Retrograde Intrarenal Surgery Versus Shock Wave Lithotripsy for Renal Stones Smaller Than 2 cm: A Randomized Clinical Trial

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Purpose: To compare outcomes of retrograde intrarenal surgery (RIRS) with extracorporeal shock wave lithotripsy (SWL) for stones ≤ 2 cm.

Materials and Methods: Patients who were diagnosed with kidney stones of ≤ 2 cm underwent RIRS or SWL in a parallel group randomized clinical trial with balanced randomization [1:1] from 2011 to 2014. The primary outcome of interest was stone free rate after a single session intervention. Patients were evaluated by ultrasonography and KUB at 1 and 3 months after the intervention for the presence of residual stone by a radiologist who was blinded to the study.

Results: The stone free rate one month after a single session intervention in the RIRS group was higher than the SWL group (90% versus 75%, $P = .03$). The success rates after two sessions of RIRS versus SWL were 96.7% versus 88.3% respectively. ($P = .08$) Patients in the RIRS group had significantly lower postoperative visual analogue pain score compared to the SWL group (5.2 ± 2.8 versus 3.1 ± 2.7, $P < .001$). Steinstrasse formation and renal hematoma were observed in 4 and one patient in the SWL group versus no patient in the RIRS group. Postoperative hospital stay was significantly shorter in the SWL group (6.7 ± 1.3 versus18.9 ± 4.3 hours, $P < .001$).

Conclusion: The RIRS procedure is a safe treatment option for renal stones of ≤2cm with less pain and higher success rate at first session compared to SWL.

Keywords: endoscopes; kidney; laser; lithotripsy; nephrolithiasis; retrograde intrarenal surgery; shockwave lithotripsy

INTRODUCTION

The current preferred treatment for renal stones less than 2 cm is extracorporeal shock wave lithotripsy (SWL) due to its minimal morbidity and simplicity.[1] However, the efficacy of SWL drops significantly for large renal stones.[2] Several factors such as stone composition and position, kidney malposition and obesity of the patient can decrease the success rate of SWL.[3] Alternative procedures to SWL include laparoscopic nephrolithotomy and percutaneous nephrolithotripsy (PNL) which are more invasive and harbor a profile of complications.[1,4] Vast development of endoscopic technology as well as introduction of holmium laser for treatment of urologic stones has made flexible ureterorenoscopy (F-URS) a good alternative procedure for the management of renal stones.[5,6] Retrograde intrarenal surgery (RIRS) seems a promising technique which is performed at many centers for patients who have previously undergone SWL or PNL[7]. Few studies that have compared efficacy and safety of RIRS with other procedures including SWL reported that RIRS can be considered as an option for treating medium sized renal stones.[6,8] Some studies reported success rates approaching 90% when RIRS is applied to single renal stones with maximal diameter of less than 3 cm.[5,6,9] This randomized clinical trial was conducted to compare outcomes and complications of SWL with RIRS for the management of renal stones ≤ 2 cm.

PATIENTS AND METHODS

Study population

Study participants were patients who were diagnosed with medium sized renal stones (maximum diameter of 6 mm to 2 cm) from March 2011 to March 2014. Patients were enrolled in the study after a routine preoperative evaluation. Inclusion criteria were presence of renal stones ≤ 2 cm in diameter. Exclusion criteria were kidney anomalies, uncontrolled coagulopathies, ureteral obstruction, history of previous renal surgery or SWL, pregnancy and renal failure (serum creatinine ≥ 3mg/dl). The nature of the study was explained to each patient and informed consent was obtained. The protocol of this study was approved by the ethics committee of the Laser Application in Medical Sciences Research Center (LAMSRC). Patients' enrollment algorithm has been illustrated in **Figure 1**.

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Table 1. Patients' demographic data and clinical characteristics.

Characteristics[a]	SWL	RIRS	*P* value
Age (years)	31.3 ± 6.5	32.4 ± 7.8	0.4
Male Gender	39 (65)	37 (61.7)	0.7
Body mass index (Kg/m^2)	27.1 ±4.3	26.7 ± 4.1	0.6
Stone diameter (mm)	16.4 ± 3.3	16.8 ± 2.1	0.4
Number of stones	1.3 ± 0.7	1.3 ± 0.6	0.9
Stone location			
Superior calyx	17 (28.4)	15 (25)	
Middle calyx	11 (18.3)	12 (20)	
Inferior calyx	5 (8.3)	6 (10)	
Pelvis	22 (36.7)	21 (35)	
Multiple	5 (8.3)	6 (10)	
Left sided stone	30 (50)	27 (45)	0.6

[a]Data is presented as mean ± SD or number (percent)

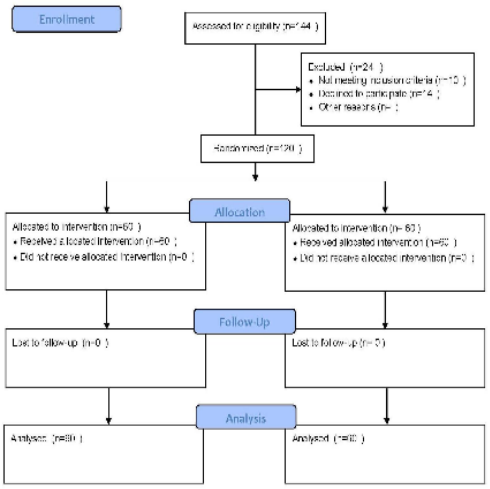

Figure 1. Patients' enrollment algorithm

One hundred and twenty patients underwent further evaluation consisting of urine analysis, urine culture and renal functional assays. A full course of antibiotics was administered before intervention in case of positive urine culture. In patients with negative urine culture, a single dose of prophylactic antibiotics was administered before SWL or RIRS. CT urography was the primary modality to determine the size, number and location of calculi, as well as the anatomy of the upper urinary tract. Routine prophylactic intravenous antibiotics were administered before surgery.

Study design

This study was a prospective single center, parallel-group randomized clinical trial with balanced randomization [1:1] which was performed in a referral hospital in Tehran, Iran. Sample size was calculated considering a 30 percent expected difference between RIRS and SWL in the primary outcome of interest. Considering type I error of 0.05 and type II error of 0.1, 59 samples were needed for each arm. Therefore 60 samples were decided to be enrolled in each arm of the study. Patients were randomly assigned to one of the two treatment groups of SWL or RIRS (sixty patients in each group). Randomization was carried out using computerized random numbers. The allocated treatment for each patient was recorded in concealed envelopes. After achieving eligibility criteria and patient's agreement on participation, the concealed envelopes were opened by one of the researchers and the allocated treatment was performed as explained below.

Surgical technique

The SWL procedure was performed using the Dornier HM3 Lithotripter (Dornier MedTech, Wessling, Germany) on sedated patient in the supine position. All SWL procedures were performed by a single urologist. The therapeutic power was started from 15 kV and increased stepwise up to 20 kV. The rate of delivered shocks was 60 to 90 per minute. The number of shock waves was limited to 3,000 per session. Shocks were given based on stone dissolution while stones were fragmented under fluoroscopic/ultrasonic guidance. The therapy head of the electromagnetic lithotripter was positioned below the treatment table and conductive gel was applied. In the RIRS group, patients received spinal anesthesia and then were turned into the lithotomy position. After inserting an 11 Fr semirigid ureteroscope (Olympus) under endovision guidance thorough the bladder, a 0.035-inch hydrophilic coated guide-wire was introduced through the channel into the ureteral orifice and then ureteroscopy was performed with hydrodilation to dilate the ureter. Thereafter, an 11 Fr ureteral access sheath was placed and a 4Fr/6Fr feeding tube was placed trans-urethrally to maintain low pressure of the bladder. An 8.5/5.3 Fr flexible ureteroscope (Olympus) was introduced under fluoroscopic guidance to the renal pelvis to identify the stone. Stone fragmentation was performed using holmium:YAG laser with 200 µm fibers. Lower and middle calyceal stones were relocated into renal pelvis or upper calyx by basketing before lithotripsy if it was not possible to fragment them in their primary position. Final ureteronephroscopy was performed after fragmentation, followed by a control fluoroscopy to detect any probable residual stones. A double-J stent was placed in the ureter for two weeks in cases of difficult dilation, prolonged procedure or residual stone. In case of no ureteral injury, a ureteral stent was inserted and fixed to the Foley catheter. The ureteral catheter was removed the day after surgery. RIRS procedures were performed by a single experienced endourologist.

Outcome assessment

The primary outcome of interest was stone free rate after one session of RIRS or SWL. Residual stones were evaluated by plain abdominal radiographs and renal ultrasonography 1 and 3 months after treatment. The radiologists who performed ultrasonography or reported KUB were totally blind to the study objectives and protocols. Patients were considered stone free if residual stones were ≤ 3 mm. A second treatment session was planned for large and/or symptomatic stones detected at one month follow up. Secondary outcomes included stone free rate after two treatment sessions, pain after procedures, hospital stay, and complications including

Table 2. Patients' intraoperative and postoperative data

Characteristics[a]	SWL	RIRS	*P* value
Postoperative fever	4 (6.7)	1 (1.6)	0.1
Renal hematoma	1 (1.6)	0(0)	0.3
Gross hematuria	8 (13.3)	4 (6.7)	0.2
Steinstrasse	4 (6.6)	0(0)	0.04
Injury to adjacent organs	1 (1.6)	0(0)	0.3
Pyelocaliceal system disruption	0(0)	0(0)	
Pain VAS	5.2 ± 2.8	3.1 ± 2.7	0.001
Number of procedures	1.6 ± 0.3	1.2 ± 0.2	0.001
Need for second session	15 (25)	6(10)	0.03
Operation duration (minutes)	48.2 ± 14.6	79.9 ± 14.1	0.001
Hospitalization duration (hours)	6.7 ± 1.3	18.9 ± 4.3	0.001
Success rate at first session	45 (75)	52 (90)	0.03
Success rate	53 (88.3)	58 (96.7)	0.08
Superior calyx	16 (94)	15 (100)	0.3
Middle calyx	11 (100)	11 (91.6)	0.3
Inferior calyx	2 (40)	6 (100)	0.02
Pelvis	21 (95.5)	21 (100)	0.3
Multiple	3 (60)	5 (83)	0.4

[a]Data is presented as mean ± SD or number (percent)

postoperative fever, renal hematoma, hematuria, pelvicaliceal system injury, and steinstrasse formation. Postoperative pain was evaluated by visual analogue pain scale (VAS) 24 hours after the procedure. Duration of the operation was defined as the time between the first and last shock for SWL and from ureteroscope insertion to Foley insertion for RIRS. Data analysis was performed using SPSS software (Statistical Package for the Social Sciences, V. 16.0; SPSS Inc, Chicago, IL, USA). Numerical variables were compared by independent samples t-test. Ordinal variables were compared by Mann-Whitney U test. Categorical variables were compared by chi square or fisher exact tests as appropriate. All analyses were planned as intention to treat.

RESULTS

As explained in the methods section, sixty patients were enrolled in each arm of the study. Ten patients were excluded from study due to exclusion criteria. Patients' demographic data in the two study groups has been outlines in **Table 1**. There was no statistically significant difference between the groups regarding stone parameters including location, number and size. Operative data and postoperative investigations have been illustrated in **Table 2**. The mean ± SD of energy used with the holmium:YAG laser for lithotripsy was 150.8 ± 11 kJ. Success rate of procedure at first session was 75% in SWL group and 90% in RIRS group which raised to 88.3% and 96.7% after the second session. There was a significant superiority of success rate for RIRS over SWL in resolving the inferior calyx stones (100% vs. 40%, $P = .02$). After excluding patients with inferior caliceal stones and patients with multiple stones which are known limitations of SWL, the success rate of SWL increases to 96% which is very close to the observed success rate of RIRS (98%) for these patients. Mean operation duration and hospital stay were significantly shorter in the SWL group (48.2 ± 14.6 minutes versus 79.9 ± 14.1 minutes, $P = .001$; 6.7 ± 1.3 hours versus 18.9 ± 4.3 hours, $P = .001$). Postoperative fever was observed in 4 patients in the SWL group and one patient in the RIRS group which was managed with broad spectrum antibiotics. Perforation of the pelvicaliceal system was not observed in any patient. One patient in the SWL group experienced anemia due to renal hematoma which was treated conservatively. One case of adrenal hematoma was observed in the same group that was managed uneventfully. Steinstrasse formation was reported in four patients in the SWL group which necessitated ureteroscopic management. Patients in the RIRS group reported lower VAS for postoperative pain and required less analgesic medication postoperatively. In two patients in the RIRS group, performing RIRS was not possible in the first session due to difficult dilation. In these two patients, a Dj catheter was inserted and RIRS was successfully performed after two weeks. In another four patients in the RIRS group Dj stent was inserted after completion of lithotripsy because of lengthy operation duration as mentioned in the methods section.

DISCUSSION

SWL has an excellent success rate in treating renal stones with diameters of less than 2 cm.[10] Some factors including anatomical variations, obesity, kidney malpositioning and stone composition can preclude

successful SWL[3]. Improvements in endoscopic technology have made retrograde stone removal a more popular approach as endourologic procedures dynamically expand their role for treatment of urinary calculi.[11-12]This comparative study was conducted to compare the efficacy and safety of RIRS in the management of renal stone ≤ 2cm with SWL as a procedure of choice in many centers. The success rate of RIRS at first session was 90% which was higher than SWL which supports the reported data from previous studies.[13] In their study, Hussein et al. suggested the diameter of 2 cm as the upper limit of stone size which assures stone clearance in a single procedure regardless of its density or location [13]; a finding that was confirmed in a review of the literature.[14] Recently some authors have evaluated the role of RIRS in the management of renal stones of >2cm diameter and suggested it as a favorable option for selected patients with renal stones of 2 to 4 cm. However, in these researches high success rate was achieved after two or three treatment sessions.[5,15] The higher success rate of RIRS after one session in the present study suggests that this method is a promising alternative for SWL. Nevertheless, it is noteworthy that the main differences in the success rates of SWL versus RIRS were observed mainly in patients with lower pole stones and also in patients with multiple stones. The success rates of SWL were essentially similar to RIRS for stones in the superior calyx, pelvis or middle calyx (**Table 2**). Holmium:YAG lithotripsy is mainly performed through photothermal mechanisms to fragment stones (12). Therefore, its efficacy in stone fragmentation and clearance is not dependent on stone composition.[16] In contrast, multiple authors have reported that SWL success varies between different stone compositions and even within stones of the same composition.[3] A principle in performing SWL is the correlation between the higher distance from the skin surface to the stone and the lower chance of stone fragmentation.[3,14] As a consequence, some urologists prefer to manage obese patients with renal calculi by PNL.[17] Increased respiratory compromise with positioning such patients in the prone position makes RIRS a potentially viable treatment method.[14] According to a recent meta-analysis, the use of RIRS in obese patients is efficient with low complications, and with an overall stone-free rate of 87.5%.[14] The Residual calculi remaining within the kidney can lead to recurrent stone formation after the SWL procedure.[18] In addition to this probable complication, expulsion of the produced stone fragments is usually followed by renal colic.[19] This fact can explain the higher reported pain scores from patients in the SWL group. Considering the probability of repeated treatment sessions for SWL and the consequential induction of multiple episodes of pain in patients, a high first session success rate for RIRS makes it a favorable modality for individual who are more susceptible to pain. Steinstrasse formation is another complication that can affect 2% to 10% of the patients who have received the SWL procedure.[20] This complication is directly correlated with increasing stone burden and was observed in four patients in the SWL group in the current study. Steinstrasse is one of the drawbacks of SWL which increases the number of auxiliary treatment in these patients.[20] Although some surgeons have suggested use of routine stenting before SWL to decrease the chance of steinstrasse formation and increase the stone-free rates, stenting is clearly associated with increased morbidity.[21,22] On the other hand, the need for insertion of ureteral stent after ureteral access is also mentioned as a limitation for the RIRS procedure.[23] Despite the advantages of ureteral access sheaths by facilitating multiple passages of the flexible ureteroscope as well as providing lower intrarenal pressures and better flow through the ureteroscope, it might be associated with ureteral injuries with reported rates as high as 46.5%.[23-25] For this reason, routine ureteral stenting is often recommended if a ureteral access sheath is used. In order to avoid the extra admission for JJ stent removal, we prefer not to introduce ureteral stent unless the case is complicated or failed. Matani et al. recommended risk factor stratification for JJ stenting and believed that its routine insertion is impractical and weakly supported.[26] Also, another study has suggested that patients could be selected for no ureteral stent if ureteroscopy was uneventful.[23] Hospital-stay duration and operation time were higher in the RIRS arm of the current study. One drawback of RIRS is long operation duration that is dependent on stone size, number, and location and experience of the surgeon. Nevertheless, in spite of having a reported duration of 30 to 60 minutes per SWL session, this procedure regularly requires repeated treatment sessions along with a high rate of extra admissions for renal colic management.[6] Required equipment for RIRS include flexible ureteroscope and holmium laser which are expensive and may be unavailable in many centers.[1] Also, unfamiliarity of urologists with this technique make RIRS a technique that is usually performed in limited referral centers.

Lack of double blind design was a limitation of our study. We did neither evaluate stones' Hounsfield units preoperatively to identify its effect on the success rate nor performed Chemical analysis of the stones. Therefore the influence of stone composition on the success of RIRS could not be evaluated. Cost effectiveness of each procedure was not included in the protocol of this study and is another limitation of this study. And at last we should mention that according to the protocol of our ward we limited the number of shockwaves to 3000. It is possible to use shockwave numbers of up to 4000. This could have made a difference in some cases. However, excluding patients with lower pole or multiple stones, SWL success was parallel to RIRS for patients with stones size of 6 mm to 2 cm.

CONCLUSIONS

Our data suggests that RIRS is a safe, successful and less painful procedure for treatment for renal stone of ≤2cm. We suggest RIRS as an option available for patients with small to medium sized renal stones especially in the lower pole in centers with available experience after consultation with the patient regarding alternative options available including SWL. The optimum treatment modality should be chosen based on the patient and stone characteristics as well as the surgeon's experience and availability of the equipment.

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CONFLICT OF INTEREST

The authors report no conflict on interests.

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