ORIGINAL PAPER

UROLITHIASIS

Comparative evaluation of retrograde intrarenal surgery, antegrade ureterorenoscopy and laparoscopic ureterolithotomy in the treatment of impacted proximal ureteral stones larger than 1.5 cm

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Introduction The aim of this article was to compare retrograde intrarenal surgery (RIRS), antegrade ureterorenoscopy (URS), and laparoscopic ureterolithotomy (LU) for impacted proximal ureter stones larger than 1.5 cm in terms of operative data, success, complications, auxiliary treatment rates, and visual analog scale (VAS) scores.

Material and methods Medical records of patients undergoing RIRS, antegrade URS, or LU were retrospectively reviewed. After exclusion criteria, 122 patients were included in advanced analyses. Patients were divided into 3 groups as RIRS (n = 43), antegrade URS (n = 38) and LU (n = 41).

Results Operation time was shortest in the antegrade URS and hospitalization time was shortest in the RIRS group ($p < 0.001$ and $p < 0.001$, respectively). VAS scores were lowest in the RIRS group and highest in the LU group ($p < 0.001$). Success (complete stone clearance) rates were 83.7%, 97.4%, and 97.5% in the RIRS, antegrade URS, and LU groups, respectively ($p < 0.001$). Auxiliary treatment rates in the RIRS, antegrade URS, and LU groups were 19.1%, 2.6%, and 4.7%, respectively ($p < 0.001$). Although there was no significant difference in terms of general complication rates, grade II complication rate (blood transfusion) was significantly higher in the antegrade URS group and grade IVb complication rate (urosepsis) was higher in the RIRS group according to the modified Clavien-Dindo classification system ($p = 0.007$ and $p = 0.02$, respectively).

Conclusions Antegrade URS or LU are more logical options than RIRS for the treatment of large impacted proximal ureter stones. Between antegrade URS or LU, antegrade URS seems to be a more reasonable option due to its less invasive nature.

Key Words: complication ‹› laparoscopy ‹› stone-free ‹› ureterolithiasis ‹› ureteroscopy

INTRODUCTION

Treatment methods used for proximal ureter stones include extracorporeal shockwave lithotripsy (SWL), retrograde ureterorenoscopy (URS) (semi-rigid URS and retrograde intrarenal surgery, RIRS), antegrade URS, open ureterolithotomy and laparoscopic ureterolithotomy (LU) [1, 2]. Before 1980, all upper ureter stones were treated with open surgery. With the entry into the practice of the SWL method in the 1980s, there were revolutionary developments in urology and this quickly spread around the world [3]. Together with technological advancements in the 1990s, semi-rigid URS and percutaneous nephrolithotomy (PNL), and in the 2000s RIRS gained popularity. In parallel with these head-turning

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developments in endourology, a range of developments occurred in laparoscopic surgery and LU began to be applied with very high success rates especially for the treatment of large ureter stones. As a result of all these developments, open surgery has nearly been abandoned [4].

Current European Association of Urology (EAU) urolithiasis guidelines recommend URS (antegrade or retrograde) as the first choice for treatment of proximal ureter stones larger than 1 cm, with SWL as the second choice. However, SWL should not be chosen for larger stones due to a reduction in success rates and lengthened treatment durations. In selected patients, antegrade URS and LU to RIRS may be alternatives [5]. Though RIRS comes to the forefront for treatment of large proximal ureter stones it has some basic disadvantages like requiring multiple sessions (hence multiple anesthesias) and working withhigh pelvicalyceal system (PCS) pressures. Unfortunately, the existing guidelines do not offer specific recommendations for impacted ureteral stones.

In the present study, we aimed to compare efficacy, complications, auxiliary treatment rates, and visual analog scale (VAS) scores of RIRS, antegrade URS, and LU for impacted proximal ureter stones larger than 1.5 cm in light of current studies.

MATERIAL AND METHODS

Study design

The medical records of patients undergoing RIRS, antegrade URS, or LU performed from January 2015 to December 2019 due to >1.5 cm proximal ureter stones were retrospectively reviewed. Inclusion criteria were being older than 18 years of age and having unilateral impacted stone with no history of stone treatment. Patients who were morbidly obese, had a solitary kidney, urinary system anomaly, skeletal deformity, or active urinary infection, with the urethra, ureter stenosis, or with coagulopathy, or with missing data were excluded from the study. After inclusion and exclusion criteria, a total of 122 patients were divided into 3 groups as RIRS (n = 43), antegrade URS (n = 38), and LU (n = 41). Groups were compared in terms of demographic data, stone characteristics, operative data, and postoperative outcomes (success and complications), and VAS scores.

All patients were assessed with non-contrast computed tomography (NCCT) study before the procedure. Definition of 'proximal ureter stones' used for stones localized to the ureter section from the renal pelvis to the upper border of the sacrum. Impacted stone was defined as the stone that had remained in the same position for at least two months. Also, it was operatively confirmed that the stone was an impacted stone where the guidewire will not pass without ancillary measures. For stone size, the longest axis of the stone was taken into consideration.

Comorbidities and physical status of patients were assessed preoperatively with the American Society of Anesthesiologists (ASA) score. Success was defined as complete stone-free status on the 3rd month NCCT check-up. Complications were classified according to the modified Clavien-Dindo classification system [6]. Sepsis was defined as a known or suspected infection in addition to the presence of two or more Systemic Inflammatory Response Syndrome criteria [7]. Pain severity in patients was assessed in the 12th hour postoperative with the VAS score (0: no pain, 10: intolerable pain).

Preoperative assessment

Before the procedure, informed consent was obtained from all patients. The patient assessment included medical anamnesis, physical examination, complete blood count, coagulation tests, renal function tests, urine analysis, and urine culture tests. The urine culture of all patients was sterile before the procedure. For antibiotic prophylaxis, a second-generation cephalosporin was used.

Retrograde intrarenal surgery technique

All RIRS operations were performed under general anesthesia and in a lithotomy position. Before the RIRS procedure, ureteral dilatation was performed with a 9.5 Fr semi-rigid ureterorenoscope. For all cases, two guidewires were used, one of which was a safety guidewire. A 9.5/11.5 Fr ureteral access sheath (Cook Medical Bloomington, IL, USA) was inserted over the guidewire under fluoroscopy. In situations where the access sheath did not pass, a 4.8 Fr JJ stent (Boston Scientific, Natick, USA) was inserted by providing partial fragmentation with a flexible ureterorenoscope without ureteral access sheath and the operation was delayed to 14 days later. All cases had a 7.5 Fr Flex-X2 (Karl Storz, Tuttlingen, Germany) used. Stones were fragmented with a holmium: YAG laser device (Sphinx, Lisa Laser, Katlenburg, Germany) and 200 μm laser fibers (energy level: 0.8–1.2 J and frequency: 12–15 Hz) until size reduced to allow spontaneous passage. Large fragments were removed with a basket catheter (1.3 F Opti Flex, Boston Scientific, Marlborough, USA). After the procedure, all patients had a 4.8 Fr JJ stent inserted (Boston Scientific, Natick, USA) which was removed 2 weeks later.

Antegrade ureterorenoscopy technique

After general anesthesia administration, in the dorsal lithotomy position, a 5 Fr open-end ureter catheter was inserted below the stone with the aid of a 17 Fr cystoscope, and the catheter was fixed to a 16 Fr Foley catheter. Then, the patient position was changed into a prone position. The pelvicalyceal system was imaged with contrast material and the upper or central calyx suitable for access was identified. The puncture was performed with an 18-gauge access needle accompanied by fluoroscopy. Nephroscopy was performed with a 10 Fr semi-rigid ureterorenoscope (Karl Storz, Tuttlingen, Germany) within an Amplatz sheath and entry to the upper ureter was ensured. Stones were fragmented with Ho: YAG laser. Large fragments were removed with a stone forceps. At the end of the procedure, a 14 Fr nephrostomy tube was inserted.

Laparoscopic ureterolithotomy technique

The operations were performed under general anesthesia in a flank position. Insufflation was provided by the Verres needle technique. A 10 mm camera port was inserted laterally of the rectus muscle at the umbilical level. The other 10 mm (right hand) and 5 mm (left hand) trocars were inserted 6–8 cm lateral to form a triangle. After freeing the colon from the Toldt line, the Gerota fascia was opened at the point where it joined with the psoas sheath and the ureter was found. The ureter was then dissected distally staying away from the adventitia until the stone site was reached. When the stone was found, the proximal endwas held with an endograsper to prevent the stone escaping proximally. Using laparoscopic scissors, longitudinal ureterotomy was performed and the stone was removed with a grasper through the 10 mm port. Before removing larger stones, they were placed inside a bag. After inserting the 4.8 Fr JJ stent into the ureter, the ureterotomy incision was closed with the interrupted technique with 4/0 vicryl sutures. The reflected colon was replaced and an 18 Fr soft abdominal tube drain was placed close to the suture line. The 10 mm port sites were closed at the end of the procedure. The JJ stents were removed 4 weeks after the operation. All operations in the study were performed by two experienced surgeons.

Statistical analysis

To have 80% power and a 5% type 1 error level, 45 individuals for each group were included in the study. A 20% loss was predicted for the exclusion criteria. All data were analyzed using SPSS Windows version 22.0 (IBM SPSS, Armonk, NY, USA). Quantitative data were expressed as mean±std values and categorical data were expressed with frequency (n) and percentages (%). The Kolmogorov Smirnov test was used to determine whether the variables were distributed normally or not. Groups were compared with the one-way ANOVA test. Bonferroni ve Tukey test were used for Posthoc analyses. The data were

Table 1. *Demographic data and stone characteristics*

	RIRS (n = 43)	Antegrade URS (n = 38)	Laparoscopic ureterolithotomy (n = 41)	p
Age, (years) (mean ±sd)	45.3 ±12.1	39.8 ±11.9	43.0 ±11.7	0.81
Gender, n (%)				
female	18 (41.8%)	14 (36.8%)	18 (43.9%)	0.21
male	25 (58.1%)	24 (63.2%)	23 (56.1%)	
BMI, (kg/m^2) (mean ±sd)	25.4 ±3.6	26.2 ±4.1	25.9 ±4.0	0.78
ASA score, (mean ±sd)	1.3 ±0.4	1.3 ±0.5	1.2 ±0.6	0.90
Comorbidity, n (%)				
diabetes mellitus	4 (9.3%)	6 (15.8%)	7 (17.7%)	
hypertension	5 (11.6%)	4 (10.5%)	6 (14.6%)	0.44
coronary artery disease	1 (0.2%)	2 (5.3%)	3 (7.3%)	
anticoagulant usage	6 (14%)	0	0	
Urosepsis, n (%)	5 (9.4%)	3 (7.9%)	4 (9.3%)	0.57
Stone size, (mm) (mean ±sd)	20.4 ±2.9	21.2 ±3.7	22.1 ±5.0	0.17
Stone volume, (mm^3)	1375 ±156	1445 ±225	1520 ±180	0.23
Laterality, n (%)				
right	20 (46.5%)	21 (55.3%)	19 (46.3%)	0.81
left	23 (53.5%)	17 (44.7%)	22 (53.7%)	

RIRS – retrograde intrarenal surgery; URS – ureteroscopy; sd – standard deviation; n – number; BMI – body mass index; ASA – American Society of Anesthesiologists

analyzed at a 95% confidence level and the threshold for statistical significance was accepted as $p < 0.05$ for all analyses.

RESULTS

There were no significant differences between the groups in terms of age, gender, body mass index (BMI), ASA score, comorbidity, history of urosepsis, stone size, stone volume, and stone laterality (Table 1).

Operation time was shortest in the antegrade URS and hospitalization time was shortest in the RIRS group ($p < 0.001$ and $p < 0.001$, respectively). VAS scores were lowest in the RIRS group and highest in the LU group ($p < 0.001$). The differences in success rates in the 3rd month between RIRS and antegrade URS were significant ($p < 0.001$), with no significance for the difference between antegrade URS and LU. In the RIRS group, 18 patients were performed two sessions of surgery, respectively ($p < 0.001$). The differences of auxiliary treatment rates (antegrade URS; 2.6%, and LU; 4.7%) were significant between the RIRS group and the other two groups ($p < 0.001$), with no significance between the antegrade URS and LU groups (Table 2).

Although there was no significant difference in terms of general complication rates, grade II complication rate (blood transfusion) was significantly higher in the antegrade URS group and grade IVb complication rate (urosepsis) was higher in the RIRS group according to the modified Clavien-Dindo classification system ($p = 0.007$ and $p = 0.02$, respectively). While in the RIRS group, 2 (4.3%) patients had ureteral stenosis, no patient had stenosis in the other two groups ($p < 0.001$) (Table 3).

In the RIRS group, a total of 12 patients (27.9%) could not have ureteral access sheath inserted and surgery was delayed by 14 days. In patients with success, the mean session number was 1.86 (range: 1–3). However, all patients in the other group were operated in one session. Four patients with urosepsis in the RIRS group had empirical antibiotic therapy (ceftriaxone 2 g/day) with the treatment given for 14 days according to antibiogram results. Two patients developing perforation had JJ stents inserted and had surgery completed 4 weeks later.

In the antegrade URS group, a total of 4 patients had a hemorrhage from the nephrostomy tube requiring a transfusion after the operation. The mean transfusion rate in these patients was 1.75 units (1–3 U). However, transfusion was not needed in the other two groups. Two patients in the antegrade URS group had ureter perforation observed during lithotripsy. Patients had nephrostomy catheter and JJ stent inserted, with the surgery completed 4 weeks later.

In the laparoscopic ureterolithotomy group, a total of 2 patients had no dissection plan found due to adhesion and open operations were performed. Stone-free status was ensured with open surgery. In this group, one prolonged urine leakage was observed and treated with nephrostomy. Another patient had an abdominal abscess treated with percutaneous abscess drainage and antibiotic therapy.

DISCUSSION

Currently, the surgical methods applied for the treatment of large proximal ureter stones are RIRS, antegrade URS, and LU [5]. Due to the use of natural

Table 2. *Operative data and postoperative outcomes*

	RIRS (n = 43)	Antegrade URS (n = 38)	Laparoscopic ureterolithotomy (n = 41)	p
Operative time (min) (mean ±sd)	60.1 ±9.8	44.2 ±6.1	147 ±67	<0.001*
Fluoroscopy time (min) (mean ±sd)	0.4 ±0.2	4.4 ±1	N/A	<0.001&
Hospitalization time (day) (mean ±sd)	2.0 ±1.3	4.1 ±1.2	4.3 ±0.8	<0.001#
VAS score (mean ±sd)	3.6 ±1.7	4.8 ±1	5.2 ±1.1	<0.001£
Success rate, n (%)	36 (83.7%)	37 (97.4%)	40 (97.5%)	<0.001˜
Auxiliary treatment, n (%)				
SWL	1 (2.3%)	1 (2.6%)	0	
RIRS	N/A	0	1 (2.5%)	<0.001x
Antegrade URS	4 (9.3%)	N/A	0	
Laparascopic ureterolithotomy	2 (4.6%)	0	N/A	
Follow-up (month) (mean ±sd)	3.2 ±0.6	3.5 ±2.4	3.2 ±2.2	0.61

&Independent T test, Bonferroni Test; *Group 1 vs. 2, p <0.001, Group 1 vs. 3, p = 0.145, Group 2 vs. 3, p <0.001; &Group 1 vs. 2, p <0.001; #Group 1 vs. 2, p <0.001, Group 1 vs. 3, p <0.001, Group 2 vs. 3, p = 0.17; £Group 1 vs. 2, p <0.001, Group 1 vs. 3, p <0.001, Group 2 vs. 3, p = 0.03; Tukey test; ˜Group 1 vs. 2, p <0.001, Group 1 vs. 3, p <0.001, Group 2 vs. 3, p = 1.0; xGroup 1 vs. 2, p <0.001, Group 1 vs. 3, p <0.001, Group 2 vs. 3, p = 1.0

RIRS – retrograde intrarenal surgery; URS – ureterorenoscopy; sd – standard deviation; VAS – Visual Analog Scale; SWL – shock wave lithotripsy; N/A – not available

Table 3. *Complications analysis*

	RIRS (n = 43)	Antegrade URS (n = 38)	Laparoscopic ureterolithotomy (n = 41)	p
Overall complications, n (%)	9 (20.9%)	9 (24%)	7 (17.7%)	0.25
Complications, n (%)				
Fever (>38°C)	1 (2.1%)	2 (5.3%)	1 (2.4%)	0.72
Urosepsis	4 (8.5%)	0	1 (2.4%)	0.10
Hb drop (mean ±sd)	0.5 ±0.2	2.9 ±0.7	0.8 ±0.3	<0.001^
Blood transfusion	0	4 (10.5%)	0	0.007
Ureteral perforation	2 (2.1%)	1 (2.6%)	0	0.14
JJ-stent discomfort	2 (4.6%)	0	1 (2.3%)	0.23
Prolonged drainage	0	2 (5.3%)	1 (2.3%)	0.28
Intraabdominal abscess	0	0	1 (2.3%)	0.37
Conversion to open surgery	0	0	2 (4.7%)	0.13
Ureteral stenosis at 3 months	2 (4.3%)	0	0	<0.001
Clavien-Dindo classification				
Grade – I	1 (2.1%)	2 (5.3%)	1 (2.4%)	0.45
Grade – II	0	4 (10.5%)	0	0.007
Grade – IIIa	0	0	0	
Grade – IIIb	4 (9.7%)	3 (7.9%)	5 (11.6%)	0.72
Grade – IVa	0	0	0	
Grade – IVb	4 (8.5%)	0	1 (2.3%)	0.02

^Hb drop; Group 1 vs., 2 and 3, p <0.001; Group 1 vs. 2, p <0.001; Group 2 vs. 3, p <0.001
RIRS – retrograde intrarenal surgery; URS – ureterorenoscopy; n – number; Hb – hemoglobin; sd – standard deviation

orifices and clearly its minimally invasive nature, RIRS is the most commonly chosen method by both patients and surgeons. However, for the treatment of large and impacted ureter stones, RIRS has low success rates, requires multiple sessions, and has a risk of urosepsis. The risk further increases, especially for patients with increased operation duration [8]. In our study, the lack of any comorbidity that could induce an infection tendency in patients with sepsis in the RIRS group confirms factors were related to the surgical technique (high PCS pressure) rather than patient-related factors. Another disadvantage of RIRS for impacted ureter stones is that the passage of fragmented stones may be negatively affected by ureter stenosis which may develop after the process of impaction. In our study, though ureter stenosis was not analyzed, we think this situation was the reason for the low success rate in the RIRS group.

Antegrade URS may be performed in situations where the stone cannot be reached by RIRS or as a primary treatment choice due to high success rates [1]. The greatest advantage of antegrade URS compared to RIRS and LU is the lack of possibility of stone movement. In RIRS and LU, the operation may result in failure due to stone pushback. In antegrade URS, much lower PCS pressure is used compared to RIRS. Probably due to these reasons, no patient in this group developed urosepsis. Contrary to this, antegrade URS has more risk of major hemorrhage compared to the other two methods. This risk especially increases for middle and upper calyx entries. We routinely used a semi-rigid ureteroscope for antegrade URS because of the fact that flexible devices were associated with cost problems and semi-rigid devices were more practical. The majority of cases were done through the middle calyx access. If a flexible ureteroscope was used, lower calyx entry could be performed ensuring less hemorrhage. However, flexible devices are more difficult to use, especially in hydronephrotic kidneys.

Though there are very high success rates for laparoscopic ureterolithotomy, it is chosen less in clinical practice due to the thought that it is more invasive. LU may be performed by transperitoneal or retroperitoneal routes. Both techniques have different advantages and disadvantages. The basic advantages of the retroperitoneal approach are that the ureter can be accessed directly, and there is less risk of intraperitoneal contamination and postoperative peritoneal irritation findings. However, the retroperitoneal approach is more difficult and complicated due to the narrowness of the surgical field [9, 10]. The transperitoneal approach offers a larger working area and clearer anatomic landmarks. This makes the learning curve shorter. Contrary to this, the transperitoneal technique has complications related more to intestinal and urinary extravasation in the intraperitoneal area [11]. In our study, due to our greater experience of the transperitoneal technique, all patients were operated with this route. Perhaps if the retroperitoneal route was chosen, the intraabdominal abscess complication seen in this group may have been prevented. In a recent meta-analysis

(7 studies, 253 patients), it was reported that retroperitoneal LU was superior to transperitoneal LU in postoperative paralytic ileus [12].

In a meta-analysis study including 12 randomized controlled studies (RCTs), it was reported that Both PNL and LU appear more effective and safer than URS for proximal ureteral stones larger than 10 mm; although, LU has a higher risk of urine leakage and is more likely incur trauma which requires additional support. Also, it was reported that there was no difference in complication and SF rates between PNL and LU [13]. In another recent meta-analysis study, it was reported that PNL was better than LU and URS in SF rates for proximal impacted ureteral stones, but considering the major bleeding risk, mini-PNL can reduce the risk of bleeding [14]. In another recent meta-analysis of 14 studies (7 RCTs and 7 non-RCTs), it was reported that LU and PNL have higher success rates compared to URS (rigid, semirigid URS or RIRS), and LU has a longer operative time and a higher complication rate with no differences in hospitalization time compared to URS. The authors noted that URS should be considered as the standard therapy for the treatment of large proximal ureteral stones [15].

Besides the success disadvantage, another important disadvantage of RIRS is the risk of ureteral stenosis. In a study comparing URS and retroperitoneal LU in proximal ureteral stones larger than 12 mm, the risk of postoperative ureteral stricture development was found to be significantly higher in the URS group (3.6%) than the retroperitoneal LU group (1.5%) [16]. This is probably due to the thermal effect created by the laser on the ureter. Also, in LU, ureteral mucosa is less manipulated and the cold incision is used. Long-term studies with a high level of evidence are needed to determine which technique is advantageous in terms of a critical complication such as ureteral stenosis.

Our study has some limitations. The most basic limitations are the retrospective nature of the study and the relatively low patient numbers. Only studies with higher volumes and longer follow-up durations will clarify which method should be chosen as the first choice. Another limitation of our study is that all surgeries in the LU group were performed with the transperitoneal route. If performed with the retroperitoneal route, intraabdominal complications and conversion to open surgery rates may have been lower. In spite of these limitations, our study will contribute to the literature and clinical applications as a first study comparing RIRS, antegrade URS, and LU for large impacted ureter stones.

CONCLUSIONS

In the clinical practice, though RIRS is considered the first choice for the treatment of large impacted ureter stones, it has lower success rates and higher additional treatment rates compared to the other two techniques. Additionally, it has notable multiple session requirements, risk of urosepsis, and ureteral stenosis. Contrary to these, RIRS has shorter hospital stays, lower pain scores, and shorter fluoroscopy duration. Antegrade URS and LU have very high success and low additional treatment rates. The basic disadvantage of antegrade URS of hemorrhage risk may be kept at acceptable levels by using miniaturized tools and entry via the lower calyx. If LU is performed via the retroperitoneal route, reductions may be ensured for pain scores, duration of hospital stay, and intraabdominal complications. The results of our study, when assessed with current meta-analysis studies, show that antegrade URS or retroperitoneal LU are more logical options than RIRS for the treatment of large impacted proximal ureter stones. Choosing between antegrade URS and LU, antegrade URS seems to be a more reasonable option due to its less invasive nature.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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