ORIGINAL PAPER

UROLITHIASIS

Efficacy and safety of fURS in stones larger than 20 mm: is it still the threshold?

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Introduction The aim of this article was to evaluate the safety and efficiency of flexible ureteroscopy (fURS) in the management of renal calculi larger than 20 mm.

Material and methods A total of 92 cases with renal calculi were managed with fURS and divided into two groups depending on the size of the stones; <20 mm and >20 mm (Group 1 and Group 2, respectively). The groups were compared with respect to treatment-related parameters including success, complication rates, hospitalization period and need for auxiliary procedures with an emphasis on the rate of infections. Success rates were also compared in each group according to stone location.

Results Overall success rates after 3 months showed that stone-free rates in both groups were 84.1% (< 20 mm) and 58.33% (>20 mm) respectively (p = 0.008). The success rates of upper/mid pole (100% vs. 80%) and pelvis stones (83.3% vs. 75%) showed no statistically significant difference (p = 0.5, p = 0.51 respectively). Success rates for stones located in the lower pole were 75% vs. 14.28% respectively (p = 0.008). The rate of infectious complications was significantly higher in cases undergoing fURS for relatively larger stones (22.9%) as compared to smaller calculi (6.8%) (p = 0.032). No complications were recorded in Group 1, while 2 cases in Group 2 (4.1%) developed ureteral stricture.

Conclusions Despite the relatively low stone-free rates in lower pole stones, our current results indicate that fURS can be an effective and safe treatment alternative to PNL in larger renal stones (>20 mm) located in the pelvis and in the upper part of the calyceal system of the involved kidney.

Key Words: urolithiasis ‹› flexible ureteroscopy ‹› retrograde intrarenal surgery ‹› furs ‹› rirs ‹› kidney stone

INTRODUCTION

Despite the successful and safe outcomes obtained in the management of moderate sized calculi (1–2 cm), the treatment of larger renal stones (>2 cm) continues to be a challenge for the practising urologist. Although percutaneous nephrolithotomy (PNL) has been performed as the preferred treatment modality with highly successful outcomes particularly in a single session [1, 2, 3], the evident invasive nature of this approach, which may cause severe complications such as bleeding and infection, has led endourologists to seek less invasive alternatives. In this respect, technological improvements coupled with the experience gained in semi-rigid ureteroscopic stone management has made it possible to perform 'flexible ureteroscopy (fURS)' in a safe and efficient manner for the majority of renal stones. However, despite the comparable stone-free rates obtained in relatively small stones (<20 mm), reported data have clearly demonstrated that as the stone size gets larger, decreased stone free rates along with an increased need for additional sessions could be anticipated in these cases [4–7].

Treatment algorithms for relatively large calculi have changed considerably over time due in part

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to the cumulative experience gained with the use of flexible scopes. This was also made possible by endourologists beginning to successfully apply the Ho-YAG laser technique in managing relatively large renal calculi during the last 20 years. However, studies focusing on the management of larger stones (> 20 mm) with fURS monotherapy have clearly shown that success rates will depend on the operator's experience and staged procedures may be needed for a completely stone-free status [4–13]. Nonetheless, data obtained to date in the management of large renal stones with fURS have clearly demonstrated that despite the lower success rates reported in a number of studies, acceptable and comparable stone-free rates can be achieved with significantly lower complication rates with this technique [14–17]. In other words, apart from the available experience, conflicting results have been reported in literature in regards to the size as well as location of the stones within the kidney, which makes it difficult to decide about the indications of fURS in the minimally invasive management of large renal stones [18, 19].

The aim of this study was to evaluate the efficacy and safety of fURS in the management of renal stones, based on both stone size (stones smaller and larger than 2 cm) and location (pelvis, upper-mid, lower), in terms of stone-free rates, mean operating time and length of hospital stay, postoperative complications and infection rates, emergency admission, and time to JJ stent removal.

MATERIAL AND METHODS

Following the approval of the study protocol by the Ethics Committee, 92 patients treated with fURS and Ho-YAG laser for kidney stones between January 2017 and November 2018 were included in the study program. Data were retrieved in a prospective manner from the stone registry system readily available in the department (Table 1). Patients with urinary tract infection, urinary system abnormalities and multiple calyceal stones were excluded from the study. In addition to a detailed patient history and thorough genitourinary examination, biochemical tests (particularly renal functional tests) were performed prior to the treatment. A urine culture was routinely obtained from all patients and if present, infection was treated according to the culture sensitivity test results in the preoperative period.

In cases with pyonephrosis and/or infectious material encountered at the beginning of the procedure, the kidneys were first drained by either percutaneous nephrostomy or JJ stenting and the treatment was postponed until the resolution of hydronehrosis and eradication of the infection. Radiological evaluation of the cases prior to the management included a plain film of the urinary tract (KUB), sonography of the whole urinary system and non-contrast spiral computed tomography (NCCT).

fURS technique

The fURS procedure was performed under general anesthesia in the lithotomy position with a flexible 7.5-Fr ureteroscope (Karl Storz, FLEX-X2, Tuttlingen, Germany) used for stone management. Patients with negative urine culture received ceftriaxone as prophylactic antibiotic treatment just before the procedure. Semi-rigid ureteroscopy (Richard Wolf, 6.5/8.5 Fr, Dual Channel, 5°, Knittlingen, Germany) was performed to facilitate the placement of the ureteral access sheath (UAS). The UAS (9.5/ 11.5–12–14 Fr) was placed over a 0.038 inch PTFE-nitinol guidewire with hydrophilic tip which had been introduced into the renal pelvis. An X-ray was obtained for optimal placement of the UAS. All renal calculi were managed using a holmium:YAG laser (Quanta; Litho DK30) (272 μ caliber fiber). Laser energy and frequency of pulsation (0.5–1.5 joule/8–20 Hertz) were adjusted during the procedure based on the stone hardness (its reaction to laser energy application) and volume. Both the dusting and fragmentation methods with different settings were used for stone disintegration where small fragments were removed with appropriate baskets. Some extracted fragments were sent for stone analysis and a 5 Fr double-J stent was placed in all cases after the procedure. Double J stents were removed 15 to 60 days after the fURS procedure. Stone-free status after fURS was defined as

Table 1. *Demographic data and stone locations*

	Group 1 (<20 mm)	Group 2 (>20 mm)	Total	P value
Number of patients (%)	47.75 (44)	52.37 (48)	100 (92)	
Average age (years)	47.75 ±14.76	52.37 ±14.5	50.16 (20–87)	0.133
Male/female (%)	25/19	33/15	58/34	0.236
Mean stone size (mm)	13.13 ±2.24	22.18 ±3.3	17.85 (7–29)	0.001
Stone laterality Right/left (%)	25/19	18/30	43/49	0.064
Stone location				0.209
Renal pelvis	30 (68.2 %)	24 (50%)	54 (58.7%)	
Upper/middle pole	6 (13.6 %)	10 (20.8%)	16 (17.4%)	
Lower pole	8 (18.2 %)	14 (29.2%)	22 (23.9%)	

the detection of no fragments or fragments <4 mm on radiologic evaluation by KUB and/or sonography at the 3-month follow-up evaluation. After the completion of all of the interventions, the cases were separated into two groups according to the size of the stone treated (stones smaller and larger than 2 cm) and all treatment-related parameters, with an emphasis on the rate of infections, were comparatively evaluated in both groups.

Data analysis was performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). Conformity to normality of distribution was tested with P-P plot and Kolmogorov-Smirov tests. Student t test analysis was used for intergroup comparisons of continuous variables and the Chi-Square test was used for the comparison of categorical variables. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Data obtained in our current study were evaluated from different aspects and the following findings were determined: The overall success rates in terms of completely stone free status after 3 months were 84.1% in patients with stones <20 mm (Group 1) and 58.33% in patients with stones >20 mm (Group 2) with a significant difference between the two groups ($p = 0.007$). When this critical evaluation was made on the basis of stone location (renal pelvis, upper-mid and lower pole), 83.3% of the patients with renal pelvic stones were stone-free in Group 1 (<20 mm), and 75% of the cases in Group 2 with stones in the same location were stone-free (fragments <4 mm) at 3 months after the fURS procedure ($p = 0.510$). The stone-free rate was higher for stones located in the upper and mid poles of the kidney in Group 1 as compared to Group 2 cases with stones in the same locations (100% vs. 80%) ($p = 0.500$). Evaluation of the success rates in both groups for stones located in the lower pole however revealed a statistically significant difference between the two groups regarding the stone-free rate after 3 months (75% vs. 14.28%) ($p = 0.008$) (Table 2).

The mean postoperative hospitalization period was shorter in Group 1 than in Group 2 (1.43 days vs. 1.75 days), but the difference was not significant ($p = 0.281$). The mean operating time was significantly longer (>60 min) in Group 2 compared to Group 1 where cases had smaller stones (6.8% vs. 54.2%) ($p = 0.001$). The duration of JJ stenting after the procedure was significantly longer in cases with larger stones as compared to the patients with smaller stones (35.77 days vs. 44.68 days) ($p = 0.001$).

As a highly important parameter related to both the size of the stone and the duration of the procedure, the rate of infectious complications was significantly higher in cases undergoing fURS for relatively larger stones (22.9%) than in the cases in Group 1 operated on for smaller calculi (6.8%) ($p = 0.032$). Presentation to the emergency department (ED) due to colic pain in the postoperative follow-up period was determined as 20.8% of the cases in Group 2, and in 13.6% of the cases in Group 1 ($p = 0.363$). Auxiliary procedures for the removal of residual fragments (re-fURS, SWL or semi-rigid URS) were required in 15.9% and 37.5% of Groups 1 and 2 respectively, and the difference between the groups was determined to be statistically significant ($p = 0.020$). Other than infection, no complications developed in any of the cases in Group 1, and ureteral stricture formation requiring JJ stent placement developed during the follow-up period in 2 cases (4.1%) in Group 2 ($p = 0.495$) (Table 2).

Table 2. *Comparison of operative parameters, clinical course and success rates*

	Group 1 (<20 mm)	Group 2 (>20 mm)	P value
Mean hospitalization (day)	1.43 ±0.75	1.75 ±1.8	0.281
Operation time >60 minutes (%)	6.8 (3/44)	54.2 (26/48)	0.001
Postoperative emergency admission (%)	13.6 (6/44)	20.8 (10/48)	0.363
JJ stent removal time (day)	35.77 ±9.96	44.68±14.33	0.001
Postoperative urinary tract infection (%)	6.8 (3/44)	22.9 (11/48)	0.032
Auxiliary procedures (%)	15.9 (7/44)	37.5 (18/48)	0.020
Postoperative complication (%)	0	4.1 (2/48)	0.495
Stone free rates (%)			
Renal pelvis	83.3 (25/30)	75 (18/24)	0.510
Upper/middle pole	100 (6/6)	80 (8/10)	0.500
Lower pole	75 (6/8)	14.28 (2/14)	0.008
Total	84.1 (37/44)	58.33 (28/48)	0.007

DISCUSSION

Both the European Association of Urology (EAU) and the American Urological Association (AUA) guidelines accept percutaneous nephrolithotomy (PNL) as the preferred treatment modality in the management of large (>20 mm) as well as complex renal stones [2, 20]. However, despite higher completely stone-free rates obtained in a single session, the risk of certain serious complications during and/or after the procedure indicates the more invasive nature of PNL. Of these complications, transfusion need (11.2% to 17.5%), fever (21% to 32.1%), pneumothorax (0% to 4%), urosepsis (0.25% to 1.5%) and

colonic injury (<1%) have been reported in literature to date [21]. Additionally, this modality may not prove to be a valuable option in patients with morbid obesity or bleeding disorders. In light of the invasive nature of PNL as well as the complications and/or limitations mentioned above, urologists began to seek other relatively less invasive procedures, such as flexible ureteroscopy (fURS), particularly in the relatively less invasive treatment of larger calculi. Regarding this issue, as a minimal invasive management alternative, the popularity of fURS has continuously increased over the last 10–15 years, mainly due to accumulated experience and recent technical advances that have resulted in the introduction of new-generation flexible ureteroscopes. The use of appropriately sized ureteral access sheaths has also made it possible to perform the procedure under lower renal collecting system pressures particularly during longer interventions and has enabled the removal of multiple stone fragments in a quick and practical manner.

As mentioned above, as a safe and efficient option, the overall success rates obtained with fURS for kidney calculi >20 mm have been reported as 77% after a single session and 93% with additional sessions as needed, and these rates have been found to be comparable with those achieved using PNL [22–28]. However, the stone free status for lower pole stones after fURS are lower in the range of 62–85% [29].

In the management of larger renal stones (>20 mm) with fURS, Grasso et al. achieved a stone-free rate of 91%, with a second procedure required in one third of the cases [5], and Breda et al. reported a success rate of 93.3%, for single renal stones between 20 and 25 mm in size with an average of 2.3 procedures [22]. In another study, Ricchiuti et al., obtained 87.5% success rates in the management of calculi 20–30 mm in size, with a second procedure required in 43% of patients [6].

Riley et al. obtained 90.9% stone-free status for stones 30 mm in size, and in the same study, 91.6% success rate with an average of 1.9 procedures for stones >30 mm and 80% success rate after an average of 1.8 procedures for stones >35 mm. For stones >40 mm, the success rate decreased to 50% with a mean of two procedures [24]. Unlike these previous studies, the stone-free rates in the current study were reported in regards to calyceal location of the stones and after only one session in both groups at 3 months after fURS. Depending on stone location, success rates were 83.3% vs 75% for stones in the pelvis and 100% vs. 80% upper/mid pole stones for Group 1 and Group 2 respectively ($p = 0.51$, $p = 0.5$). The stone-free rate of lower pole stones, however, was significantly lower in Group 2 (75% vs. 14.28%) ($p = 0.008$) indicating the inadequate efficacy of fURS with only one session in these cases. In such cases with residual fragments (85.72%), a higher-stone free rate of >80% with an auxiliary session could be anticipated and this finding could be attributed to the diminished stone volume as well as the effect of JJ stenting after the procedure.

All of the results reported so far for stones >20 mm, have clearly indicated that staged fURS could be a successful treatment alternative when the more invasive nature of PNL associated with certain severe complications is considered. Despite adequate reports in literature focusing on the high overall stone-free rates obtained with staged fURS for large stones (>20 mm) and comparative evaluations of retrograde intrarenal surgery (RIRS) with other techniques, there remains a limited amount of data regarding the unsatisfactory outcomes of fURS in large lower pole calculi and particularly that of the evaluation for fURS-related parameters, (success and complication rates) in such stones regarding the stone related parameters (size and especially location). The aim of the present study was to evaluate the efficacy and safety of a single fURS procedure from a different perspective as a minimally invasive management alternative for such calculi.

Data obtained in the study clearly indicated the importance of a thorough preoperative evaluation of the renal calculi to be treated with fURS on the basis of stone size and location. We were able to note that in addition to the higher success rates obtained in smaller stones after fURS (<20 mm), similar success rates with a complete stone-free status could be anticipated for relatively large stones (>20 mm) located in the renal pelvis as well as in the mid and upper calyces of the involved kidney, but not for lower pole calculi.

As an important operative parameter particularly during fURS procedures with respect to the possible infective complications during short-term follow-up, the relatively longer operative duration of endoscopic management of large renal stones in particular during the fURS procedures has been emphasized in literature. Although the data is limited, in one study the operative time was reported to be acceptable with a mean duration of 66 minutes (range, 25–240 min) in the treatment of renal calculi 20–40 mm in size [25]. In the current study the operating time was significantly longer (>60 min) in cases with larger stones as expected when compared to the cases with smaller stones (6.8% vs. 54.2%). Ultrasonographic evaluation of 2 patients in Group 2 with colic pain during follow up after the removal of JJ stents revealed moderate hydronephrosis and on diagnostic ureterosco-

py an ureteral stricture, possibly due to the longer operation time and longer exposure of ureteral access sheath, was detected. Evaluation of other relevant and to some extent important parameters in the current study revealed that, although not statistically significant, the postoperative hospitalization period was shorter in cases with stones <20 mm. (1.43 days vs. 1.75 days). Similarly, the duration of JJ stenting after the procedure was significantly longer in cases with larger stones as compared to patients with smaller stones (35.77 vs. 44.68 days). Both of these parameters seem to be important as they will affect the time of return to daily life and work after the procedure. In addition, the presence of a JJ stent has a negative effect on the quality of life after the procedure requiring removal after a certain period of time. Regarding the quality of life after this procedure, presentation at ED because of colic pain during the post-operative follow-up period was seen to be more prominent in cases with larger stones, together with a high rate of auxiliary procedures due to the fragments requiring a secondary intervention.

The infection rate can be considered as a highly important parameter evaluated in the study as it was found to mainly be associated with the duration of the procedure. A significantly higher rate of infectious complications was determined in cases undergoing fURS for relatively larger stones (22.9%) as compared to the cases operated on for smaller calculi (6.8%).

In light of the current study findings and the published data in literature, it is clear that, although use of fURS as a minimally invasive management alternative for moderate size stones (<20 mm) is safe and effective with stone-free rates comparable to those of other available modalities (SWL and PNL), this modality could also be performed successfully with acceptable complication rates in the management of relatively larger (>20 mm) stones. However, in order to obtain the desired completely stone-free rates, patients need to be well informed about staged procedures and evaluated in respect to the size and location of the stones in the kidney. While larger stones located in the renal pelvis and mid – upper calyceal position can be fragmented and eliminated and/or removed in a highly successful and safe manner, larger stones in the lower pole should be treated with the PNL approach to achieve a completely stone-free status in a single session. Operating times and postoperative length of stay in the hospital are longer and the risk of infection seems to be higher in the management of such stones. Therefore, all cases need to be evaluated on an individual basis with respect to stone characteristics, to predict the likelihood of success after fURS in the management of larger stones.

The current study may have several limitations, with the relatively low number of patients being considered as the most important. We believe that further multi-centre studies with larger series of cases with such stones are certainly needed. A second limitation can be stated as the prospective evaluation of retrospectively-obtained data for analysis. A prospective study would be better to demonstrate the actual role of fURS in the minimally invasive management of larger renal stones located in different parts of the kidney. However, despite these limitations, we believe that as the first study focusing on the role of fURS in large stones based on stone location characteristics, our preliminary data will be contributive enough to the existing data in the literature.

CONCLUSIONS

The results of this study indicate that fURS can be an effective and safe treatment alternative to PNL in larger renal stones (>20 mm) located in the pelvis and the upper part of the calyceal system of the involved kidney. An individualized approach to these cases, focusing on the stone-related parameters will enable the prediction of success and postoperative complications. There is certainly a need for further studies with larger numbers of cases to confirm these results.

ETHICAL APPROVAL

This article does not contain any studies with animals performed by any of the authors.

INFORMED CONSENT

Informed consent was obtained from all of the participants that were included in the study.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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