Asymptomatic Lower Pole Small Renal Stones: Shock Wave Lithotripsy, Flexible Ureteroscopy, or Observation? A Prospective Randomized Trial

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OBJECTIVE To present the outcomes of flexible ureteroscopy (F-URS), shock wave lithotripsy (SWL), and observation in the management of asymptomatic lower calyceal stones.

METHODS A total of 150 patients with asymptomatic lower calyceal stones were randomized into F-URS (group 1), SWL (group 2), and observation (group 3) groups. The main criteria for patient enrollment were having asymptomatic single lower pole stones <1 cm.

RESULTS In F-URS, the mean stone-free rate was 92% (46 of 50). The mean number of sessions for the SWL group was 1.48 ± 0.65. Stone-free rate was 90% (45 of 50). In the observation group, patients were followed up for a mean of 21.02 ± 3.65 months. Three stones passed spontaneously without any symptoms. Pain developed in 3 patients during follow-up, and 2 of them passed a stone and responded to analgesics without further treatment. Complication rates for groups 1 and 2 were similar, but group 2 had higher Clavien grades.

CONCLUSION For asymptomatic small-sized lower calyceal stones, SWL and F-URS are established treatment modalities. However, with low auxiliary treatment rates, observation may be an option for the management of nonsymptomatic small-sized lower pole kidney stones. UROLOGY ■: ■—■, 2014.

Management of asymptomatic lower calyceal stones is one of the most controversial topics in endourology as the natural history is poorly defined and the progression risk is not clear.[1] Even though various types of modality are available for the management of asymptomatic lower calyceal stones including extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy (PNL), and ureteroscopy, there is no consensus on the appropriate time or intervention type for small, nonobstructing, asymptomatic lower pole calyceal stones.[2]

However, even though the indications for the treatment of lower pole stones are well defined (such as increasing stone size, localized obstruction, associated infection, and acute and/or chronic pain), the natural history of asymptomatic lower pole stones has not been defined to decide whether a prophylactic intervention is required.[3] Although some groups advocate observation in patients with asymptomatic lower calyceal stones, a symptomatic episode or the need for intervention was required at approximately 10% per year and is expected to be >50% of cases in 5 years.[4] Kang et al[5] reported that 50% of cases under observation required intervention in 19 months time.

In this study, it was aimed to present the outcomes of flexible ureteroscopy (F-URS), shock wave lithotripsy (SWL), and observation when managing asymptomatic lower calyceal stones.

METHODS

Approval for the study was granted by the local ethics committee. Patients who presented at our clinic with single lower pole stones <1 cm between December 2011 and February 2014 were enrolled in the study. Analysis in search of 80% power revealed that groups at an average of 48 patients each would be required to demonstrate the outcomes with a type I error of .05, so a total of 150 patients with asymptomatic lower calyceal stones were prospectively randomized into F-URS (group 1), SWL (group 2), and observation (group 3) groups. The main criteria for patient enrollment were asymptomatic single lower

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Table 1. Patient demographics

Parameters	F-URS (N = 50)	SWL (N = 50)	Observation (N = 50)	*P* Value
Patient age (mean + SD), y	36.84 (11.70)	34.5 (11.04)	32.52 (13.29)	.202
Stone size (mean + SD), mm	8.2 ± 1.2	7.9 ± 1.1	7.9 ± 0.7	.424
Gender, %				
Male	35	37	29	.618
Female	15	13	21	.723

F-URS, flexible ureteroscopy; SD, standard deviation; SWL, shock wave lithotripsy.

pole stones <1 cm. Patients with semiopaque or nonopaque stones, anomalous kidneys, ureteropelvic junction obstruction, a history of open or percutaneous interventions to the ipsilateral kidney, a solitary kidney, steep infundibulopelvic angle (<30°), and a dilated pelvicalyceal system were excluded from the study. The study protocol was explained to the patients with a full discussion of success, possible complications, invasiveness, the need for anesthetics, and hospitalization, and patients were actively involved in the decision-making process. After informed consent was obtained from the patients for all options, randomization was applied using an online randomization tool.[6]

Flexible ureterorenoscope (Flex-X2; Karl Storz, Tuttlingen, Germany) and holmium laser (Ho:YAG Laser; Dornier MedTech, Munich, Germany) were used for flexible ureterorenoscopy. In the F-URS group, preoperative stenting was not performed. An access sheath of 11-13 Fr was surgically placed. The stones were placed onto the upper pole or renal pelvis and disintegrated there. The operation was ended when the biggest stone was <3 mm in diameter. After the procedure, a JJ stent was not placed unless a complication occurred. The patients treated by F-URS were hospitalized and discharged the following day.

SWL was performed as an outpatient procedure, without general or regional anesthesia by the same experienced urologist. An electrohydraulic extracorporeal lithotripter (MULTIMED Classic; ELMED, Ankara, Turkey) was used for SWL (in each lithotripsy session, 2500-3000 shocks were given at 14-17 kV.). Patients in the SWL group underwent three courses at the most of SWL therapy. The patients were evaluated for fragmentation by kidney-ureter-bladder (KUB) radiography, 1 week after the SWL session. When stone-free status was established in KUB, an abdominal computerized tomography (CT) scan was applied for confirmation.

To evaluate and compare the complications of procedures, a modified Clavien classification was used.

In the observation group, primary endpoint was 24 months. Kang et al[5] proposed that 50% of patients required intervention in their groups of patients under observation. We planned, on this knowledge, to report the data after approximately 24 months. All patients were evaluated every 3 months. Physical examination, serum creatinine levels, urinalysis, and plain radiographs of the KUB were applied at each visit. Stone length was defined as the largest diameter on KUB radiography. Development of symptoms, such as ureteral or calyceal obstruction, urinary tract infection, and hematuria, during follow-up or stone growth was described as disease progression. Intractable pain or pain causing impairment of quality of life was also an indication for active intervention. These patients were referred for SWL, F-URS, or PNL after prompt medical treatment.

For each procedure, primary outcome measures were: fragmentation <3 mm was considered successful 3 months after the procedure (SWL and F-URS), and success for observation was defined as no requirement for any intervention until the end of the observation period.

Follow-up

All patients underwent a detailed evaluation including KUB radiography, intravenous urography, and spiral CT at the initial visit. Postoperative analysis was performed by KUB radiography for each SWL session and F-URS procedure after 1 week. To assess stone status, the observation group were assessed with KUB radiography every 3 months and CT in every 6 months. In the F-URS and SWL groups, CT imaging was applied at 3rd and 12th months after the intervention.

Statistical Analysis

All groups were compared using the 1-way analysis of variance or the Kruskal-Wallis test for continuous variables and the chi-square or the Fisher exact tests for categorical variables. Odds ratios were calculated and statistical determinations were within the 95% confidence interval. Two-tailed *P* values <.05 were considered as statistically significant. Data are shown as mean ± standard deviation. Data were entered into an Excel for Mac 14.0 database (Microsoft Corp, Redmond, WA) and analyzed using Statistical Package for Social Sciences 20 software for Mac (SPSS Inc, Chicago, IL).

RESULTS

Each group consisted of 50 patients. The mean stone sizes in groups 1, 2, and 3 were 8.2 ± 1.2, 7.9 ± 1.1, and 7.9 ± 0.7 mm, respectively. The demographic parameters of the patients are listed in Table 1.

In F-URS group, the mean stone-free rate was 92% (46 of 50). The main reason for residual stones was a limitation of the ureterorenoscopy deflection in lower pole stones of 4 patients. These patients were treated with PNL. Three patients (6%) in this group had intraoperative complications. All patients had grade 1 ureteral laceration and treated via double J stenting intraoperatively. They were categorized as Clavien grade 3A because no additional general anesthesia was planned. They required local double J stent removal as an auxiliary measure. Four patients (8%) in group 1 had postoperative complications. Three of these patients had fever in the first 24 hours postoperatively (Clavien grade 1), and 1 patient had a urinary tract infection, which was treated with oral ciprofloxacin (Clavien grade 1).

The mean number of sessions for the SWL group was 1.48 ± 0.65. Sixteen patients were treated in 2 sessions, and 4 patients were treated in 3 sessions. The remaining 30 patients were managed in 1 session. After a mean of 1.48 sessions, the stone-free rate was 90% (45 of 50). The mean complication rate for the SWL group was 6% (3 of 50): 1 patient had renal colic after SWL treatment but

Table 2. Procedure outcomes

Parameters	F-URS (N = 50)	SWL (N = 50)	Observation (N = 50)	*P* Value
Number of sessions	1	1.48 ± 0.65	n/a	<.001
Stone free after 3 mo, % (n)	92 (46/50)	92 (46/50)	2 (1/50)	<.001
Stone free at the end of the study, % (n)	92 (46/50)	100 (50/50)	10 (5/50)	<.001
Auxiliary measures, % (n)	8 (4/50)	6 (3/50)	1% (6/50)	.555
Uneventful course, % (n)	86 (43/50)	94 (47/50)	88 (44/50)	.397
Efficacy quotient*	0.85	0.79	0.09	n/a
Complications, % (n)	14 (7/50)	6 (3/50)	n/a	.318
Minor (Clavien grade I-II) complications, % (n)	8 (4/50)	4 (2/50)	n/a	.687
Major (Clavien grade III-V) complications, % (n)	6 (3/50)	2 (1/50)	n/a	.617

n/a, not applicable; other abbreviations as in Table 1.
* Efficacy quotient was calculated as: % stone-free rate/(100 + auxiliary measures + re-treatment).[7]

treated with analgesic medication (Clavien grade 1), 1 patient having renal colic had to undergo ureteroscopy for a ureter-migrated stone (Clavien grade 3b), 1 patient had a perirenal hematoma treated conservatively (Clavien grade 1), and 1 patient (2%) passed residual fragments spontaneously. All patients were stone free at the end of 12 months. Two of the 3 patients with symptomatic residual stones after SWL were rendered stone free with F-URS, and 1 patient was rendered stone free with PNL as auxiliary treatment.

In the observation group, patients were followed up for a mean of 21.02 ± 3.65 (17-24) months. Six patients had to be treated with auxiliary procedures and were removed from the observation group, and 3 patients were lost to follow-up after 17 months. Three stones passed spontaneously (1 in first 3 months and 2 in 8th and 19th months) without any symptoms. Pain developed in 3 patients during follow-up, and 2 of them passed a stone after 5 and 6 months, respectively and responded to analgesics without further treatment. Six patients, who had developed symptoms, recurrent urinary tract infections, pain, an obstructing ureteropelvic stone, and/or increased stone size required active intervention during follow-up, consisting of PNL in 1 (2%), SWL in 3 (6%), and F-URS in 2 (4%) patients. The overall noneventful follow-up ratio was 88% (44 of 50). Preobservation stone size was 7.96 ± 0.76 mm. After 2 years, the mean stone size was 8.07 ± 0.75 mm. Seventeen stones did not increase in size (34%). Of the 66% of stones increased, mean increase in size was 0.15 ± 0.7 mm (2.0%).

Clayman et al[7] developed a calculation (efficiency quotient) to compare the results of different approaches for stone treatment. For groups 1, 2, and 3, efficiency quotients were 0.85, 0.79, and 0.09, respectively.

When the noneventful ratio is considered as success, the success rates ($P = .801$) and complication rates ($P = .555$) among the groups were similar (Table 2).

COMMENT

For nonsymptomatic calyceal stones, several treatment options are possible. SWL is a viable option as well as F-URS. Although there is consensus on the efficacy and safety of these procedures, there are conflicting reports on observation as a management option.

The European Urological Association recommends observation for nonsymptomatic calyceal stones.[2] However, they indicate active stone removal in the following conditions: infection, stone growth, obstruction, stones >15 mm, patient preference, and treatment choice.

Inci et al[8] followed up 24 patients for a mean of 52.3 months and found a progression rate of 33.3% and an intervention rate of 11.1%. Three migrating stones without any symptoms were also reported. Glowacki et al[9] investigated the outcome of nonsymptomatic urolithiasis and reported an incidence rate of 10% per year, with a 5-year probability of nearly 50%. In another study, with a follow-up duration of 2.2 years, researchers did not find any difference between observation and SWL groups in terms of symptoms, additional therapy requirements, or quality of life.[10] Yuruk et al[11] randomized patients with nonsymptomatic lower pole stones into SWL, observation, and PNL groups. They reported >20% stone-related incidents in the observation group and concluded that PNL has outstanding outcomes. Kang et al[5] followed up patients with stones of a mean size of 4 mm for a mean of 31 months and revealed a 29.1% spontaneous passage incidence. They also found a 45.2% progression rate. They proposed that 50% of patients developed symptoms in 19 months time. Koh et al[12] revealed a similar 45.9% progression rate in their study of 50 patients. Burgher et al[13] demonstrated a 77% progression rate in their study of 300 patients with mean 10.8-mm sized stones. In the present study, 88% noneventful patients were reported from an approximate 2-year follow-up. However, stone enlargement of approximately 1 mm was reported over the course of 2 years.

The authors of this study had previously performed a prospective randomized study comparing SWL and F-URS in lower pole stones <1 cm. In that study, the superiority of F-URS over SWL was demonstrated.[14] El-Nahas et al[15] compared the outcomes of SWL and F-URS procedures in lower pole stones between 10 and 20 mm. A success rate of 86.5% and a complication rate of 8% were determined in the F-URS group. In a study by Pearle et al[16] comparing SWL and F-URS in small-size lower pole stones, success rates of 72% for F-URS and

Table 3. Comparison of outcomes

Articles	Number of Patients	Mean Stone Size	Follow-up Duration, mo	Observation			Shock Wave Lithotripsy			Flexible Ureteroscopy	
				Spontaneous Passage Rate, %	Progression Rate, %	Intervention Rate, %	Number of Sessions	Stone-free Rate, %	Complication Rate, %	Stone-free Rate, %	Complication Rate, %
Koh et al[12]	50	5.7 mm	46	20	45.9	7.1	n/a	n/a	n/a	n/a	n/a
Kang et al[5]	347	4.39 mm	31	29.1	45.2	24.5	n/a	n/a	n/a	n/a	n/a
Inci et al[8]	24	8.8 mm	52.3	12.5	33.3	11.1	n/a	n/a	n/a	n/a	n/a
Yuruk et al[11]	94 (31, PNL; 31, SWL; 32, observation)	136.7 mm^2*	19.3	3.1	n/a	18.7	2.06	54.8	6.4	n/a	n/a
Burgher et al[13]	300	10.8 mm	39	n/a	77	26	n/a	n/a	n/a	n/a	n/a
Glowacki et al[9]	107	n/a	32	15	n/a	16.8	n/a	n/a	n/a	n/a	n/a
Sener et al[14]	140 (70, SWL; 70, F-URS)	8.0 mm	n/a	n/a	n/a	n/a	2.7	91.5	5.7	100	2.8
Pearle et al[16]	67 (32, SWL; 35, F-URS)	7.3 mm	n/a	n/a	n/a	n/a	1	35	22	50	20
Present study	150 (50, F-URS; 50, SWL; 50, observation)	8 mm	21.2	6	66	12	1.48	90	6	92	14

PNL, percutaneous nephrolithotomy; other abbreviations as in Tables 1 and 2.
* Stone area in mm^2.

65% for SWL were reported. In the present study comparing F-URS, SWL, and observation in small lower calyceal stones, a success rate of 92% was determined in the F-URS group. Patients treated by SWL achieved a success rate of 90% in 1.48 sessions. The success rates are similar, but for patients undergoing SWL, this rate was obtained in >1 session. Some patients underwent as many as 3 sessions of treatment without any success. The outcomes of our study were compared with similar studies and demonstrated in Table 3.

Several complications can arise in treatment choices. When considering SWL, renal colic was reported at a rate of 4%[17] and sepsis in 1%-2.7% of patients.[18] Hematoma may develop in approximately 20% of patients.[19] There are case reports of morbid cardiac events and even bowel perforation.[20] F-URS seems to have rare complications, such as mucosal injury (about 1.5%), avulsion (0.1%), and ureteral stricture (0.1%).[21] In the present study, 14% of the F-URS group patients had complications, whereas this rate was 6% in the SWL group. These rates seem similar, but most complications of the F-URS group seemed to have higher Clavien grades. As patients were only monitored for approximately 2 years, long-term complications, such as strictures could not be observed. The main advantage of observation option may be the absence of these long-term complications.

These modalities should be discussed separately according to success. Even though F-URS seem to have higher success rates than other modalities, it should always be kept in mind that F-URS is a surgical intervention, requires anesthesia, and may cause major complications as seen in our study. SWL is not a surgical intervention and can be performed without the need of anesthesia in the adult population but it still may cause serious complications. However, it has the main advantage of stone-free state without anesthesia. Observation may seem the most harmless modality among others; however, success rates can be defined as not having adverse events due to stone existence. Although observation may delay intervention in most patients, this study reveals around 12% of patients require auxiliary measures during observation period.

For small-sized lower calyceal stones, SWL and F-URS are considered to be equally safe and effective, but observation and deferred treatment could also be an option because of the high probability of a noneventful duration. Patients may be followed up until the onset of symptoms. Over the course of 2 years time, the rate of stones enlarging or symptoms developing was approximately 12%.

The limitations of this study are the small cohort for the groups and the lack of follow-up after SWL and F-URS.

CONCLUSION

For asymptomatic small-sized lower calyceal stones, SWL and F-URS are established treatment modalities. However,

observation may delay the need for treatment for most patients and even be an option for the management of nonsymptomatic small-sized lower pole kidney stones.

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