2015; 194:137–143.

16. Huang JS, Xie J, Huang XJ, Yuan Q, Jiang HT, Xiao KF. Flexible ureteroscopy and laser lithotripsy for renal stones 2 cm or greater: A single institutional experience. Medicine (Baltimore) 2020; 99:e22704.

17. Kasmani Z, Ravindraanandan M, Mahmalji W. Flexible ureteroscopy: global user experience using disposable devices. Cureus 2023; 15:e46626.

18. Nour H, Wishahi M, Elesaily K, Badawy M. Laparoscopic ureterolithotomy: bridging the gaps between open surgery and ureteroscopy and/or shock wave lithotripsy. Egypt J Surg 2021; 40:393–398.