# The effectiveness of percutaneous nephrolithotomy for the treatment of large impacted upper ureteral stones

<sup>®</sup>Kubilay Sarıkaya, <sup>®</sup>Çağrı Şenocak, <sup>®</sup>Mehmet Çiftci, <sup>®</sup>Muhammed Arif İbiş, <sup>®</sup>Ömer Faruk Bozkurt

Health Sciences University Keçiören Training and Research Hospital Ankara, Turkey

**Cite this article as**: Sarıkaya K, Şenocak Ç, Çiftci M, İbiş MA, Bozkurt ÖF. The effectiveness of percutaneous nephrolithotomy for the treatment of large impacted upper ureteral stones. Anatolian Curr Med J 2021; 3(2); 165-170.

## ABSTRACT

**Objective:** To compare the efficacy of combined semi-rigid+ flexible ureterorenoscopic surgery (URS+RIRC) and percutaneous nephrolithotomy (PNL), which is the standard method for the surgery of  $\geq 2$  cm upper ureteral impacted stones.

**Material and Method:** The data of 123 patients who underwent stone surgery for  $\geq 2$  cm impacted ureteral stones in the upper ureter in our clinic were retrospectively analyzed. The patients were divided into two groups as URS+RIRC (n=59) and PNL (n=64) according to the type of operation. Patients with stones impacted in the ureter at the level between the L4 vertebra and ureteropelvic junction were included in the study. Preoperative demographic data and postoperative results of the patients in two groups were compared.

**Results:** Average operation time was similar in both groups (p=0.147). Mean hospital stay was significantly higher in the PNL group compared to the URS+RIRC group ( $3.28\pm0.57$  days vs  $1.11\pm0.32$  days, p=0.001). Mucosal injury was developed in 10 (16.9%) patients in the URS+RIRC group during the operation, while it was only 3 (4.7%) in the PNL group (p=0.027). Postoperative urinary tract infection development was found to be similar in URS+RIRC and PNL groups (8.5% vs 4.7%, p=0.479).Postoperativestone-free rate was found to be significantly higher in the PNL group compared to the URS+RIRC group (95.3% vs 79.7%, p=0.008).

**Conclusion:** PNL is a very effective and safe procedure in the surgical treatment of stones  $\geq 2$  cm in diameter impacted in the upper ureter. The complication rate of PNL is comparable with URS+RIRC; however, it is seen that the PNL is more advantageous than URS+RIRC in terms of postoperative total stone-free rate.

Keywords: Urolithiasis, percutaneous nephrolithotomy, ureteroscopic surgery

# INTRODUCTION

Urinary system stones are a common health problem affecting more than 12% of the general population (1). Completely obstructed stones impacted into the ureter cause symptoms such as pain, high fever, infection and result in loss of renal function in the later period (2). Although extracorporeal shock wave lithotripsy (ESWL) is recommended as the first-line treatment method in upper ureteral stones, it is known that its effectiveness is decreased, especially in stones with a  $\geq 1.5$  cm in diamater (3). Therefore, semi-rigid ureteroscopy (URS) and combined retrograde intrarenal surgery (RIRC) are used as the common treatment choice in many centers in the treatment of upper ureteral stones with a diameter of  $\geq 1.5$  cm (4). However, it has been reported that the effectiveness of only semirigid-URS decreases in stones larger than 1 cm and therefore additional

surgery is required (5). Retrograde migration of stone fragmentsduring the operation into the kidney and the inability to find some stone fragments in the kidney is a common problem in semi-rigid URS (6). Therefore, in recent years, percutaneous nephrolithotomy (PNL) has been used more frequently in many centers in the surgical treatment of upper ureteral stones with a diamater of  $\geq$ 1.5 cm and its successful results have been reported (7). When the literature is reviewed, it is seen that all of the studies in this area were carried out on upper ureteral stones with a diameter of  $\geq 1.5$  cm (2-4,6,7). Therefore, in this study, we aimed to report our experience with PNL in the surgical treatment of larger upper ureteral stones with a diameter of  $\geq 2$  cm in our clinic, which is one of the centers that urinary system stone surgery is performed intensively.



#### MATERIAL AND METHOD

After obtaining the approval of the Keçiören Training and Research Hospital Clinical Researches Ethics Committee (Date: 23.02.2021, Protocol no: 2012-KAEK-15/2238), the data of 123 patients who were operated for upper ureteral stones larger than 2 cm in diameter between January 2012 and January 2020 in our clinic were retrospectively analyzed. The trial was conducted in accordance with the Helsinki Declaration principles. While 59 of the patients had retrograde URS+RIRC, 64 patients had PNL. Patients with stones impacted in the ureter with a diameter of  $\geq 2$  cm located between the lower border of the spinal L4 vertebra and the ureteropelvic junction were included in the study. The stone that did not allow any passage at contrast graphies or computed tomography (CT) and that stayed at the same localization for more than 1 month and which resulted with hydronephrosis was defined as impacted stone. Before the operation, patients were informed in detail about URS+RIRC and PNL procedures, and the choice of treatment was decided by mutual consensus between the patient and the physician. Patients with nonfunctioning kidney or stones <2 cm were excluded from the study.Patients with additional stones in the renal collecting system other than ureter stones were excluded from the study. Patients who were observed to have pus drainage from the obstructed urinary system during URS+RIRC or PNL and who were terminated by inserting a ureteral double-J Stent or nephrostomy for this situation were not included in the study. Patients with additional urinary tract anomaly, pregnancy, coagulopathy, and active urinary tract infection were also excluded from the study. Another exclusion criterion was the previous unsuccessful ESWL and the scattering of the stones into the ureter or renal collecting system.

All patients were evaluated preoperatively with routine blood tests, urine analysis, urine culture, and non-contrast abdominal computed tomography (CT). Excretory urography was performed if the serum creatinine was normal. Dynamic renal scintigraphy (Tc-99m-DTPA) was performed in patients with severe reduction of renal parenchyma thickness and renal functions were evaluated. According to the antibiogram results, appropriate antibiotic treatment was initiated for the patients whose bacterial growth was detected in the urine culture and the operations were delayed until the urine culture was cleared. All operations were performed by a total of 5 urologists working in the same clinic.

#### **Surgical Procedures**

**URS+RIRC:** All of the URS+RIRC operations were underwent under general anesthesia. Under direct vision, a 0.035-inch hydrophilic guide-wire was advanced into the kidney from the ureter orifice on the stone side. A

9.8F semi-rigid ureteroscope (Olympus<sup>®</sup>) was used for ureteroscopy and access was provided up to the stone. The stone was fragmented with a 200  $\mu$ m or 500  $\mu$ m Ho: YAG laser energy (Stone light<sup>®</sup>)and removed using a 2.2 F nitinol stone basket. In cases where the stone migrated into the renal pelvis or renal caliceal system, the stone was found and fragmentated using a flexible ureteroscope (Olympus<sup>®</sup>-9.5 F). A5-6 F double-j stent was placed in the ureter for spontaneous drainage of small fractured residual stone fragments and easy recovery of mucosal edema. However, double-j stentwas not placed in cases where there was no residual stone and no significant mucosal edema.An urethral 16-18F foley catheter was placed into the bladder and removed on postoperative day 1 and the double-j stent was removed on postoperative 3<sup>rd</sup> week.

PNL: Following given a lithotomy position an external 5 F ureteral catheter was inserted to the target ureter with direct vision under general anesthesia. Then the patient was rotated to the prone position with a pack under the ipsilateral hemi-pelvis. After the appropriate position was given, radiopaque liquid diluted with 50% saline was given into the renal collecting system through ureteral catheter and it was screened using fluoroscopy. In cases which sufficient radiopaque material could not reached into the renal collecting system, the ultrasound-guided entry technique was used. An 18-gauge percutaneous needle was used to enter the renal collecting system, and the needle was removed so that the outer sheath remained in the renal collecting system by providing the targeted renal calix entry. In order to reach of the upper ureter with a nephroscope, a middle calix-tract entry was preferred and the the operation was performed in a single percutaneous axess. Mini-PNL was not preferred in patients with stone size >2 cm, as it would significantly prolong the operation time.

Afterwards, radiopaque fluid was injected into the renal collecting system through the outer sheath of the percutaneous needle, and the collecting system was visualized, and the entrance location and anatomical structure were evaluated. After proper renal calix insertion was provided, a 0.035-inch hydrophilic guide wire was advanced into the renal collecting system through the outer sheath of the needle, followed by percutaneous dilatation with percutaneous dilatators ranging from 24F-30 F, allowing percutaneous access to the renal collecting system with rigid nephroscope (Karl-storz<sup>®</sup> -22F). Following the percutaneous entry, the stone was fragmented and removed with use of an ultrasonic lithotripter (EMS®), or pneumatic lithotripter (EMS®). A flexible nephroscope (Olympus®-21F) was used in some stones that can not be reached with rigid nephroscope.As a result of fluroscopic control, antegrade double-j stent was placed in patients who had escaped stone fragments into the distal of the ureter or had significant mucosal edema.

Following the procedure, a 16F catheter was placed in all patients as a nephrostomy. Nephrostomy of the patients was taken on the 3<sup>rd</sup> postoperative day. Patients who were placed with double-j stents were called for control at postoperative 3<sup>rd</sup> week and their double-j stents were removed. Patients in both groups were called for control in the postoperative 1<sup>st</sup> month and evaluated with non-contrast CT. Successful treatment was defined as complete removal of the stone or the presence of <4 mm small insignificant stone. The authors state that residual stones <4 mm in size drain spontaneously and do not require additional intervention (8). On the other hand, ESWL or second session URS+RIRC was recommended for patients with residual stones greater than a  $\geq$ 4 mm diamater.

Groups were compared according to sucess rates, perioperative outcomes and postoperative complication rates.

#### **Statistical Analysis**

All statistical analyses were performed using the SPSS 24.0 (IBM Corp., Chicago) software for Windows. In the univariate analysis, the Chi-Square Test was used for nominal data, while the Mann-Whitney U test was used for nonparametric variables. Mean±Standart deviation, Median, minimum, and maximum were used to define the variables. A p-value of <0.05 was considered as statistically significant.

#### RESULTS

The median age of the patients was 42 (23-75) years and the male/female (M/F) ratio was 72/51 (Table 1). The median age of the patients in URS+RIRC group was 43 (23-75) years, while the median age of the patients in PNL group was 41 (23-72) years (p=0.939). M/F ratios were also found to be similar between groups (URS+RIRC: 34/25 vs PNL: 38/26, p=0.844). While the mean stone diameter was 24.22±3.53 mm in URS+RIRC group, it was found to be 25.28±4.38 mm in PNL group (p=0.230). Mean Hounsfield unit of the stone was 790.37±138.30 in URS+RIRC group, and it was mean 816.94±155.55 in PNL group (p=0.320). Preoperative mean hydronephrosis degrees of the groups were similar (p=0.582). There was no difference between the groups in terms of mean operation times (URS+RIRC=69.49±21.02 min vs PNL=75.46±22.44 min, p=0.147). The average hospital stay was significantly lower in URS+RIRC group than PNL group (1.11±0.32 days vs 3.28±0.57 days, p=0.0001). While 10 (16.9%) patients had peroperative mucosal injury in URS+RIRC group, only 3 (4.7%) patients in PNL group had mucosal injury (p=0.027). On the other hand, there was no bleeding that would require transfusion in any patient in URS+RIRC group, while blood transfusion was required in 3 (4.7%) patients in PNL group; however, there was no significant difference between the groups (p=0.245). While in URS+RIRC group

17 (28.81%) of the patients had stone migration to the renal collecting system during the operation, there was no stone migration in PNL group (p=0.0001). While 91.5% of the patients in URS+RIRC group had a peroperative ureteral double-j catheter, only 20.3% of the patients in PNL group required a double-j catheter (p=0.0001). There was no significant difference between the groups in terms of postoperative complications according to Clavien grade system (p=0.168); however, postoperative stone-free rate was found to be significantly higher in PNL group than URS+RIRC group (95.3% vs 79.7%, p=0.008) (**Table 2**).

Table 1. Patient's characteristics and outcomes (n=123)				
Age, median (minimum-maximum), years	42(23-75)			
M/F ratio, n	72/51			
Stone diameter (mm), mean±SD	24.77±4.02			
Operation time (min), mean±SD	72.60±21.89			
Hospital stay (days), mean±SD	$2.24{\pm}1.18$			
Stone-free rate, n (%)	108 (87.8)			
*M/F: Male/Female *SD:Standart deviation				

Table 2. Patient's characteristics and comparison of the groups				
	URS+RIRC (n=59)	PNL (n=64)	p value	
Age, median (minimum -maximum), years	43 (23-75)	41 (23-72)	0.939	
M/F ratio, n	34/25	38/26	0.844	
Stone diameter (mm), mean±SD	24.22±3.53	25.28±4.38	0.230	
Previous ipsilateral renal surgery, n (%)	13 (22)	16 (25)	0.699	
Preoperative HN, n (%)			0.582	
Grade 1	15 (25.4)	16 (25.0)		
Grade 2	25 (42.4)	23 (35.9)		
Grade 3	19 (32.2)	25 (39.0)		
Preoperative Hounsfield Unit, mean±SD	790.37±138.30	816.94±155.55	0.320	
Operation time (min), mean±SD	69.49±21.02	75.46±22.44	0.147	
Hospital stay (days), mean±SD	1.11±0.32	3.28±0.57	0.001*	
Preoperative serum creatinine (mg/d L), mean±SD	1.09±0.29	1.06±0.27	0.719	
Postoperative serum creatinine (mg/d L), mean±SD	1.20±0.28	1.17±0.26	0.634	
Peroperative outcomes, n (%)				
Mucozal injury	10 (16.9)	3 (4.7)	0.027*	
Bleeding	0 (0)	3 (4.7)	0.245	
D-J catheterization	54 (91.5)	13 (20.3)	0.001*	
Stone migration	17 (28.8)	0 (0)	0.001*	
Postoperative urinary tract infection, n (%)	5 (8.5%)	3 (4.7)	0.479	
Postoperative complications by Clavien grade, n (%) 0.16				
Grade0	49 (83)	61 (95.2)		
Grade1	2 (3.4)	1 (1.6)		
Grade2	4 (6.8)	1 (1.6)		
Grade3	4 (6.8)	1 (1.6)		
Grade4	0 (0)	0 (0)		
Grade5	0 (0)	0 (0)		
Stone-free rate, n (%)	47 (79.7)	61 (95.3)	0.008*	
*M/F: Male/Female *SD: Standart deviation *D-J catheterization: Double-j stent catheterization *HN: Hydroureteronephrosis				

# DISCUSSION

Stones impacted in the ureter cause complete obstruction that prevents urine flow from the ureter, resulting in hydronephrosis (2-4). The increased backflow resulting from intrapelvic pressure leads to a decline in renal blood flow with progressive focal ischemia, compression of the papillae with a decrease in the glomerular filtration rate, thinning of the parenchyma and decrease in renal functions due to a loss of nephrons (9). The main treatment options for upper ureteral stones are ESWL,semirigid or flexible URS, PNL, laparoscopic or open ureteral stone surgey (10). ESWL is widely preferred in the first-line treatment of upper ureteral stones with a diameter of <1.5 cm and not causing complete obstruction (3). Although ESWL is frequently preferred as a minimally invasive method in the treatment of ureteral stones, the success rate decreases significantly, especially in impacted ureteral stones with a diameter of  $\geq$ 1.5 cm and (5). In addition to the stone size, the hounsfield units of the stone also play an important role in the success of ESWL.In the study performed by Celik et al. (11) on 254 ESWL patients, it was reported that the stone-free rate was significantly higher in the patient group with low HU compared to the patient group with high HU. In our study, HU values were quite high in both groups. In addition, repeated multiple ESWL sessions can cause serious complications such as renal injury, subcapsular hematoma and renal scarring (12).

Success rates of semi-rigid or flexible URS have been reported up to 87% in minimally invasive surgical treatment option of ureteral stones (13). Using both pneumaticultrasonic lithotripter and Holmium YAG: laser technology individually or in combination when necessary increases the success rate of URS in ureter stones  $\geq$ 1.5 in diameter (14). However, the difficulty of reaching the stone, which occurs as a result of the migration of the complete stone or fragments of the stone into the renal collecting system due to pressure effect of irrigation fluid or lithotripter during operation is one of the most important problems of semirigid URS (15). Although the use of stone cone prevents this situation, it is not always possible to pass the proximal of the stone and the risk of mucosal damage increases. In this situation, fragmentation of the stone seriously increases the stone-free rate of the operation by reaching the stone fragments migrated into the renal collecting system with the help of a flexible ureteroscope in the same session (16). In the present study, a flexible URS combination was used with semi-rigid URS, and similar to the literature, a high stone-free rate was obtained (79.7%).

Nowadays, PNL is the most preferred surgical treatment method, especially in the treatment of renal stones larger than 2 cm in diameter, and its success rate has been reported between 85% and 100% (17). In addition, stone-free rates of up to 86% to 98.5% and higher than all other treatment options have been reported in upper ureteral stones with a diameter of 1.5 cm in PNL (18). In the presentstudy, stonefree rate of PNL in upper ureteral stones with a diameter of  $\geq$ 2 cm was found to be quite high (95.3%). Juan et al. (19) reported the results of their study, in which they performed PNL in 22 patients and URS in 31 patients in the treatment of ureter impacted stones >1.5 cm in diameter. According to this study, the mean operation time was 115.4±49.5 min in the PNL group and 88.6±28.5 min in the URS group (p=0.001).In the same study, the mean hospital stay was 4.7±2.0 days in the PNL group, while it was 1.9±1.1 days in the URS group (p=0.009). However, in the same study, stone free rate was found to be 95.4% in the PNL group and 58% in the URS group, and PNL was reported to be quite advantageous (p=0.001).In another similar study, Yang et al. (20) reported the results of their study involving a total of 182 patients in which they performed PNL in 91 patients and URS in 91 patients due to upper ureter impacted stones. Also according to this study, the mean operative time was found to be significantly higher in the PNL group than the URS group (27.4±2.3 min vs 45.2±3.1 min, p<0.001). In addition, in this study, it was reported that the mean blood loss in the PNL group was significantly higher than the URS group (40.2±5.3 ml vs 15.6±1.8 ml, p<0.001).On the other hand, it has been reported that the total stone clearance rate in the PNL group is considerably higher than the URS group (p<0.001).

Combination of semi-rigid URS with RIRC is known to reduce the postoperative stone-free rate. Mugiya et al. reported the results of 54 patients treated with URS+RIRC (13). According to this study, 48 of the patients were treated solely using retrograde ureteroscopy. In 47 patients (87%), the stones were fragmented completely by a single endoscopic procedure.İn their study, additional shock wave lithotripsy was performed after endoscopic debulking in 2 patients, and any stones remaining in the ureter were easily treated by shock wave lithotripsy. Pyelonephritis resulting from obstruction caused by ureteral stones was observed in 4 patients, 3 of whom required percutaneous nephrostomy and 1 of whom required stent insertion before the endoscopic procedure. They reported that, these patients then underwent retrograde endoscopic lithotripsy, which completely cleared the calculi in one session with any complication. In another recent study, Kozyrakis et al. reported the effectiveness of retrograde semirigid and flexible ureteroscopic lithotripsy for the treatment of large ureteral stones equal of or greater than 15 mm in 19 patients (21). According to their study, a subsequent RIRS during the same session was necessary in 2 cases. They satated that, after a single procedure a stone free state was achieved in 15 cases (78.9%), while 4 others required a second session (ESWL or second ureterolithotripsy, 2 cases each).İn their study, only 1 patient, the stone-free state was not achieved after a 1.2 procedure per patient (overall

success rate 94.7%). In precent study, no significant difference was found between the groups in terms of mean operation time, but similar to the literature, the length of hospital stay was significantly higher in the PNL group.In addition, in our study, similar to the literature, the stone-free rate was found to be significantly higher in the PNL group compared to the URS+RIRC group.This result indicates that PNL is quite advantageous in terms of stone-free rate compared to URS in the surgical treatment of upper ureteral stones with larger diameter ( $\geq 2$  cm) as well as in ureter impacted stones with  $\geq 1.5$  cm diameter.

Karalar et al. (22) evaluated the effects of parenchymal thickness and stone density values on PNL outcomes. According to this study, no correlation was detected between stone density and success rate (p>0.05), but drop in Hb (%) was only correlated with parenchymal thickness (p<0.01). They were also stated that the stone-free rate in patients with thicker renal parenchyma was higher than in patients with lower parenchymal thickness (p<0.01). Also in our study it was considered that, in patients with low renal parenchymal thickness on CT images, bleeding will be more during the operation, and recovery is longer after nephrostomy removal.In present study, no blood transfusion was required due to bleeding in any of the patients underwent PNL.

Wang et al. (23) reported the results of their studies in which they performed URS, mini-PNL and laparoscopic ureterolithotomy (RPLU) at a ratio of 1: 1: 1 to 150 patients with stones >15mm in diameter impacted into the upper ureter. In their study, it was reported that mini-PNL and RPLU are more appropriate treatment options for upper ureteral stones with a diameter of >15 mm, and URS would be more appropriate for selected patients with high general anesthesia risk. In addition, this study reported that there was no significant difference between the three groups in terms of complication rates (p>0.05). In another similar study, Bozkurt et al.(24) performed URS in 41 and PNL in 45 of 86 patients with a  $\geq$ 1.5 cm diameter impacted upper ureter stones. According to this study, PNL was found to be quite advantageous over URS in terms of stonefree rate (97.8% vs 82.9%, p=0.025), while postoperative complication rates were shown to be close to each other according to the Clavien grade system (Grade 0: 35/34%, Grade 1: 3/2%, Grade 2: 7/5%, Grade 3-4-5: 0/0%). Similar to literature data, in the present study, no significant difference was found between the groups in terms of postoperative complications according to Clavien grade system (p=0.168). This result indicates that both URS and PNL can be safely applied with low complication rate in the treatment of larger impacted upper ureteral stones with a diameter of  $\geq 2$  cm as well as in stones with a diameter of  $\geq 1.5$  cm.

**Limitations:** The most important limitation of our study is its retrospective nature and the lack of randomization. The small sample size due to the fact that it is a single center study can be considered as another limitation. In addition, the lack of long-term patient satisfaction status may be determined as another important limitation.

#### CONCLUSION

Combined URS+RIRC and PNL are very effective and safe treatment options in the treatment of stones  $\geq 2$  cm in diameter. The complication rates of both procedures are similar. URS+RIRC is a more minimally invasive treatment option and is more advantageous than PNL in terms of hospital stay. However, in terms of total stone free rate, PNL provides a significantly higher success rate than URS+RIRC. The operation option, the advantages and disadvantages of both procedures should be determined with the patient-physician consensus after discussing the patient in detail.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** After obtaining the approval of Keçiören Training and Research Hospital Clinical Researches Ethics Committee (Date: 23.02.2021, Protocol no:2012-KAEK-15/2238).

**Informed Consent:** Because the study was designed retrospectively, no written informed consentform was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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