

Study of ureteral and renal morphometry on the outcome of ureterorenoscopic lithotripsy: The critical role of maximum ureteral wall thickness at the site of ureteral stone impaction

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Abstract

Purpose: The purpose is to study the association of stone, ureteral, and renal morphometric parameters with the relevant outcome variables, i.e., complication rate, stone-free rate (SFR), and operating time of ureterorenoscopic lithotripsy. Although a safe procedure, it still occasionally has major complications. Computed tomography (CT) scan is often performed to diagnose ureteral calculi, providing opportunities for ureteral morphometry that may have a bearing on the outcome of the procedure.

Materials and Methods: Ureteric, renal, and stone morphometric parameters were measured from CT of the abdomen and pelvis of the 110 patients with ureteral calculi who underwent ureteroscopic lithotripsy (URSL). Data were collected retrospectively in 25 patients and prospectively in 85 patients. Association of these parameters with the outcome variables of the procedure mentioned above was studied.

Results: On univariate analysis, body mass index, stone size, and maximum ureteral wall thickness (MUWT) were found to have a significant association with URSL complications, SFR, and duration of surgery. On multivariable analysis, only MUWT was found to be an independent risk factor for URSL complications. In 90% of total patients with residual stones, MUWT was found to be >4.8 mm.

Conclusion: Ureteral wall thickness of >4.8 mm is associated with prolonged duration of surgery and lower SFR. Patients with ureteral wall thickness of >4.8 mm at the site of ureteral stone who are planned for URSL must be counseled about the higher chances of residual stones and the need for additional procedure.

Keywords: Complications, duration of surgery, ureteral wall thickness, ureterorenoscopic lithotripsy

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Received: 24.06.2019, **Accepted:** 22.11.2019, **Published:** 10.06.2020.

INTRODUCTION

Ureterorenoscopy came into being in the 1980s, and with the progressive development of more flexible, smaller, and less traumatic ureteroscopes, the procedure has become more reliable and widely accepted among urologists the

world over. As a routinely performed procedure, it is relatively safe with overall complication rates ranging from 12% to 27% in various studies and major complication rates have reduced to a mere 0.5%–1%. Development of newer ureteroscopes that are of finer caliber and the application of

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How to cite this article: Mishra AK, Kumar S, Dorairajan LN, Manikandan R, Ramkumar G, Sreerag KS, *et al.* Study of ureteral and renal morphometry on the outcome of ureterorenoscopic lithotripsy: The critical role of maximum ureteral wall thickness at the site of ureteral stone impaction. *Urol Ann* 2020;12:212-9.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_95_19

advanced digital technology has made ureteroscopy safer. Nevertheless, despite significant technologic advances, the incidence of iatrogenic ureteral avulsion, tears, perforations by basketing, intussusception, and sepsis are still substantial. The subset of patients in which these are more common is patients with impacted stones in ureters, ureters that are inflamed, larger stone size >1 cm, proximal ureteric stones, postfailed extracorporeal shockwave lithotripsy or endourological manipulation cases, and longer periods of impaction.^[1,2]

The routine use of computed tomography (CT) for diagnosing ureteral calculi in the last decade has made it feasible to measure various parameters, including ureteral wall thickness that was earlier not possible with conventional radiography such as X-ray kidney, ureter, and bladder (KUB), or intravenous urography. Thickness of the ureteral wall where the stone is impacted, intuitively, could be a reflection of the degree of local inflammation, which in turn could be due to the mechanical pressure, infection, or ischemic effect of the stone on the ureteral wall. Generally, larger stones and a longer period of impaction exert greater pressure at the impact site and cause severe and chronic inflammation at the ureteral mucosa because of decreased blood flow. The inflammation, interstitial fibrosis, and urothelial hypertrophy associated with stone impaction may cause ureteral edema and polyps and may involve surrounding tissues, increasing UWT in the impacted area. It would seem logical that this might be associated with the complication rate in ureteroscopic lithotripsy (URSL). This hypothesis is also supported by a recent study, in which ureteral wall thickness was found to have a direct association with complications in patients undergoing shock-wave lithotripsy (SWL) for the treatment of ureteral calculi.^[3] However, there are no studies that have looked at the ureteral wall and renal morphometry as predictor of outcome of URSL.

In this study, we measured multiple ureteral and renal morphometric and other parameters such as ureteral wall thickness, proximal ureter diameter, presence of periureteral stranding, renal transverse pelvic diameter) and explored whether they are helpful in predicting complications of URSL. We also tried to see if it would be possible to identify using these parameters the subgroup of such patients with ureteric calculi in whom the complication rate would be higher so that additional precautions can be taken in these patients while performing URSL.

MATERIALS AND METHODS

The present study was conducted from November 2014

to May 2015 in a retrospective manner and from May 2015 to December 2016 prospectively after obtaining the approval of the Institute Ethics committee (Human Studies). All patients >12 years of age who had undergone URSL or were scheduled to undergo URSL for a solitary ureteral calculus disease during the study period were included. Patients with urethral and ureteral stricture disease, coagulopathy, pregnancy, preplaced ureteral stent, and/or percutaneous nephrostomy were excluded from the study. Relevant details from history and physical examination findings including body mass index (BMI), biochemical evaluation (serum creatinine, blood urea nitrogen), urinalysis, and urine culture-sensitivity test results were recorded from case files. All patients were treated with appropriate perioperative antibiotics. Patients with sterile preoperative urine culture were given two doses of injection cefoperazone (500 mg) ± sulbactam (500 mg), one at the time of induction of anesthesia and a second dose 12 h later. For patients with a positive preoperative culture, intravenous antibiotics were started 24 h before the procedure and continued postoperatively for 5 days as per the department's standard protocol. BMI was categorized as low and normal if <25 and high if >25. The following radiological parameters measured from axial images obtained from noncontrast CT of the KUB region (NCCT-KUB) were recorded. Stone parameters included stone size in millimeters defined as the maximum transverse diameter of stone, stone location (proximal if located above the upper border of the sacroiliac joint and distal if located below it), and stone density measured by placing a maximum size circular or oval region of interest completely within the stone from axial NCCT image and recording the average CT density in Hounsfield units [Figure 1]. Ureteral and renal morphometric

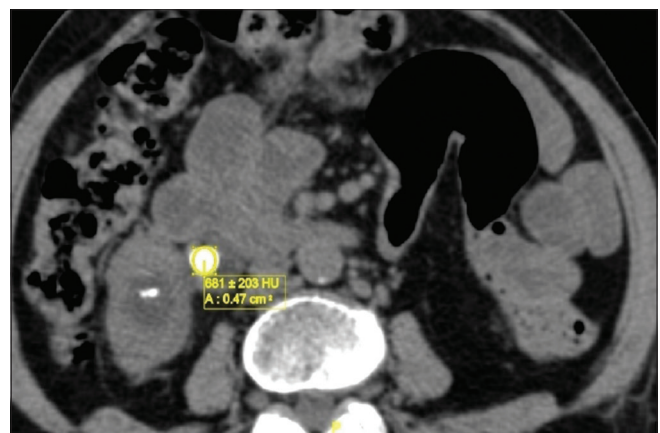


Figure 1: Axial cross-sectional noncontrast computed tomography of the kidney, ureter, and bladder image showing measurement of average stone density by placing a maximum size circular or oval region of interest completely within the stone from axial computed tomography scan image (Hounsfield units)

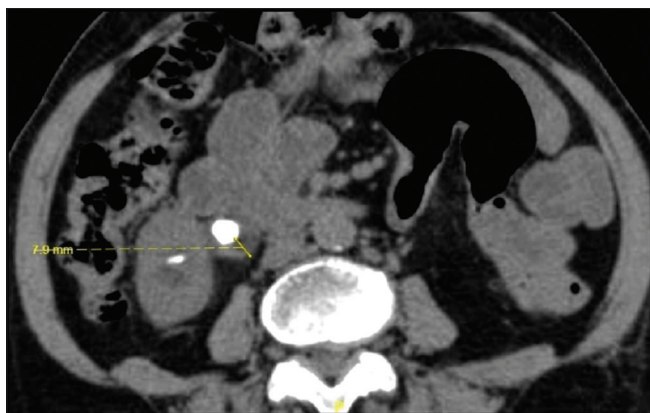


Figure 2: Axial cross-sectional noncontrast computed tomography of the kidney, ureter, and bladder image showing maximum thickness of ureteral wall measured at the site of impaction of stone from axial computed tomography scan images, i.e., maximum ureteral wall thickness (mm)

parameters, including the MUWT measured at the site of stone impaction [Figure 2], the proximal ureteral diameter measured as the maximum transverse diameter of the ureter anywhere proximal to the stone impaction site but distal to the pelvic ureteric junction, the maximum renal parenchymal thickness measured in axial images at the level of hilum, the maximum renal transverse pelvic diameter measured in anteroposterior axis and the presence or absence of periureteral stranding at the level of impaction of stone, were all recorded. All the measurements were done in Universal Viewer Zero Footprint Client™ by GE Healthcare, USA.

URSL procedure was performed in standard lithotomy position under regional anesthesia with an 8/9.2 Fr Karl Storz™ semirigid ureteroscope with 6° telescope lens. The calculus was fragmented with the help of laser or pneumatic lithotripter. Settings for Ho: YAG laser lithotripsy with a 365 μ -mm fiber were energy 0.8–1.2 J and frequency 10–15 Hz. Settings for pneumatic lithotripsy (Swiss LithoClast Master™) was energy 4 bar and frequency 5–10 Hz. Routinely, a 6 Fr size 26-cm long double pigtail stent and a per urethral catheter were placed at the end of the procedure. Postoperative X-ray KUB was routinely obtained. In those with residual fragments, X-ray/ultrasonography (USG)-KUB was repeated after 2 weeks. CT scan to confirm stone clearance was performed only in those patients who were symptomatic or had residual hydronephrosis in the USG-KUB performed after 2 weeks. The ureteral stent was removed at that time provided the patient was “stone-free.” “Stone-free” state for the purpose of the study was defined as no residual fragment of stone that more than 2 mm in size. Any auxiliary procedure such as repeat URSL or SWL performed for residual calculi and complications were noted. Duration of surgery, defined

as the time taken from the point of introduction of cystoscope to the time of perurethral catheter insertion after completing the procedure, was recorded.

Statistical methods

The sample size was estimated using two primary outcome measures: First, for comparing the difference in ureteral morphometric parameters between the patient groups with and without complications and based on the expected overall complication rate. The expected difference in MUWT between the groups with and without complications based on a previous study was 1.42 with a standard deviation of 1.62 mm.^[3] The sample size was estimated at 5% level of significance and 90% power. Second, assuming the expected overall complication rate among the patients undergoing URSL as 27%,^[4] we expected to get 30 patients with complications and to achieve these 110 patients were included in the study and screened for the complications. The latter calculation that yielded a higher sample size was considered.

The effect of demographic parameters, stone parameters, presence of infection (positive preoperative culture), and ureteral morphometric and renal parameters on the outcome variable such as complications, SFRs, and duration of surgery was analyzed. Univariate analysis (Chi-square/Fisher's exact test or *t*-test) and multivariable analysis were performed to determine statistically significant independent factors. If parameters did not show normal dispersion, Mann–Whitney *U*-test was performed as the nonparametric equivalent of *t*-test. All statistical analysis was carried out at 5% level of significance, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS Statistics for Windows, Version 19.0. (Armonk, NY, USA: IBM Corp).

RESULTS

A total of 110 patients undergoing URSL from November 2014 to January 2016 who fulfilled the inclusion and exclusion criteria were studied. Of these, data on 25 patients were obtained by retrospective record review, while in the prospective group, 85 patients were studied. Details regarding patients' mean value of demographic, clinical, stone parameters, ureteral and renal morphometric parameters are illustrated in Table 1.

In 23 patients (20.9%), complications occurred included minor intraoperative complications such as bleeding (6 cases), ureteric mucosal injury (1 case), postoperative complications such as residual calculi (9 cases – Clavien–Dindo [CD] Grade III), urinary tract infections (UTI) (2 cases – CD Grade II), and major

Table 1: Various variables of study population

Variable	Value
Demographic and clinical variables	
Total number of patients	110
Gender (%)	
Male	72 (65)
Female	38 (35)
Age (years), mean±SD	42.4±13.30
Preoperative urine culture	
Positive	24 (22)
Sterile	86 (78)
BMI	
BMI ≤25	52 (47)
BMI >25	58 (53)
Stone parameters	
Stone size (mm), mean±SD	7.72±2.35
Stone density (HU), mean±SD	786.87±264.25
Stone location (%)	
Proximal	68 (62)
Distal	42 (38)
Ureteral and renal morphometry	
Ureteral wall thickness (mm), mean±SD	4.09±1.66
Maximum renal parenchymal thickness (midpole) (mm), mean±SD	21.41±6.32
Maximum proximal ureteric diameter (mm), mean±SD	16.23±5.24
Maximum transverse renal pelvic diameter (mm), mean±SD	20.67±8.14
Periureteric stranding (%)	
Present	52 (47)
Absent	58 (53)
Outcome parameters	
Duration of surgery (min), mean±SD	32.75±7.28
Complications (%)	
Yes	23 (21)
No	87 (79)

SD: Standard deviation, BMI: Body mass index, HU: Hounsfield unit

Table 2: Stone location and complications

Stone location	Total number	Complications	Type of complications
Proximal	68	15	Residual calculi Incomplete fragmentation-2 Up-migration-5 Perforation-1, mucosal injury-2 Fever and UTI-3 Bleeding-2
Distal	42	8	Hematuria-2 Mucosal injury-1 Residual calculi-2 UTI-1, dysuria and voiding LUTS-2

UTI: Urinary tract infection, LUTS: Lower urinary tract symptom

complications such as urosepsis (2 cases – CD Grade IV) and ureteral perforation intraoperatively (1 case). The proportion and types of complication associated with stone location is shown in Table 2. The Clavien Dindo grade of severity of the different complications observed are shown in Table 3 and the proportion of patients with based on the mode of lithotripsy used is shown in Table 4. After URSL, 100 patients (91%) out of a total of 110 patients were completely stone free at 2 weeks. A total of 11 (10%) patients had residual calculus on postoperative imaging, and 10 out of them needed auxiliary procedures, namely

Table 3: Clavien–Dindo classification of complications

Clavien grade	Complication	Patient number
I	Fever	3
	Pain, nausea, vomiting	5
	Hematuria	4
	Dysuria and voiding LUTS	2
II	Hypertension	1
	UTI	4
	Mucosal injury	3
III	Perforation	1
	Stone migration	4
IV	Incomplete fragmentation	5
	Urosepsis	2

LUTS: Lower urinary tract symptom, UTI: Urinary tract infection

Table 4: Mode of lithotripsy versus complications

Mode	Location	Total number	Complications	P (laser vs. pneumatic)
Laser lithotripsy	Proximal	40	5	0.10
Pneumatic lithotripsy	Proximal	28	10	
	Distal	42	8	

The differences are not significant

ureteroscopic stone removal or SWL, to become stone-free while one patient passed out the stone with medical expulsive therapy within the next 14 days.

Age, BMI, stone size, MUWT, and preoperative urine culture were found to have a statistically significant association with URSL complications. Furthermore, infective postoperative complications were found in five patients, out of 24 who had a positive preoperative urine culture (20.8%) and none among 86 patients who had a sterile preoperative culture, and this difference was statistically significant ($P < 0.001$) [Table 5]. Furthermore, it was found that patients with positive preoperative urine culture had a higher mean MUWT (5.05 ± 1.73 mm) as compared to patients with sterile preoperative urine culture (3.83 ± 1.56 mm) and this was statistically significant ($P = 0.0013$). On logistic regression analysis, only age ($P = 0.034$), preoperative urine culture ($P = 0.009$), and MUWT ($P = 0.006$) were found to be independent risk factors for URSL complications. It was found that SFR was significantly associated with age, BMI, stone size, stone density, and MUWT on univariate analysis [Table 6]. However, on logistic regression analysis of these risk factors, only MUWT ($P = 0.008$) was found to be an independent determinant of SFR. The duration of surgery was found to show significant positive correlation with stone size, BMI, and MUWT [Table 7]. On multiple linear regression analysis, duration of surgery was found to have an independent association with MUWT only ($P < 0.004$). Receiver operating characteristic analysis of MUWT with SFR and occurrence of any complication revealed that the chances of residual stone being present were 1.3% when the MUWT was < 4.8 mm versus 28.1%

Table 5: Association of various categorical variables with ureteroscopic lithotripsy complications

Fisher's exact test*	Complications (23)	No complications (87)	Significance (P)
Sex			
Female	7	31	0.806
Male	16	56	
BMI (high/low)			
High	18	40	0.009
Low	5	47	
Preoperative urine culture-sensitivity			
Positive	13	11	<0.001
Negative	10	76	
Stone location			
Distal	8	34	0.811
Proximal	15	53	
Periureteral standing			
No	9	49	0.109
Yes	14	38	
Mann-Whitney U-test#		P	
Age (years)		0.019	
Stone size (mm)		0.015	
Stone density		0.571	
Maximum ureteral wall thickness (mm)		<0.001	
Maximum proximal ureter diameter (mm)		1.000	
Maximum renal parenchymal thickness (mm)		0.922	
Maximum TPD (mm)		0.922	

*Evaluated by Fisher's exact test, #Evaluated by Mann-Whitney U-test. TPD: Transverse pelvic diameter

Table 6: Association of various categorical variables with stone-free rate

Fisher's exact test*	Complete clearance	Residual calculus	Significance (P)
Sex			
Female	35	3	1.00
Male	65	7	
BMI (high/low)			
High	49	9	0.018
Low	51	1	
Stone location			
Distal	41	1	0.086
Proximal	59	9	
Periureteral standing			
No	54	4	0.512
Yes	46	6	
Mann-Whitney U-test/t-test#		P	
Age (years)		0.031	
Stone size (mm)		0.012	
Stone density		0.028	
Maximum ureteral wall thickness (mm)		0.001	
Maximum proximal ureter diameter (mm)		0.766	
Maximum renal parenchymal thickness (mm)		0.979	
Maximum TPD (mm)		0.198	

*Evaluated by Fisher's exact test, #Evaluated by Mann-Whitney U-test. TPD: Transverse pelvic diameter

when MUWT was >4.8 mm [Figure 3]. 90% of total patients with residual stones had MUWT >4.8 mm. Furthermore, using the same cutoff value, it was found that the risk of any complication occurring was 7.7% when the MUWT was <4.8 mm versus 53.1% when the MUWT was >4.8 mm.

DISCUSSION

In spite of its myriad advantages, URSL is associated with various minor complications such as bleeding, mucosal injury, and UTI to occasionally major complications such as

ureteral avulsion, ureteral perforation, and urosepsis. In our study, we had complications in 21% of patients, including bleeding in six patients, mucosal injury, and ureteral perforation in one patient each; urosepsis and UTI in two patients each; and residual calculi due to stone ascension in 11 patients. Abdelrahim *et al.*^[4] evaluated various factors related to intraoperative complications during rigid ureteroscopy and reported complications in 27.4% cases which included stone up-migration in 12%, bleeding in 6%, mucosal injury in 5%, and perforation of the ureter in 2% of cases. Overall, our results were almost similar to

Table 7: Association of various variables with duration of surgery

Variables	Correlation	Duration of surgery (min)
Age (years)	Pearson correlation	0.074
	Significance (two-tailed)	0.441
	<i>n</i>	110
BMI	Pearson correlation	0.312**
	Significance (two-tailed)	0.001
Stone size (mm)	Pearson correlation	0.266**
	Significance (two-tailed)	0.005
Stone density	Pearson correlation	-0.005
	Significance (two-tailed)	0.957
Maximum ureteral wall thickness (mm)	Pearson correlation	0.504**
	Significance (two-tailed)	<0.001
Maximum proximal ureter diameter (mm)	Pearson correlation	-0.002
	Significance (two-tailed)	0.981
Maximum renal parenchymal thickness (mm)	Pearson correlation	0.098
	Significance (two-tailed)	0.309
Maximum TPD (mm)	Pearson correlation	-0.034
	Significance (two-tailed)	0.722

**Highly significant with $P < 0.01$. TPD: Transverse pelvic diameter

the above study, except that in 0.5% of their cases, ureteral avulsion also occurred which did not take place in our study perhaps due to the smaller numbers that we studied. Geavlete *et al.*^[1] studied a series of 2000 URSL procedures. Out of these, fever and sepsis occurred in 1.1% of patients, hematuria in 2%, loin pain in 0.2%, stent migration in 0.6%; intraoperatively, 1% had ureteral mucosal injury, 0.6% had ureteral perforation, while 0.1% had both bleeding and avulsion. In our study, the complication rate was a little higher (21%) because we included residual calculi due to stone up-migration or insufficient fragmentation as a complication which the above-mentioned authors have not included in their studies as a complication. In our study, 22% males and 18% females had complications and the association between gender and complication rate was insignificant ($P = 0.80$) in concurrence with Özsoy *et al.*^[5] Similarly, BMI and stone location were not found to be independent risk factors for complications in our study as inferred by Drăguțescu *et al.*^[6] while analyzing the impact of BMI on the complications of URSL and Schuster *et al.*^[7] regarding association between stone location and URSL complications. All the patients who developed infective complications in our study had a positive preoperative urine culture, and preoperative culture was the sole risk factor associated with postoperative infective complications and was also found to be a highly significant and independent risk factor for the development of overall postoperative complications. Pricop *et al.*^[8] also found the association to be highly significant ($P < 0.001$) and recommended mandate of a negative urine culture before performing the procedure. In fact, our study confirms the importance of ensuring a sterile preoperative urine culture in reducing infective complications of URSL.

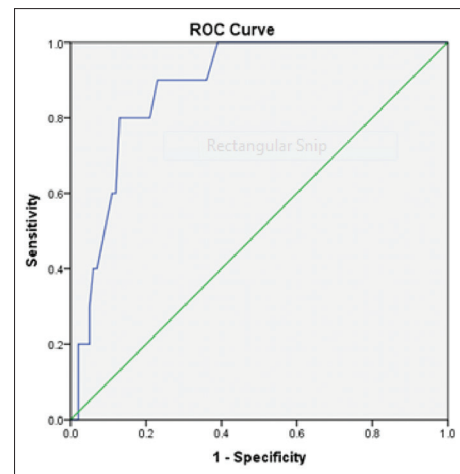


Figure 3: Receiver operating characteristic curve of maximum ureteral wall thickness against stone-free rate showing strong association, (area under curve = 0.9) between maximum ureteral wall thickness and stone-free rate

El-Nahas *et al.*^[9] found an increased risk of complications in cases where the mean transverse diameter of the stone was 8 mm and concluded that width of the stone was the factor leading to maximum difficulty in stone extraction. In our study also, the mean transverse diameter of the stone in patients having complications was 8.9 mm and the association of complications with stone size was found to be statistically significant on univariate analysis. However, in multivariable analysis, only MUWT, age, and preoperative urine culture were the significant predictors. The mean MUWT in the complications group was 5.49 mm, and the association of complications with MUWT was highly statistically significant ($P < 0.0001$). Sarica *et al.*^[3] studied the association of ureteral wall thickness with SWL complications and found that patients with ureteric wall thickness more than 3.5 mm required more auxiliary procedures and this number was statistically significant. They concluded that higher the extent of stone impaction, lesser is the chance of stone fragmentation by shock waves. In our study, the association of the mean duration of surgery with complications was found to be highly statistically significant ($P < 0.001$). More than 90% of complications occurred when the duration of surgery was more than 36 min. When the duration of surgery was < 36 min, the proportion of cases that had complications was 2.7%, as compared to 54% when the duration of surgery was 36 min or more. Similarly, the duration of surgery was 40 min or more in all patients with residual stone fragments. When the duration of surgery was 40 min or more, the proportion of cases that were stone-free at 2 weeks was $< 50\%$, as compared to 100% when the duration of surgery was < 40 min. In a study of 320 cases done by Schuster *et al.*, they found only a single

contributory factor, i.e., increased duration of surgery to be significantly associated with perforation of ureter.

Abdelrahim *et al.*^[4] also studied the association of duration of surgery with complication rate and concluded that the association was statistically significant on both, bivariate and multivariate studies. Sugihara *et al.*^[10] studied the complications of URSL in a series of more than 12,000 patients and concluded that increased duration of surgery, especially those surgeries of more than 90 min duration, were significantly associated with more, as well as severe complications. Sugihara *et al.*^[10] found that longer duration of surgery, female gender, elderly patients, and comorbidities were highly correlated with severe complications and lesser SFR. However, in their study, only longer duration of surgery was the independent risk factor of complications and success rate on multivariate analysis.

Our result was in concordance with the abovementioned studies. This implies that factors that determine operating time are important determinants of complications. Our study showed that MUWT was the sole preoperative predictor of operating time. There was no statistically significant correlation between SFR and gender, stone density, proximal ureteral diameter, renal parenchymal thickness, and transverse pelvic diameter as was shown by Georgescu *et al.*^[2] who also found that variables such as gender of patient, transverse pelvic diameter, anomalies of the kidney and ureter did not correlate with SFR. Higher SFR was associated with stones lesser than 7.54 mm in size. Yu *et al.*^[11] also found increased rate of auxiliary procedures for stones which were impacted and larger in dimension. Fong *et al.*^[12] also reported significantly higher rate of secondary procedures with increasing stone size (>5 mm). In our study also, stone size was found to be significantly associated with SFR on univariate analysis but on multivariable analysis. MUWT was the sole predictor of SFR. Perez Castro *et al.*^[13] studied the stone clearance rate which was maximum in case of distally located stones (94%) and least in proximally located stones (84%). As already mentioned, 90% of patients with residual stones had ureteral wall thickness more than 4.8 mm. Sarica *et al.*^[3] also found, on multivariate analysis, a significant association of ureteral wall thickness with SFR in patients undergoing SWL for ureteral calculus disease.

Similarly, auxiliary procedure rate was also higher in patients with MUWT >4.8 mm. These findings were similar to study conducted by Kim *et al.*^[14] who found that ureteral wall thickness (tissue rim sign) is the sole preoperative predictor of the urologists' level of difficulty which, in turn, increases the duration of surgery. Many researchers have reported

that there is a higher incidence of complications and greater intraoperative difficulty in cases with larger stone size and impacted stone in proximal ureter.^[5,9,13] Impaction of a large stone leads to greater mucosal edema and inflammation which in turn increases the chance of causing ureteric injury or creating a false passage. All these factors lead to increased level of urologists difficulty, greater duration of surgery and more severe complications.

We feel that ureteral wall thickness which is determined by the amount of edema of the ureteral wall which in turn is determined by the size of the stone, severity of obstruction and duration of impaction, and presence of infection (positive culture) is, thus, a composite measure of the abovementioned adverse factors. This hypothesis is confirmed by our study where MUWT was an independent preoperative predictor of complications and the sole predictor of residual stones that may need auxiliary procedures.

CONCLUSION

Our study also shows MUWT at the site of ureteral stone impaction is a very important predictor of complications, SFR, and duration of surgery of URSL. When the MUWT is greater, especially if it is more than 4.8 mm, the surgeon should anticipate greater difficulty, longer operative time, more complications, and higher chance of residual stones that may need auxiliary procedure. Since NCCT-KUB is routinely being performed for diagnosis of ureteral calculi, radiologists should always comment on MUWT and the operating urologist should use this knowledge to counsel the patient accordingly, regarding the chances of complications, residual calculi, and need for auxiliary procedures.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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