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Predictive Factors for the Peri-operative Outcome of Ureteroscopic Lithotripsy for Proximal Ureteric Stones

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ABSTRACT

Background: Proximal ureteric stones are considered one of challenging location for lithotripsy using semirigid ureteroscopes. Aim of the study was to assess clinical and radiological characteristics associated with outcome of lithotripsy using semirigid ureteroscope for proximal ureteric stones.

Methods: Prospective observational study was done on patients who underwent semirigid ureteroscopic lithotripsy for proximal ureteric stone. Stone and ureteral mormphomeric parameters were documented from computed tomography urogram. Stone free status and complication rates were studied. To determine predictive factors for outcomes, multivariate regression analysis and receiver operative curve were used.

Results: One hundred patients were included in study. Demographic characteristics, stone size, density and mode of lithotripsy had no impact on stone free rate or complications. The mean ureteral wall thickness($p = 0.002$), distance of stone from pelvi-ureteric junction($p = 0.005$), degree of hydronephrosis($p = 0.0001$) and peri-ureteric fat stranding ($p = 0.038$) were found to have significant association with stone free rate on univariate analysis. On multivariate analysis, mild hydronephrosis($p = 0.003$) and distance of stone from pelvi-ureteric junction($p = 0.022$) were significant for stone free rate.

Conclusions: Mean ureteral wall thickness, stone distance from pelvi-ureteric junction, presence of peri-ureteric fat stranding and hydronephrosis affect stone free rate on univariate analysis. On multivariate analysis for stone free rate, stone distance from pelvi-ureteric junction and mild hydronephrosis were significant. There was no significant impact of any stone or ureteral morphometry on complication rate.

Keywords: Complications; proximal ureteric stone; semirigid ureteroscopic lithotripsy; stone free rate

INTRODUCTION

Semi-rigid ureteroscopy (SURS) is popular, reliable, and widely accepted treatment modality for the treatment of ureteral stones.[1, 2] Flexible ureteroscopy is increasingly gaining popularity and is gradually replacing SURS for the treatment of proximal ureteric stones. However, SURS still have the advantages of better irrigant flow, superior optics with a wider field of view, larger working-instrument channels and greater durability.

However lithotripsy for proximal ureter stones using semirigid scopes is considered a challenging location owing to difficult access, and lower stone free rate (SFR) is documented than in distal locations.[3]

An accurate estimate of treatment success is crucial for optimal decision making and informed patient counseling. Studies assessing predictive factors in SURS for proximal ureteral stones are limited. This study was conducted to explore preoperative factors that could influence the outcome of SURS in proximal ureteric stones.

METHODS

A prospective observational study was conducted in the Department of Urology, National Academy of Medical

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Sciences, Bir Hospital, Kathmandu, Nepal on patients undergoing semi-rigid ureteroscopic lithotripsy for proximal ureteric stones from December 2021 to August 2022. Ethical clearance was obtained from Institutional review board (Ref. 976/2078/79) and written informed consent was obtained from all patients. The sample size was 96.

Patients of age 16 years and above with solitary proximal ureteric stone undergoing semirigid ureteroscopic lithotripsy (URSL) during the study period were included. Patients with ureteral or urethral stricture, pregnancy, coagulopathy, preplaced ureteral stent, concomitant renal stones, previous history of ureteral reconstruction surgery and those in whom stones retropulsed before lithotripsy were excluded from the study.

Detailed history, clinical examination and relevant investigations reports of all patients were recorded. Investigations performed were serum creatinine, blood urea nitrogen, urine analysis, urine culture-sensitivity and computed tomography intravenous urogram (CT IVU). Stone parameters such as stone size, stone volume, stone location, 3-D stone density (HU) and ureteral morphometry such as maximal ureteral wall thickness at the site of impaction, distance of stone from pelvi-ureteric junction (PUJ), proximal ureteric diameter, peri-ureteric stranding at the site of impaction, presence and degree of hydronephrosis were measured from CT IVU by an experienced consultant radiologist from the institute.

Surgical Technique: Prophylactic antibiotic, ceftriaxone 1 gram was given half an hour before the procedure. URSL was performed in standard lithotomy position under regional anesthesia. A 6.5/7.5 Fr semirigid ureteroscope (Wolf, Germany) was introduced in ureter over 0.0035 inches glide wire. Calculus was fragmented with pneumatic (Nidhi, India), Holmium: YAG laser (Lumenis, Israel) and ultrasonic lithotripter (Olympus, Tokyo, Japan). Settings for lithotripter were as follows: pneumatic (3.6 Kg/cm^2 pressure, frequency 4 Hz) and Holmium: YAG laser (Energy: 0.6-0.8 Joules, frequency 8-10 Hz, laser fiber diameter: 365 micron). At the end of procedure ureteral stent and Foley catheter was placed in all patients.

Patients were discharged on first postoperative day after removal of Foley catheter and were followed up with X-ray kidney ureter bladder (KUB) and ultrasound (USG) KUB after two weeks. Patients with no residual stones had their stent removed at 2 weeks and those with residual stones in the imaging studies at two weeks were followed up at four weeks with USG and X-ray KUB. Stone-free status were defined as no residual fragments in USG and X -ray KUB at four weeks.

Operational definitions: Proximal ureter was defined as the portion of the ureter from PUJ to the upper border of sacroiliac joint. The stone size was calculated using the maximum transverse diameter as determined in CT scan. The proximal ureteral diameter was measured as the maximum transverse diameter of the ureter anywhere between stone impaction site and the PUJ. Maximum ureteral wall thickness and fat standings were noted at the level of stone. Duration of surgery was defined as the duration between introduction of ureteroscope to per-urethral catheter insertion at the completion of the procedure. Complications were defined as per Clavien-Dindo classification.[4]SFR and complication rates were considered primary and secondary outcome respectively.

Data analysis was done using the IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA). Baseline characteristics were done using the Chi-square test/Fisher's exact test for categorical variables and the Student t-test/ Mann Whitney U test for continuous variable. To determine potential risk factors for URS success, univariate and multivariate regression analysis was used. The results were expressed as adjusted OR with 95% CI. Receiver operated curve (ROC) was plotted for stone free rate.

RESULTS

One hundred and twenty-five underwent semirigid URSL during the study period and after exclusion of patients with multiple stones (n=17) and retropulsion before lithotripsy (n=8) one hundred patients were included in the final analysis.

The preoperative demographic, clinical characteristics, ureteral and stone related parameters are reported in Table 1. There was male predominance (66%). The mean stone size was 11.22±4.16 mm. The mean duration of surgery was 32.86± 16.94 minutes.

Out of the complications, most of the patients had grade I complications such as fever (1), pain (16), nausea/ vomiting (9), one patient had retention due to clot and 1 had ureteric perforation (Table 2).

While comparing all the variables with SFR, stone free status significantly increased with decreased maximal ureteral wall thickness (p=0.002). Similarly, SFR was significantly low for decreased distance of PUJ from

stone (p=0.005). SFR was low in patients with peri-ureteric stranding compared to those in whom stranding was absent (p=0.038). Patients with mild hydronephrosis were significantly stone free (p=0.0001) and increment in BMI was associated with higher SFR. However, there were no significant association between age, sex, and stone free status. Altogether 31 patients underwent laser lithotripsy, among which 11 had stone fragments retropulsion. However, at four weeks, 24 achieved stone free status with the SFR of 77.4%. A total of 66 patients underwent pneumatic lithotripsy, 30 patients had stone retropulsion at the time of surgery. At four weeks, 46 patients achieved stone free status (69.7%). Three patient had ultrasonic lithotripsy among them, one had stone retropulsion however all of them were stone free at four weeks (100%). However, there was no significant association of the mode of lithotripsy with stone free status (p=0.504) (Table 3).

On univariate analysis ,BMI , mild hydronephrosis, maximum ureteral wall thickness, stone distance from PUJ and peri-ureteric stranding were the factor associated with SFR while on multivariate regression analysis, factors associated with stone free status were only mild hydronephrosis (OR = 0.282, 95%[CI] = 0.122-0.653, p = 0.003)and stone distance from PUJ (OR = 1.043, 95%[CI] = 1.006-1.082, p = 0.022).

Table 1. Demographic and preoperative clinical characteristics of the participants.

Variables	Value
Sex, n (%)	
Male	66 (66.0)
Female	34 (34.0)
Age (years) (Mean ± SD)	39.55 ±1.34
Serum Creatinine (Mean ± SD)	1.22±1.04
BMI	
< 18.5	3 (3.0)
18.5-24.9	41 (41.0)
25-29.9	43 (43.0)
≥30	13 (13.0)
Duration of symptoms (months) (Mean ± SD)	5.02±3.82
Stone morphometry parameters	
Stone size (Mean ± SD)	11.22±4.16
Stone density (HU) (Mean ± SD)	1032.83±274.66
Ureteral morphometric parameters	

Table 1. Demographic and preoperative clinical characteristics of the participants.

Variables	Value
Maximum ureteral wall thickness (Mean ± SD)	2.24±0.74
Distance of stone from PUJ (Mean ± SD)	31.35±17.64
Maximum ureteric diameter (Mean ± SD)	11.38±2.72
Peri-ureteral stranding, n (%)	
Present	46 (46.0)
Absent	54 (54.0)
Hydronephrosis, n (%)	
No	2 (2.0)
Mild	59 (59.0)
Moderate	32 (32.0)
Severe	7 (7.0)

BMI, Body Mass Index

Table 2. Distribution of complications according to Clavien-Dindo classification.

Clavien Grade	Complication	n (%)
I	Fever	1 (3.5)
	Pain	16 (57.1)
	Nausea/vomiting	9 (32.1)
IIIa	Retention due to blood clot	1 (3.5)
IIIb	Ureteric perforation	1 (3.5)

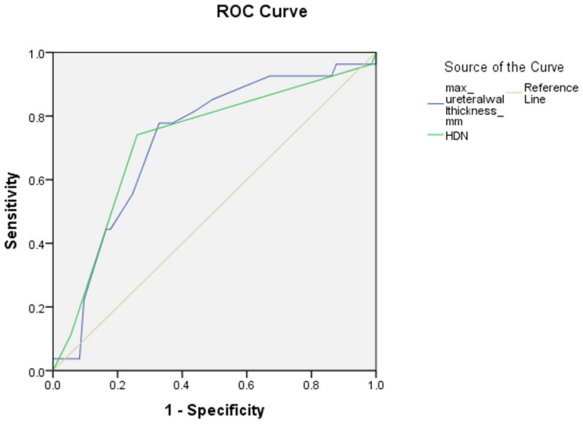

Fig 1. ROC curve for stone free status.

Table 3. Association of variables with stone free status.

Characteristics	Stone Free status		p-value
	Yes (n=73)	No (n=27)	
Sex n (%)*			0.932*
Male	48 (72.7)	18 (27.3)	
Female	25 (73.5)	9 (26.5)	
Stranding at the site of impaction n (%)*			**0.038***
Present	29 (63.0)	17 (37.0)	
Absent	44 (81.5)	10 (18.5)	
Hydronephrosis n (%)*			**0.0001***
No	1 (50.0)	1 (50.0)	
Mild	53 (89.8)	6 (10.2)	
Moderate	15 (46.9)	17 (53.1)	
Severe	4 (57.1)	3 (42.9)	
BMI n (%)*			0.013*
Underweight (<18.5)	0	3 (100.0)	
Normal (18.5-24.9)	33 (80.5)	8 (19.5)	
Overweight (25-29.9)	29 (67.4)	14 (32.6)	
Obese (≥30)	11 (84.6)	2 (15.4)	
Maximum ureteral wall thickness (mm)** Mean± SD	2.11±0.64	2.61±0.87	**0.002****
Stone distance from PUJ (mm) ** Mean± SD	34.31±18.05	23.37±13.84	**0.005****
Maximal proximal ureteral diameter (mm)** Mean± SD	11.12±2.83	12.08±2.27	0.116**
Stone size (mm) Mean± SD**	11.47±4.24	10.09±3.66	0.206**
Stone density (HU) Mean± SD**	1049.84±279.22	955.33±245.13	0.188**
Mode of lithotripsy			0.504***
Laser	24 (77.4)	7 (22.6)	
Pnuematic	46 (69.7)	20 (30.3)	
Ultrasonic	3 (100)	0	

* Chi-square test; ** Independent t-test; ***Fisher's exact test.

Table 4. Predictive factors for stone free status on univariate and multivariate regression analyses.

Variables	Stone free status			
	Univariate analysis		Multivariate analysis	
	odds ratio (95% CI)	p-value	odds ratio (95% CI)	p-value
BMI	1.533 (.714-2.289)	0.013*	1.620 (.784 -3.351)	.193
Hydronephrosis(mild)	.172 (.055 .538)	0.0001*	.282 (.122 -.653)	.003*
Maximum ureteral wall thickness(mm)	.439 (.147-1.312)	0.002**	.556 (.216 -- 1.433)	.225
Stone distance from PUJ (mm)	1.061(1.019-1.105)	0.005**	1.043 (1.006 --1.082)	.022*
Stranding at the site of stone impaction	1.262 (.347-1.593)	0.038*	1.010 (.295 -3.465)	.987

CI-confidence interval.

Table 5. Association of variables with complication.

Characteristics	Complications		p-value
	Yes (n=28)	No (n=72)	
Sex n (%)			
Male	14 (21.2)	52 (78.8)	0.035*
Female	14 (21.2	20 (58.8)	
Stranding at the site of impaction, n (%)			
Present	10 (21.7)	36 (78.3)	0.198*
Absent	18 (33.3)	36 (66.7)	
Hydronephrosis n (%)			
No	1 (50.0)	1 (50.0)	0.401*
Mild	19 (32.2)	40 (67.8)	
Moderate	6 (18.8)	26 (81.2)	
Severe	2 (28.6)	5 (71.4)	
BMI, n (%)			
Underweight (<18.5)	1 (33.3)	2 (66.7)	0.939*
Normal (18.5-24.9)	12 (29.3)	29 (70.7)	
Overweight (25-29.9)	11 (25.6)	32 (74.4)	
Obese (≥30)	4 (30.8)	9 (69.2)	
Maximum ureteral wall thickness (mm) Mean±SD	2.20±0.71	2.26±0.75	0.689**
Stone distance from PUJ (mm) Mean±SD	33.03±17.86	33.7±17.63	0.556**
Maximal proximal ureteral diameter (mm) Mean±SD	10.78±2.92	11.61±2.62	0.177**
Stone size (mm) Mean±SD	11.0± 5.24	11.3±3.69	0.745**
Stone density (HU) Mean±SD	1030.14±279.79	1033.88±274.62	0.952**
Mode of lithotripsy			0.917***
Laser	8 (25.8)	23 (74.2)	
Pnuematic	19 (28.8)	47 (71.2)	
Ultrasonic	1 (33.3)	2 (66.7)	

*Chi-square test; **Independent t-test; ***Fisher's exact test.

Among mild hydronephrosis ,ureteral wall thickness, periureteric stranding, stone distance from PUJ and BMI, ureteral wall thickness and mild hydronephrosis were best predictor for stone free status. Patients with mild hydronephrosis had 88.5% stone clearance (AUC=0.722, accuracy 74%) and in those with ureteral wall thickness <2.35 mm, the SFR was 89%(AUC=0.722, accuracy74%).

While comparing the association of variables with complications, female sex had significantly higher rate of complications (p=0.035). Five patients who underwent laser lithotripsy, had grade I complications, one had ureteric perforation and one had colic due to clot retention. The perforation was identified at the time of surgery and was managed conservatively with ureteral stent placement for six weeks. The patient was stone free and the ureteric injury was healed when examined with URS and RPG at six weeks. For colic due to clot retention, cystoscopic clot evacuation was done and as there was no active bleeding, the patient was discharged at 72 hours. Nineteen patients undergoing pneumatic lithotripsy and one patient undergoing ultrasonic lithotripsy had grade I complication. However, there was no significant association of the mode of lithotripsy and complication. Rest of the variables had no significant impact on complication rate (Table 4). However, on multivariate analysis none of the factors significantly affected complication rates.

DISCUSSION

The SFR in proximal ureteric stones are lower than in other ureteric locations.[5, 6] Various factors including available equipment, patient characteristics like age, sex, BMI, stone and ureteral characteristics, degree of hydronephrosis along with surgeon's expertise have shown to affect the success of URSL.[7-11]

The overall SFR following ureteroscopic lithotripsy for proximal ureteric stones assessed at four weeks in this study was 73% which is similar to those reported in other studies.[12-14] However, higher SFR were documented in other studies (range, 78.8 - 94%).[6,7,15,16] The reasons for lower SFR in current study could be the predominant use of pneumatic lithotripsy which is associated with higher retropulsion rate than other modalities. In current study also the -SFR was better with laser lithotripsy than pneumatic lithotripsy (77.4% vs 69.7%), however it was not significant and laser was used in fewer cases. Another reason could be the utilization of USG and X-ray KUB for assessing SFR instead of only X-ray KUB used in other studies. Ultrasonic lithotripsy was found to have stone free rate of 100% , however there are no

other studies comparing ultrasonic lithotripsy and only small subset of patient(n=3) had ultrasonic lithotripsy, so limited number patients make it preliminary to draw conclusions.

Stone morphometry and demographic features like age, sex and BMI did not seem to have any impact on stone clearance in this study unlike previous studies.[8, 15, 17, 18]

The mean ureteral wall thickness had been associated with the SFR, in various studies, those with wall thickness less than 5 mm had better SFR.[8, 9]We also observed similar findings of higher SFR in those patients with lower ureteral wall thickness. The lower SFR in those with increased ureteral wall thickness could be explained by the mucosal edema and inflammation implying stone impaction at the site further increasing the risk of ureteric injury or creating a false passage during ureteroscopy.

Okçelik et al. found that use Ho:YAG lithotripsy as well as increased distance of the stone to the PUJ increases the success rate of semi rigid URSL, however in current study only distance from PUJ influenced the SFR with no effect of mode of lithotripsy on outcome.[6] It can be attributed to high chances of retropulsion with less distance between stone and PUJ.

Presence of peri-ureteric fat stranding, which is a sign of impaction was associated with decreased stone clearance in present study similar to previous studies.[15, 19]Degree of hydronephrosis also had inverse relation with SFR with maximum clearance for mild hydronephrosis similar to a previous study.[8] However, on multivariate analysis only stone distance from PUJ (p = 0.022) and mild hydronephrosis (p = 0.003) were significant for SFR in this study.

In the current study complications were observed in 28% of patients, however most of them were grade I complications which resolved on their own, which is comparable to those reported in various studies.[18, 20] Female gender was associated with higher complication rate, however, all the complications were grade I. Association of female gender to increased complication may be attributed to older age and unnoticed comorbid factors.[21] There was no relation observed between the ureteral wall thickness, peri-ureteric fat standing with the complication rates in our study which were in contrast to those documented by Mishra et al. and Sarica et al.[8, 9] The difference could be due the lower mean maximum ureteral wall thickness (2.24±0.74 mm) in this study which was below 4.8 mm cut off value in previous studies.

The stone morphometry did not influence the complication rate in our study which is in contrast to studies by Sen et al., Sancak et al., Mishra et al., and Bangash et al. where stone morphometry influenced the complications.[7, 9, 15, 18] It may be attributed to smaller stone size in current study compared to other studies. However, on multivariate analysis no significant factors were identified for complications.

The operative duration was 32.86±16.94 minutes in the present study. The forceps were not used to extract stones post lithotripsy which explain the shorter operative duration.

Some limitations of current study included multiple surgeons with different level of expertise, co-morbidities of patients and cost effectiveness not taken into account. Mode of lithotripsy was also not randomized and as the patient were followed till only four weeks, we also could not access the long-term complications like ureteral stricture and the type of auxiliary procedure provided to the patients with residual stones.

CONCLUSIONS

Increased mean ureteral wall thickness, decreased stone distance from PUJ, presence of fat stranding and moderate and severe hydronephrosis adversely affect SFR in semi rigid URSL for proximal ureteric stones on univariate analysis, however, stone distance from PUJ and mild hydronephrosis are the only key factors as seen in multivariate analysis for SFR. There is no significant impact of any stone or ureteral morphometry on complication rate while undertaking semirigid ureteroscopy for proximal ureteric stones.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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