CT-Based Predictors of Spontaneous Ureteral Stone Passage

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ABSTRACT

Objective: To assess CT-scan based parameters, particularly ureteral wall thickness (UWT), in predicting spontaneous ureteral stone passage.

Study Design: Cross-sectional, analytical study.

Place and Duration of the Study: Section of Urology, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan, from June to November 2023.

Methodology: Patients with symptomatic, single, radio-opaque, unilateral ureteral stones having size ≤10 mm with normal kidney functions, diagnosed by non-contrast CT-scan KUB, and treated by conservative option for four weeks were enrolled. Clinical and radiological predictors for stone passage (SP), including stone size, area, laterality, location, density, degree of hydronephrosis, maximal UWT at the stone site, and ureteral diameter and density above and below the stone, were evaluated. Binary logistic regression analysis was employed to identify predictors of stone passage. Receiver operating characteristic (ROC) curve was used to find the optimal cut-off for UWT.

Results: Among 34 eligible patients, 22 (64.7%) passed their stones spontaneously. Patients who passed had smaller stone size and area and lesser UWT. Stone location, laterality, degree of hydronephrosis, stone density, ureteral wall diameter, and density above and below stones were not associated with SP. Multivariate analysis revealed maximum UWT as the independent predictor of SP, with a cut-off of 1.95 mm and an accuracy of 0.94.

Conclusion: UWT was the single most convincing factor for the spontaneous passage of ureteral stone in this study. By applying UWT's optimal cut-off value, it might be an extremely significant tool when taking decisions in daily practice.

Key Words: *Ureteral wall thickness, Medical expulsive therapy, Non-contrast computed tomography*.

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INTRODUCTION

Symptomatic calculus in ureter represents one of the most prevalent urological conditions. Depending on various factors, such as presentation and stone characteristics, treatment modalities including expectant treatment with medical expulsive therapy (MET) or intervention such as ureteroscopy are recommended. For a period of 4-6 weeks, patients with simple ureteral calculi that measure 10 mm or less should be recommended to undergo expectant management or MET, as per guidelines from the American Urological Association (AUA).[1]

The decision between MET / observation and intervention has been subjected to controversy due to conflicting evidence in the recent literature.[2]

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Nevertheless, there are studies supporting MET / observation for specific patients with proper counselling.[3,4] It is critical to identify people who are most likely to gain from conservative treatment or prompt action, such as those with ureteral stones who present to the emergency department repeatedly because of flank pain, repeated UTIs, and causing kidney damage.[2,5] Therefore, it is imperative to promptly identify significant factors that can accurately predict spontaneous stone passage (SP) to guide patient counselling and avoid unnecessary delays in treatment for patients unlikely to experience SP.[6]

Non-contrast CT (NCCT) is the first-line radiological investigation for patients presenting in the emergency department with ureteric pain. Various radiological features related to calculus, such as maximal length, density, and part of the ureter stone seen at first presentation, were investigated in the past to forecast spontaneous SP.[7] As CT replaces old modalities in diagnosis, its parameters have also gained popularity in the expectant management of ureteral calculus. Inflammation of the ureteral mucosa caused by ureteral stones results in oedema and ureteral wall hypertrophy, potentially leading to failed spontaneous SP and difficulties in stone management by ureteroscopy and shock wave lithotripsy, with increased complication rates.[8,9]

Recently, Kachroo *et al*. identified ureteral wall thickness (UWT) as an important marker for spontaneous SP, with a cut-off point of 2.3 mm.[10] The current study was motivated by the paucity of data on the relationship between UWT and the spontaneous passage of ureteric stones. Its primary objective was to determine the significance of UWT and its cut-off value in predicting spontaneous calculus passage, while its secondary goal is to investigate other NCCT characteristics.

METHODOLOGY

This study was conducted at the Section of Urology, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan, from June to November 2023. The protocol was approved by the Institutional Ethical Review Committee (ERC# 2023-8773-24966). The sample size was determined using OpenEpi software 3.01 installed. A minimum sample size of 34 patients with unilateral, simple ureteral stones and 10% inflation was calculated. The predicted mean CT parameter for ureteral stones was 1.8 ± 0.09 for Group 1 (spontaneous stone passage) and 1.9 ± 0.10 for Group 2 (failed stone passage) with a level of significance of 5%, and a power of 80%, and a confidence interval of 95%.[10]

All adult patients (>18 years) presenting to the emergency department or outpatient clinic during the study period at the study centre with symptomatic radio-opaque unilateral ureteral stones <10 mm in longest dimension, diagnosed on non-contrast CT (NCCT), and advised conservative management with medical expulsive therapy using an alpha-blocker (Tamsulosin 0.4 mg at bedtime) and analgesics (NSAID or opioid-based), were prospectively enrolled. Patients underwent thorough evaluation by the principal investigator or co-investigator by taking proper history, general and focal examination, laboratory tests including serum creatinine, urine detail report or dipsticks, and if needed urine culture, and NCCT. Patients were instructed on their first visit to filter their urine to check for the passage of stones and catch it for future analysis.

Patients with multiple or bilateral stones, congenital urinary anomalies, known ureteral strictures, those requiring immediate admission due to persistent pain, sepsis, or urgent intervention (such as stenting or nephrostomy tube placement), those with urinalysis indicating infection, baseline renal impairment (cut-off of serum creatinine was different for males and females and it was >1.3mg/dl and >1.2mg/dl, respectively), those with NCCT from outside the study centre, history of previous intervention for the same stone, allergy / contraindication to Tamsulosin, or those who did not visit for follow-up were excluded.

All CT scans were carried out using one of the two 64-MDCT scanners, both of the same model, used for non-contrast CT scans. The volume dataset of all scans were acquired at 1 mm slice collimation, and the isotropic data were reviewed after multiplanar reformation at 1 mm axial, coronal, and sagittal sections to improve detection and characterisation of urinary calculi.[11] In the latest CT machines, slice collimation remains largely fixed, leaving radiation dose as the primary concern. With an increase in the number of detectors, beam geometry is enhanced. Therefore, the collimation options in 64-MDCT scanners do not affect radiation dose.[12] A computer-based operating system was used to calculate the results of parameters when needed. An experienced radiologist (with >10 years experience), blinded to clinical decision-making and outcomes, recorded radiological parameters from the CT scans. Stone-related factors including stone position, size, and density were documented. Density was calculated by Hounsfield units (HU) at three different locations, and the average was added in the results. Stone size was also calculated at two different angles, i.e. at the point of maximum length and at a 90-degree angle to it.

UWT was calculated by using a measuring scale at the point of greatest soft tissue thickness from inside to outside, involving the ureteral wall as well as oedema around it along its entire length.[13] Magnification of 5X was used on CT scan with standard settings (Figure 1).

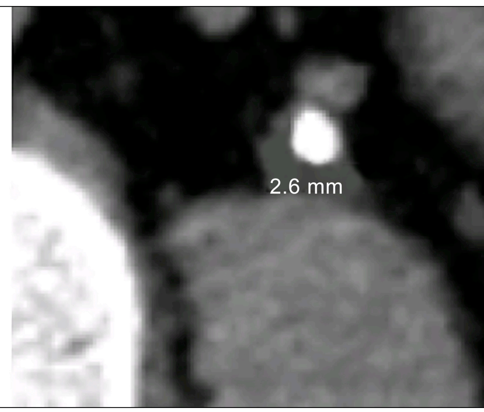

Figure 1: NCCT for ureteral stone showing maximal UWT on axial section.

Ureteral density and diameter, both above and below the stone, were assessed. Each stone's location was documented, allowing classification into upper, mid, or lower ureter stones based on their respective positions. Stones which were seen above the upper border of the sacroiliac (SI) joint were considered as upper ureter calculus, those anterior were classified as mid-ureteral calculus, and those positioned below were designated as lower ureter calculus. Hydronephrosis severity was also recorded, if present. Mild hydronephrosis was characterised by renal pelvis dilatation without calyceal dilatation. Moderate hydronephrosis included renal pelvis and calyceal dilatation, fornix blunting, and papillary flattening, while severe hydronephrosis was defined by gross renal pelvis and calyceal dilatation and loss of borders between them.[14]

Patients were followed up for 4 weeks to monitor spontaneous SP or absence thereof. Only patients with confirmed spontaneous passage (physical stone retrieval) or those with follow-up imaging, and subsequent intervention were included in the final analysis.

Patients' demographic data and radiological indicators associated with stones were noted and contrasted between two groups: Those who passed calculus and those who did not.

Using SPSS v.21, data were entered and examined. Normality of variables was assessed using Shapiro-Wilk's test. For continuous variables (such as stone size, density, and ureteral wall thickness), descriptive statistics were presented as mean ± SD / median (IQR) and subjected to the Mann-Whitney test analysis. Gender, laterality, and stone position were examples of categorical variables. These were analysed using Chi-squared analysis and presented as frequencies and percentages.

In order to find determinants of successful stone passage, binary logistic regression was used for both univariate and multivariate analyses. The area under the receiver operating characteristic (ROC) curve was used to calculate area under curve (AUC) to identify the ideal cut-off point for UWT for predicting spontaneous SP, and to calculate the sensitivity and specificity for the cut-off value. Every test was conducted in duplicate, with a significance threshold of $p < 0.05$.

RESULTS

During the study period, 104 patients presented with ureteric colic, of whom 34 patients met the study inclusion criteria and were consequently included in the final analysis. The remaining 70 patients were excluded for various reasons; 20 were lost to follow-up, 12 had impaired renal function, 14 had undergone imaging outside the institution, nine had having bilateral or multiple stones, and 15 had undergone emergency procedures [ureteroscopy (11 patients) and percutaneous nephrostomy (4 patients)]. Patient-related characteristics, NCCT findings, and stone expulsion rates are summarised in Table I.

Table I: Patients' characteristics, SP *vs.* failed group.

	SP Group (n = 22)	Failed Group (n = 12)	p-value[3]	Total sample
Age (years)[1]	38.5 (17.5)	38.5 (29.5)	p = 0.51	38.5 (16.75)
Gender[2]	14 (41.2%)	10 (29.4%)	p = 0.22	70.6%
Male	08 (23.5%)	02 (5.8%)		29.4%
Female				
BMI (kg/m^2)[1]	25.84 (2.95)	27.38 (10.7)	p = 0.52	26.18 (3.94)
Serum creatinine[1]	1.0 (0.22)	1.1 (0.27)	p = 0.17	1.05 (0.30)
Stone location[2]	06 (17.6%)	07 (20.6%)	p = 0.18	38.2%
Proximal	01 (2.9%)	00		2.9%
Mid	15 (44.1%)	05 (14.7%)		58.8%
Distal				
Laterality	12 (35.3%)	08 (23.5%)	p = 0.49	58.8%
Right	10 (29.4%)	04 (11.8%)		41.2%
Left				
Hydronephrosis	01 (2.9%)	00	p = 0.69	2.9%
None	20 (58.8%)	11 (32.4%)		91.2%
Mild	01 (2.9%)	01 (2.9%)		5.8%
Moderate	00	00		0.0
Severe				
Maximum stone size (mm)[1]	3.7 (1.58)	6.9 (4.13)	p = 0.002	4.05 (3.85)
Stone area (mm^2)[1]	10.2 (8.13)	31.01 (28.64)	p = 0.01	12.02 (24.4)
Stone density (HU)[1]	359 (351)	531 (475)	p = 0.21	425.5 (401.25)
Maximal ureteral Wall thickness[1]	1.0 (0.77)	2.3 (0.58)	p = 0.0001	1.5 (1.0)
Ureteral density above stone[1]	18.5 (14.88)	15 (21.15)	p = 0.30	17.5 (18.0)
Ureteral density below stone[1]	21 (26.8)	21 (7.0)	p = 0.65	21 (22.28)
Ureteral density ratio[1]	0.66 (0.34)	0.68 (0.66)	p = 0.92	0.66 (0.45)
Ureteral diameter above stone[1]	6.2 (2.83)	6.9 (3.9)	p = 0.30	6.4 (3.23)
Ureteral diameter below stone[1]	3.7 (1.1)	3.4 (2.8)	p = 0.77	3.7 (1.75)
Ureteral diameter ratio[1]	1.75 (0.81)	1.97 (0.84)	p = 0.16	1.75 (0.74)

[1] Values expressed as median (IQR). [2] Values expressed as number of patients (% of total sample). [3] p-value calculated using Chi-squared test for categorical variables (gender, laterality, location, and hydronephrosis) and Mann-Whitney test for continuous variables (stone size, area, density, UWT, and diameter).

Table II: Univariate and multivariate analysis of variables in spontaneous SP group.

Variable	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age (years)	0.973 (0.925 - 1.023)	0.28		
Gender	2.857 (0.497 - 16.427)	0.24		
BMI, Kg/m^2	0.884 (0.733 - 1.07)	0.19		
Serum creatinine	0.027 (0.000 - 4.679)	0.17		
Stone location	3.50 (0.791 - 15.5)	0.10		
Stone density	0.998 (0.996 - 1.001)	0.22		
Stone size	0.590 (0.397 - 0.875)	0.009	2.087 (0.197 - 22.128)	0.54
Stone area	0.911 (0.853 - 0.072)	0.005	0.816 (0.553 - 1.204)	0.31
Maximum ureteral Wall thickness	0.011 (0.0001 - 0.249)	0.005	0.013 (0.0001 - 0.507)	0.02
Ureteral density ratio	1.320 (0.653 - 2.670)	0.44		
Ureteral diameter ratio	0.398 (0.114 - 1.389)	0.15		

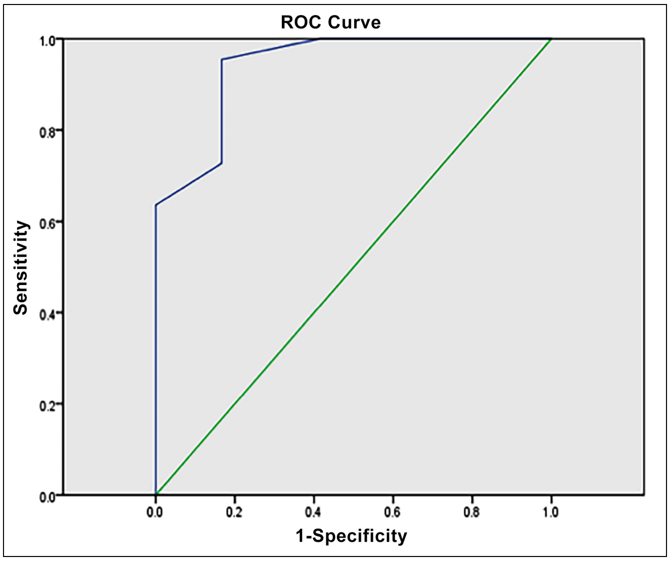

Figure 2: ROC for maximal ureteral wall thickness with AUC = 0.94, with sensitivity of 95.5%, and specificity of 83%.

The mean age of the study population was 42 ± 14.3 years with 59% stones seen below the lower border of the SI joint i.e., lower ureter. Not a single patient in the study population presented or categorised in the severe hydronephrosis group. Among the included patients, 22 (64.7%) passed the stone spontaneously, while 12 (35.3%) patients failed to pass the stone within the stipulated 4 weeks. SP was confirmed through physical collection in 22 (64.7%) patients, radiological imaging in 4 (11.7%) patients, while 8 (23.5%) patients required ureteroscopy.

Patient-related factors such as age (p = 0.51), gender (p = 0.22), and BMI (p = 0.52) were not found to be predictors of spontaneous SP. Among stone-related factors, stone size (p = 0.002) and stone area (p = 0.01) were significant predictors of stone passage, whereas stone laterality (p = 0.49), stone density (p = 0.21), stone location (p = 0.12), and degree of hydronephrosis (p = 0.69) were not significant predictors. Among the CT-based stone impaction-related factors, only UWT showed statistical significance (p <0.001), with non-stone passers exhibiting approximately twice the maximal UWT compared to those with spontaneous SP.

In the univariate analysis, conducted using binary logistic regression, stones were more inclined to pass spontaneously in cases with smaller size [odds ratio (OR) = 0.973 (95% confidence interval: 0.925-1.023), p = 0.009], reduced stone area [OR = 0.911 (95% CI: 0.853-0.972), p = 0.005], and lesser maximal UWT at the stone site [OR = 0.011 (95% CI: 0.0001-0.249), p = 0.005]. However, upon conducting multivariate analysis, maximal UWT emerged as the sole significant predictor of successful SP [OR = 0.013 (95% CI: 0.001-0.507), p = 0.02]. These findings are presented in Table II.

The ROC analysis showed results which were favourable with maximal UWT having high accuracy in predicting SP [(AUC) = 0.94, p <0.001, Figure 2]. The optimal cut-off value for maximal UWT was calculated to be 1.95mm, with a sensitivity of 95% and specificity of 83% for predicting SP. Applying this cut-off value to this study population, it accurately predicted SP in 91% of patients (31 patients), while incorrectly predicting SP in 2 patients (UWT <1.95mm) who ultimately failed to pass the stone, and one patient who predicted to fail SP but actually passed the stone spontaneously.

DISCUSSION

Symptomatic ureteral stones pose a significant healthcare burden,[15] with conservative management being the primary treatment recommendation as it is cost-effective and has less complications, allowing patients to avoid surgery and pass calculus naturally.[1] Accurately predicting successful spontaneous SP with conservative management can alleviate this burden and prevent unnecessary delays in intervention when required. Various trials have been conducted in the past to identify the factors of spontaneous passage of ureteral and renal calculus.

Anatomical studies have indicated an average cross-sectional ureteral wall thickness of around 1 mm.[16] Ureteral stones can alter local ureteral anatomy, leading to inflammatory changes that cause epithelial hypertrophy, polyp formation, and extensive ureteral / periureteral oedema, resulting in stone impaction.[17]

Traditionally, larger stone size and density were believed to be associated with stone impaction; however, even smaller stones can become impacted. Impacted stones are not only challenging to pass spontaneously but are also linked with increased rates of complications during surgery as well as with limited results.[18]

UWT measurement on NCCT scans can serve as a non-invasive substitute indicator for the possibility of impaction of stone.[13] This study analysed CT-based stone factors and impaction markers for predicting SP, with a successful SP rate of 64.7%. When compared between both groups (spontaneous SP *vs*. failed group), it was found that among stone-related factors, calculus size, calculus area, and UWT (as impaction markers) were significant factors of spontaneous passage, consistent with the results of Kachroo *et al*.[10] However, unlike Kachroo *et al.*, stone location, stone density, ureteral density above the stone, ureteral density ratio, and ureteral diameter above the stone were insignificant predictors of spontaneous SP. While they did not conduct a multivariate analysis or evaluate any cut-off value, Sahin *et al*. evaluated CT-based parameters for predicting SP of ureteral stones in 129 patients and discovered that stone size, proximal ureteric diameter, and UWT were significantly associated with successful spontaneous SP.[5]

Although the mean UWT in the study population was 1.54 mm, it was notably higher (2.21 mm) in non-passers compared to

1.18 mm in patients with spontaneous passage. Multivariate analysis in this study showed UWT to be the single independent significant predictor of SP, consistent with Kachroo *et al*.[10] The cut-off for UWT set in this study (1.95 mm) was comparatively lower than that set by Kachroo *et al.*, which was 2.3 mm. UWT is a non-invasive measure conducted on preoperative CT scans to predict stone impaction and, consequently, the outcome. In a meta-analysis of 14 studies with nearly 3,000 patients, Dean *et al*. found that thinner UWT has favourable outcomes in all parameters of stone management, including spontaneous passage of stone, good fragmentation with ESWL and ureterorenoscopy (URS), with less complication rate. On URS, it also helps in successful guidewire and ureteral stent placement.[19]

Sarica *et al*. determined a cut-off of 3.55 mm on NCCT with a predictive accuracy of 0.924 and identified the essential predictive function of UWT in the success rate of SWL for treating impacted ureteral stones.[9] Yoshida *et al*. reported UWT as the single important factor in the impaction of calculus, surgical outcomes, and complications during ureteroscopy, with a cut-off value of 3.49 mm.[13] Another previously published study found a cut-off value of 3.5 mm for impacted stones observed during ureteroscopy.[20]

The cut-off value (1.95 mm) in this study exhibited high sensitivity (93%) and specificity (83%) and correctly predicted SP in 91% of patients. Other studies based on retrospective analysis utilised non-uniform treatment approaches.[19] This study has a prospective design, and the patients received uniform treatment in the form of Tamsulosin 0.4 mg.

There is diversity in the NCCT protocols for examining outcomes associated with UWT, and this wide range may result in different results or cut-off levels in different studies. This study used 1 mm thickness cuts of CT scans, which ensures more accurate measurements as employed fixed (5X) magnification to facilitate accurate ureteral borders identification and magnification can increase the chances of considering artefacts as significant and this may affect the results.[8]

The limitation of this study is its relatively underpowered nature due to the small patient population as it was performed only in the authors' low-volume centre. Another limitation is that these measurements were performed manually, and person-to-person ability at different times so one person's ability may vary at different times. A software-based measurement may nullify this bias and produce consistency in measurement. Chandhoke *et al*. have proposed a novel surrogate measure peri-calculus ureteric thickness (P-CUT) for a 3D representation which may decrease the method that the authors used and many other contemporary studies also used.[21] Yamashita *et al*. have used a semi-automated software (Aquaris Intuition Viewer) to introduce the maximal ureteric area and ureteral volume as UWT surrogates.[22]

The authors recommend multicentred studies with large prospective cohorts using automated analytical measurement of UWT for external validation of this study's findings. This may lead to the development of a nomogram, which in future could precisely predict the percentage chances of spontaneous SP in a patient based on UWT.

CONCLUSION

Alongside various clinical and radiological indicators, maximal UWT stands out as a notable predictor of ureteral SP. Utilising the optimal cut-off value of UWT, the future clinical decision will be very easy regarding the choice between conservative management (MET) and intervention for non-complicated unilateral ureteral stones.

ETHICAL APPROVAL:
This study was conducted after obtaining approval from the Institutional Ethical Review Committee of the Aga Khan University Hospital, Karachi, Pakistan (ERC # 2023-8773-24966).

PATIENTS' CONSENT:
Not applicable since all the data was obtained from patient's medical records and no interaction with the patients was involved, so consent was exempted by the Ethical Review Committee.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
RUK, SMN: Concept of the study, design, data analysis, data interpretation, and revision for important intellectual content.
SA: Concept of the study, design, data analysis, and data interpretation.
All authors approved the final version of the manuscript to be published.

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