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ORIGINAL ARTICLE

The efficacy and safety of bilateral same-session ureteroscopy with holmium laser lithotripsy in the treatment of bilateral ureteral stones

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ABSTRACT

BACKGROUND: A staged ureteroscopic procedure is the generally preferred method in the treatment of bilateral ureteral stones due to the risk of bilateral injury. In this study we aimed to evaluate the safety and efficacy of bilateral same-session ureteroscopy (BS-URS) in terms of complications, operation time, serum creatinine, hospital stay and stone-free rates.

METHODS: A total of 75 patients who underwent BS-URS and holmium laser lithotripsy were evaluated, retrospectively. The patients were re-evaluated postoperatively after four weeks with ultrasonography, X-ray or computed tomography. Pre- and postoperative variables were analyzed. The results of BS-URS were also compared with unilateral URS cases performed in the same time period.

RESULTS: BS-URS was performed in 58 men and 16 women with a mean age of 46.3 years. The mean operating time was 69 min. In patients with stone burden ≥20 mm, the mean operative time was longer. Intraoperative complications were observed in eight patients, Clavien grade I in seven, and Clavien grade IIIb in one. Early postoperative complications included fever and hematuria were seen in 10.6% of the patients. One patient underwent secondary URS for residual stone. Stone free rate after four weeks was 98.6%. Overall complication and and stone-free rates were similar in BS-URS and unilateral URS groups (P>0.05). The mean operating time was significantly longer in BS-URS patients (P=0.001).

CONCLUSIONS: BS-URS is as safe and efficient procedure as unilateral ureteroscopy with high stone-free and minimal morbidity rates in the treatment of bilateral ureteral stones in appropriate patients.

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Surgical treatment of the urinary stone disease is one of the most common practices in urology. Multiple stones are seen in 20-25% of patients with urolithiasis and bilateral ureteral stones also are not uncommon.[1, 2] The treatment options for bilateral ureteral stones are extracorporeal shock wave lithotripsy (ESWL), ureteroscopy (URS), percutaneous nephrolithotomy (PCNL), open surgery, laparoscopic or robot-assisted surgery and sometimes their combinations. PCNL is limited for the ureteral stones which are located at the ureteropelvic junction. Recently described simultaneous bilateral endoscopic surgery (SBES) could be an alternative treatment method in patients with bilateral proximal ureteral stones whom one side is suitable for PCNL and the other side is suitable for flexible URS.[3] Similarly, the indications of open and laparoscopic surgery for ureteral stones are very limited. The ESWL for ureteral stones has been shown to be associ-

ated with lower stone-free rates (SFR) and higher re-treatments rates when compared to URS.[2, 4] Additionally, since patients with bilateral ureteral stones are more likely to have an obstructive acute renal failure, URS can be considered a more efficient treatment modality than ESWL in bilateral obstructive ureteric stones. In a large multi-center study, it has been reported that URS had 7.4% overall complication rate.[5] Due to the risk of bilateral ureteral injury in the same session URS and higher complication rates in the earlier series, the staged URS has become the preferred method of the management of bilateral stones.[6, 7] On the other hand, potential benefits of bilateral same-session ureteroscopy (BS-URS) include less length of stay, avoidance of second anesthesia and reducing hospital costs.[8]

With the development of smaller caliber semi-rigid and flexible ureteroscope combined with holmium: yttrium-aluminum-garnet (Ho:YAG) laser and increasing experience, URS has become a safe and efficient modality not only for the treatment of distal ureteral stones, but for proximal stones also.[9, 10] More recent BS-URS series have reported lower rates of complications with different lithotripsy techniques.[11-13] In this study we aimed to evaluate the safety and efficacy of BS-URS and compared with unilateral URS for the treatment of bilateral ureteral stones.

Materials and methods

After institutional board's approval, the medical records of 75 patients who underwent BS-URS and laser lithotripsy for bilateral ureteral stones between April 2013 and May 2018 were evaluated retrospectively. Patients who underwent BS-URS for indications other than urinary stone disease, staged bilateral URS or concurrent retrograde intrarenal surgery (RIRS) for kidney stones were excluded. All patients had preoperative non-contrast computed tomography (NCCT) scan, urine culture and serum creatinine. The stone size was calculated in millimeter (mm) as the largest diameter in axial or coronal planes of NCCT. Stone density in Hounsfield Unit (HU) was also recorded. Patients with positive urine cultures were treated with appropriate antibiotics preoperatively. Patient characteristics including age, gender, American Society of Anesthesiologists (ASA) preoperative evaluation score, the presence of congenital urinary system abnormalities, prior ureteral stenting and history of previous URS were evaluated. Preoperative variables including stone location, stone size and density, serum creatinine and intra-operative characteristics such as operative time, anesthesia type, type of URS (semi-rigid/flexible), access sheath use (yes/no), the presence of impacted stone (yes/no), intraoperative complications and postoperative stent placement (yes/no) were recorded. In the postoperative period, serum creatinine, postoperative complications, length of hospital stay, SFR were evaluated. Complications were categorized according to the Clavien-Dindo classification.[14] The day after surgery, kidney-urinary-bladder (KUB) film was taken to confirm the clearance of stone fragments and the position of the ureteral double-J (DJ) stent, then patients were discharged if uncomplicated. Patient re-admissions or emergency service visits after discharging and repeated surgeries within 4 weeks were also recorded.

As a routine, the patients were followed up post-operatively after four weeks at our out-patient clinic and all patients were evaluated with KUB film, ultrasonography (USG) and urine culture. NCCT scan was obtained when necessary. A stone analysis was also performed if enough stone fragment could be removed during the operation. The stone free status was defined as no stone fragment in USG and KUB or fragments ≤2 mm in NCCT with no clinical symptoms after four weeks.

Additionally, operation times, length of stay, overall complication rates and SFRs were compared to 75 consecutive unilateral URS cases performed in the same way over the same time period.

Technique

Patients with negative urine cultures received 1 g of cefazolin intravenously one hour prior to anesthesia unless the patient has allergy to cephalosporins. All operations were performed by experienced senior urologists under general or spinal anesthesia. Normal saline was used as irrigation fluid with Y set and hand pump. Af-

ter urethrocystoscopy and advancing of 0.035" floopy tip safety guide-wire (Sensor™, Boston Scientific, Marlborough, MA, USA) to the ureter under fluoroscopy, 7-Fr semi-rigid ureteroscope (Karl Storz, Tuttlingen, Germany) was inserted to the ureter. Then, stone fragmentation or dusting was performed with 30-W Ho:YAG laser (Litho-Laser, International Medical Lasers, Portland, ME, USA). Laser settings were 0.5-1.5 J and 8-50 Hz. For distal and mid ureteral stones semi-rigid URS and 355-µm laser fiber were used. For proximal ureteral stones, we started the procedure with semi-rigid URS. If we could not reach to the stone with semi-rigid-URS, 7.5-Fr fiberoptic flexible ureteroscope (Flex-X,[2] Karl Storz) was forwarded to the upper ureter through a guide-wire or 11/13-Fr, 36- or 46-cm ureteral access sheath (UAS) (Navigator™, Boston Scientific) and stone was fragmented with a 200-µm laser fiber. Small stone fragments were retrieved with a forceps or 2.2-Fr nitinol stone extractor (NGage®, Cook Medical, Bloomington, IN, USA) when necessary. Stone fragments smaller than 2 mm were accepted as insignificant and left for spontaneous passage. In cases of UAS usage, impacted ureteral stone or ureteral injury, 24- to 28-cm, 4.8-Fr standard DJ stent was inserted routinely and left for two to four weeks. Otherwise, the surgeon decided the need for ureteral stenting.

Statistical analysis

The SPSS software v. 24.0 (IBM, Armonk, NY, USA) was used for the statistical analyses. Student's *t*-test was used to compare means and Fisher's exact, two tailed to compare number of events and a P value <0.05 was considered statistically significant.

Results

A total of 75 BS-URS procedures were performed in 58 men (78.3%) and 16 women (21.7%) with a mean age of 46.3±12.5 years (range 21 to 78 years) in 74 patients with one patient who underwent BS-URS twice. Three of 74 (4%) patients had congenital urinary tract abnormalities (horseshoe kidney deformity in two and ureteral duplication in one). History of previous URS was present in 24 of 74 (32.4%) patients. Before the procedure, 14 patients had DJ stents, unilaterally in ten and bilaterally in four, respectively. The mean preoperative serum creatinine level was 1.2±0.8 mg/dL (range 0.5 to 6.7 mg/dL). In 18 of 75 (24.3%) BS-URS cases, preoperative serum creatinine level was above 1.2 mg/dL and 5 of these (6.6%) were in oliguria or anuria state. In the preoperative risk evaluation of patients, 49 (65.3%), 21 (28%) and five (6.6%) were in categories of ASA I, ASA II and ASA III, respectively. The stone characteristics are shown in Table I. The BS-URS was performed under general anesthesia in 50 of 75 (66.6%) and spinal anesthesia in 25 of 75 (33.4%). No ureteral dilatation was needed in any case. BS-URS was performed with semi-rigid URS in 64 of 75 (85.3%), with flexible URS only in three of 75 (4%) and semi-rigid URS + flexible URS in eight of 75 (10.7%).

The operative and postoperative outcomes are shown in Table II. In patients with stone burden ≥20 mm, the mean operative time was longer. The ureteral injury was identified in eight of 150 (5.3%) ureters during ureteroscopy. The most of these injuries were grade I, superficial mucosal erosions according to the Clavien-Dindo system which noted at completion of the procedure and just treated with DJ stent placement. One patient with impacted stone had grade IIIb injury of the ureter due to laser perforation but stone fragmentation was completed and also managed with DJ stent only. None of the injured ureters had been pre-stented before the procedure. No

TABLE I.—*Stone characteristics.*

Characteristics	Value
Mean stone size, mm	9.6±4.1
Stone size range, mm	3.2-26
Total stone burden	
<20 mm	43 (57.3%)
≥20 mm	32 (42.7%)
Stone location	
Upper ureter/upper ureter	34/150 (22.6%)
Upper ureter/lower ureter	40/150 (26.6%)
Lower ureter/lower ureter	76/150 (50.8%)
Mean stone density, HU	950±350
Stone density range, HU	250-1450
Impacted stone	
Yes	39/150 (26%)
No	111/150 (74%)

TABLE II.—*Operative and postoperative outcomes of BS-URS.*

Variables	Value
Mean operative time, min	
Total stone burden <20 mm	52±18
Total stone burden ≥20 mm	85±42
Overall	69±31
Intraoperative complications	
Ureteral mucosal erosion	7/150 (4.7%)
Ureteral perforation with contrast extravasation	1/150 (0.6%)
Postoperative ureteral stenting	
Unilateral	41/75 (54.7%)
Bilateral	34/75 (45.3%)
Short term complications	
Stent pain and discomfort	4/75 (5.3%)
Febrile urinary tract infection	2/75 (2.6%)
Bleeding/clot retention	2/75 (2.6%)
Mean length of stay, days	1.2±0.5
Length of stay range, days	1-3
Mean postop creatinine level, mg/dL	1.0±0.8
Postop creatinine level range, mg/dL	0.7-5.8
SFR after 2 weeks	
Upper ureter	50/54 (92.5%)
Middle ureter	24/26 (92.3%)
Lower ureter	69/70 (98.5%)
Overall	143/150 (95.3%)

stone was visualized unilaterally in two of 75 BS-URS. Intraoperatively, we determined that 71 of 75 (94.6%) BS-URS was bilaterally stone-free while in four patients had residual stones unilaterally. The postoperative period was unremarkable in the majority of the patients. Early postoperative complications were seen in eight patients (10.6%) including grade I in six and grade II in two patients (Table II). These patients were treated with conservatively and stayed one or two more days while other patients were discharged the day after surgery without any complaints. Only one of the patients with febrile urinary tract infection had been pre-stented. Out of six, in all patients with preoperative elevated levels, the serum creatinine levels decreased to normal limits within two weeks. Five of these patients the postoperative creatinine was below 2 mg/dL. In one patient, creatinine level above 5 mg/dL persisted.

Five patients (6.6%) were re-admitted to the out-patient clinic or emergency room (ER) for severe pain in three patients and for prolonged hematuria in two patients related to DJ stent. In two of these patients, DJ stent was removed before the scheduled date. Postoperatively, after four weeks, 72 (96%) patients were evaluated with KUB, USG and urine culture. Twenty-five out of 72 patients (33.3%) were additionally evaluated with NCCT. In seven of 75 (9.3%) patients asymptomatic urinary tract infection was detected in urine culture and treated with appropriate antibiotics. Most of the patients could not be followed for a long-term and their medical records were not available. Residual stones were detected with NCCT in five patients (6.6%). The spontaneous expulsion with medical expulsive treatment (MET) was successful in four patients. The other patient (1.3%) underwent to a second URS for residual stone fragment whose spontaneous passage failed despite MET for two weeks. The stone composition analysis could be done only in 12 patients (16%). Stone compositions were reported as calcium oxalate dehydrate in eight, uric acid in two, and mixed (calcium oxalate monohydrate, dehydrate, and calcium phosphate) in two patients.

The initial SFR was 93.3% and the final SFR at four weeks was 98.6%. The highest SFR was achieved in patients whom both stones were in distal ureter. When BS-URS was compared to unilateral URS performed in the same period, patient demographics and stone characteristics were not statistically different (P=0.45). There was no significant difference between the groups in terms of intra-operative complications, length of stay and SFR. However, operating time was significantly longer in BS-URS group (P=0.003). Table III shows the differences between BS-URS and unilateral URS groups.

TABLE III.—*Comparison of BS-URS and unilateral URS in the same period.*

Variables	BS-URS	Unilateral URS	P value
Pre-stenting	18/150 (12%)	5/75 (6.6%)	0.004
Mean stone size	9.6±4.1	10.1±5	0.32
Mean operating time, min	69±31	32±21	0.003
Intraoperative complications	8/150 (5.3%)	5/75 (6.6%)	0.52
Postoperative complications	8/75 (10.6%)	6/75 (8%)	0.65
Mean length of stay, days	1.3±1	1.1±1	0.45
Patients needing re-treatment	1 (1.3%)	0 (0%)	0.36
SFR at 4 weeks	98.6%	97.3%	0.47

Discussion

For the treatment of proximal and distal ureteral stones, the European Association of Urology (EAU) and the American Urological Association (AUA) guidelines recommend both ESWL and URS as options when active removal is needed.[15, 16] In AUA guidelines URS is the first choice for the treatment of proximal and distal ureteral stones regardless of diameter, while the EAU guidelines recommends URS as a first choice only in ureteral stones above 10 mm. However, there is currently no recommendation for the management of bilateral ureteral stones in current guidelines. ESWL as an out-patient procedure, has advantages of patient acceptance and the lack of requirement of anesthesia. Compared to ESWL, URS has significantly higher SFRs up to four weeks but the difference was not significant at three months.[9, 15] Additionally, URS is the preferred method of treatment in larger, impacted or high-density ureteral stones[15] and in obese patients.[17] However, still there is no consensus in the management of bilateral ureteral stones with BS-URS. Despite its good SFRs, it has been reported that overall complication rate after URS was 9-25%.[18, 19] The most of these were minor complications which did not require intervention. On the other hand, Cindolo *et al.* reported 12 Clavien grade IIIb-IV complications after URS and concluded that major life-threatening complications after URS were still considerable.[20] Although, with the advances in endourology the complication rate and morbidity of URS have been significantly reduced,[4] staged URS instead of BS-URS is still preferred by the most. The concerns over BS-URS are due to the potential increased risk for bilateral injury and complications compared to staged URS.

In early studies on BS-URS, higher complication rates were reported.[6, 7, 21, 22] Anuric renal failure has been reported after atraumatic flexible BS-URS.[23] Deliveliotis *et al.* reported a 22% rate of ureteral perforation in BS-URS[21] with 10.5-11F large caliber ureteroscope. Hollenback *et al.* found a 29% risk of complications of BS-URS which higher than staged URS, however, reported complications were mostly in the late postoperative period.[7] The high complication rates in earlier studies can be explained using a large caliber ureteroscope and pneumatic lithotripsy (PL). In a systematic review of 11 studies with BS-URS,[24] there were significantly more complications with PL compared to Ho:YAG laser lithotripsy (54.9 *vs.* 16.7%). In this analysis including more contemporary studies with Ho:YAG laser, the overall complication rate was 25.6%. Most complications were Clavien grade I-II. It has been claimed that experience and case volume were also affecting factors of the complication rate. In series which only semi-rigid URS was used, stone location was a significant risk factor with a higher incidence of intraoperative complications in proximal ureteral stones.[11, 12, 25, 26] In our study, the overall complication rate was 22.6% which was similar to the previous studies. There was no additional risk in proximal ureteral stones. Although the BS-URS group had significantly higher overall complication rate compared to the unilateral URS, intraoperative and early postoperative complication rates were similar (5.3% *vs.* 6.6%, P=0.45). The difference in postoperative complications and hospital re-admission rates was mainly due to stent related complaints since postoperative stenting was more likely used after BS-URS. Ingimarsson *et al.* reported their retrospective series of 117 BS-URS mainly with flexible URS and compared it to 134 unilateral URS.[27] The postoperative complication rate did not differ from the BS-URS group. However postoperative stenting rate in unilateral URS group was not clear. In this study the median length of follow-up was 2.8 years and end-stage renal failure developed in two patients at four and five years postoperatively, respectively. Since a significant number of our patients were from other cities, we could not follow our patients for a long time.

Longer operating times are not unexpected in BS-URS. After the introducing of Ho:YAG laser and smaller size ureteroscope, shorter operative times with fewer complications could be achieved. Recently, in a multicentric, global study by Clinical Research Office of the Endourological Society (CROES), 273 BS-URS cases were evaluated.[28] They compared the results of ipsilateral and bilateral URS for multiple ureteral stones with the results of URS for single ureteral stones and found that BS-URS results

were comparable with unilateral URS results except for longer operative times in BS-URS. Furthermore, no difference was seen in the complication rates between URS for multiple stones and URS for single stone while BS-URS has 5% lower SFR rate, 6% higher re-treatment rate and longer operating time compared to URS for single stone. Postoperative stent placement rate was also higher in BS-URS group. Geraghty *et al.* found that the mean operating time was 68.7 min in a systematic review of 11 studies on BS-URS.[24] In a meta-analysis of 11 studies by Ge *et al.*, the operation durations were between 50 and 100 minutes.[29] The mean operating time in our study is similar to the previous studies. The previous studies revealed that post-operative stenting rate was higher in patients that underwent BS-URS.[24, 28] Hollenbeck at al. reported that patients were 70% more likely to have a post-operative complication when the uretral stent was not placed after ureteroscopic intervention.[7] Although we do not routinely place ureteral stent after unilateral URS, we placed at least a unilateral DJ stent in patients that underwent BS-URS to prevent postoperative obstruction.

In studies on BS-URS, the SFRs for ureteral stones differ between 84.2% and 100%.[7, 11, 22, 25, 26] The overall ureteral SFR is 94%.[24] Initially, the reported series have limited patient numbers with various lithotripsy techniques and mostly small, distal ureteral stones. Mustaque *et al.* performed BS-URS with PL in 60 patients and followed them up to 12 months.[25] They reported 85% SFR of which only 76.4% were stone-free intraoperatively with a 26.6% minor complication rate. Similarly, Gunlusoy *et al*. reported 90% SFR in a single procedure with PL.[11] In their series of 89 patients, El-Hefnawy *et al.* found 86% SFR with PL and Ho:YAG laser lithotripsy.[26] However, it was not clear the percentage of lithotripsy methods in this study. In CROES study, it has been considered that the difference of SFR between BS-URS and unilateral URS could be explained with different types of stone composition.[28] In our study, the initial 93.3% and final 98.6% SFRs are comparable to previously published series on BS-URS for bilateral ureteral stones. However, the evaluation of SFR mostly depends on imaging modality and definition of SFR. In our study, NCCT evaluation in the follow-up period was performed only in 33.3% of the patients.

Limitations of the study

This study has several limitations that need to be considered in interpreting the findings, including its retrospective nature and lack of long-term follow-up for the patients. Therefore, long-term complications such as ureteral stricture or renal insufficiency could not be determined. In addition, SFR evaluation with NCCT was available only in 33% of the patients. This may effect SFRs in patients with asymptomatic stone fragments which could not be identified with KUB and USG. Finally, only a small group of patients had stone composition analysis.

Conclusions

BS-URS is safe and efficient procedure in the treatment of bilateral ureteral stones which may prevent repeated surgeries and reduce overall hospital costs. It can obtain comparable stone-free and complication rates with unilateral or staged bilateral procedures. Prospective and randomized studies with larger patient population are required to better define the role of bilateral URS in patients with bilateral ureteral stone.

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