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ORIGINAL PAPER

CT-related parameters and Framingham score as predictors of spontaneous passage of ureteral stones ≤ 10 mm: results from a prospective, observational, multicenter study

Ismail Selvi[1,5] · Numan Baydilli[2] · Turgut Tursem Tokmak[3] · Emre Can Akinsal[2] · Halil Basar[4]

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Abstract

To investigate the reliability of newly defined CT-related parameters and cardiovascular risk factors in groups adjusted for stone size and location to predict spontaneous stone passage (SP) of uncomplicated ureteral stones ≤ 10 mm. The data of 280 adult patients with solitary unilateral ureteral stones ≤ 10 mm in diameter in non-contrast computed tomography were prospectively recorded. All patients undergoing a four-week observation protocol with medical expulsive therapy using tamsulosin were divided into two groups according to SP or no SP. Demographic, clinical and radiological findings of these groups were recorded. Spontaneous stone passage was observed in 176 (62.9%) of the patients, whereas the SP rate was 57.6% for 118 upper ureteral stones and 66.7% for 162 lower ureteral stones. The SP rate was 13.3 times greater with ureteral wall thickness < 1.88 mm, 4.4 times greater with a ratio of ureter to stone diameter of < 1.24, 3.4 times greater with Framingham score of < 11.5%, 2 times greater with neutrophil lymphocyte ratio < 1.96, 1.9 times greater with ureteral diameter < 6.33 mm and 1.5 times greater with stone volume < 38.54 mm^3. Lower levels of ureteral wall thickness, ratio of ureter to stone diameter, Framingham score, neutrophil lymphocyte ratio, ureteral diameter, stone volume and absence of hydronephrosis were found to be more successful predictors. We consider that the success rate can be increased by selection of the proper option (observation or active treatment) according to these predictors.

Keywords Framingham risk score · Neutrophil lymphocyte ratio · Spontaneous stone passage · Ureteral diameter · Ureteral stone · Ureteral wall thickness

Introduction

Urolithiasis is a common health problem. The rates are 1–5% in Asia, 5–9% in Europe and 13% in the United States, whereas it is seen on average in 10–15% of the whole world population [1]. Ureteral stones consist of 20% of all urinary tract stones [1]. Because there is a possibility for spontaneous stone passage (SP) for uncomplicated ureteral stones ≤ 10 mm, the first reasonable approach is observation with or without medical expulsive therapy (MET) for 4–6 weeks [1, 2]. The basis of MET with alpha blockers or calcium channel blockers is to increase the SP rate, reduce the time to expulsion and improve the quality of life by reducing colic pain. It has been emphasized by the European Association of Urology guidelines that the greatest benefit of α-blockers for MET may be for patients with > 5 mm distal ureteral stones [2]. Extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy (URS) are active interventions

✉ Ismail Selvi
ismselvi33@hotmail.com

1 Department of Urology, Karabük University Training and Research Hospital, Karabük, Turkey

2 Department of Urology, Erciyes University Medical School, Kayseri, Turkey

3 Department of Radiology, Kayseri City Training and Research Hospital, Kayseri, Turkey

4 Department of Urology, Health Science University Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara, Turkey

5 Present Address: Department of Urology, Başakşehir Çam ve Sakura City Hospital, Istanbul 34480, Turkey

that can be performed in case of complicated ureteral stones or stones that are not expected to pass [3].

The main risk with observation is failure in SP. This failure may result in unbearable colic pain, urosepsis, impaired renal function or deterioration in quality of life because of the obstructing stone. The potential risks in active intervention are upper urinary tract infections, ureteral injury and complications due to anesthesia [4]. However, it is not easy to predict the proper initial management of ureteral stones. Although guidelines recommend observation or medical expulsive therapy (MET) for 4–6 weeks for patients with uncomplicated distal ureteral stones > 5 mm, sometimes individualized treatment may need to be chosen on a patient basis [2]. Although stone size and location are widely used traditional parameters for predicting SP, some newly defined CT-related parameters such as ureteral wall thickness (UWT), ureteral diameter (UD) and the ratio of ureter to stone diameter (USD) have been investigated in the last few years [1, 5, 6]. These findings have revealed that there is still a need to investigate more reliable predictors that accurately estimate the possibility of SP or stone-related complications.

A relationship between metabolic syndrome components, urolithiasis and ureteral peristalsis has been reported [3, 7]. The components of the Framingham score, a scale that predicts cardiovascular risk, also constitute the metabolic syndrome [8]. In the present study, we aimed to investigate the reliability and clinical significance of CT-related parameters and Framingham score in predicting SP of uncomplicated ureteral stones ≤ 10 mm when adjusted for stone size and localization.

Materials and methods

This prospective, observational, multicenter study was designed after approval of the local ethics committee (protocol number 77192459–050.99-E.10736, 6/13) and obtaining written informed patient consent. Between October 2019 and March 2020, 301 adult patients (> 18 years) who presented following the first episode of renal colic and those with solitary unilateral ureteral stones ≤ 10 mm in diameter in non-contrast computed tomography (CT) were included in the study. The exclusion criteria are listed below:

- Patients with anamnesis of congenital genitourinary tract anomaly, solitary kidney
- Patients with a history of urethral or ureteral stenosis and anastomotic urinary tract surgery were excluded because of the idea that SP could be hindered
- Patients with multiple ureteral stones, renal stones, > 10 mm ureteral stones
- Patients who initially needed emergency intervention due to severe urinary tract infection or acute renal failure or grade 3 (severe) hydronephrosis
- Patients with fever ≥ 38 °C, acute urinary tract infection, active infection of other origin, hematological disease, malignancy, inflammatory disease, liver failure and those taking medications such as contraceptives and glucocorticoids were excluded since these conditions can potentially affect complete blood count levels during the measurement of neutrophil lymphocyte ratio (NLR)
- Patients who refused to participate in the study

A total of 280 patients with complete data were included in our study. All patients were selected from the same sociocultural background, ethnic region and those sharing a similar lifestyle to reduce any substantial bias. Figure 1 shows the flowchart of our study.

The data of age, gender, body mass index (BMI) and history of urinary stones were recorded. Hydronephrosis (HN) grade on CT was noted according to the HN grading classification commonly used in CT [9]. The presence of stone-related complications such as persistent colic, febrile urinary infection and deterioration in renal function were recorded during observation.

Radiological evaluation

All CT examinations were performed with a non-contrast enhanced stone protocol (Kv: 120, mAs: automatic, slice thickness: 1 mm) (Siemens Somatom Definition, Siemens Healtcare, Forchheim, Germany). Sagittal and coronal reformatted images and volume rendering images were obtained. Maximum anterior–posterior, tranverse and longitudinal lengths of ureter stones were measured using axial, sagittal and coronal CT images. Stone volumes were measured automatically on volume rendering images with the GE Centricity PACS program (GE Healthcare, UK). Stone densities were measured with the freehand option at the largest level of the stone on axial images [10] (Fig. 2).

Stone side (right/left), stone location (upper/lower), transverse stone diameter (TSD), longitudinal stone diameter (LSD), sagittal stone diameter, HN grade, stone density [(Hounsfield unit (HU)] and stone volume (mm^3) were recorded. Upper and lower ureteral localization was defined as above or below the iliac vessels.

Ureteral diameter was measured on three CT slices (3 mm) proximal to the stone on axial CT. The ratio of ureter to stone diameter was measured as UD divided by TSD [8]. Ureteral wall thickness was measured as the point of greatest soft-tissue thickness around the stone. This distance consisted of ureteral wall ± peri-ureteral edema [1]. All these CT-related parameters were measured by the same experienced radiologist.

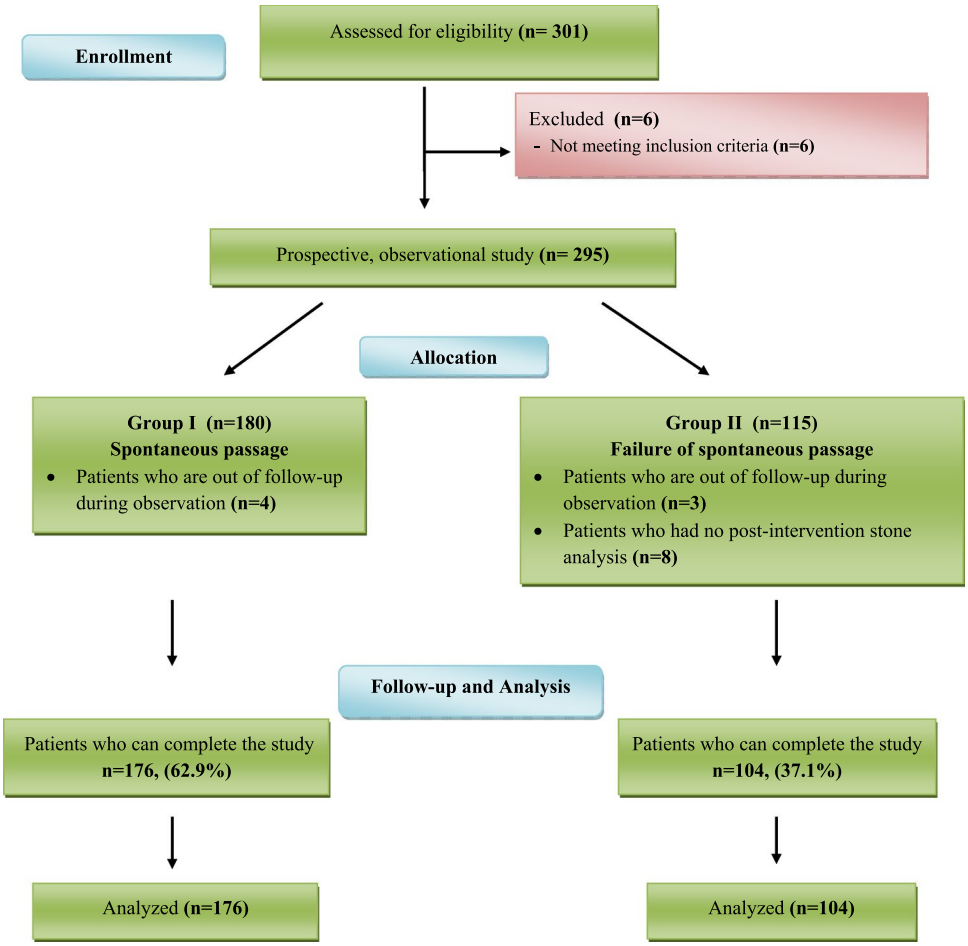

Fig. 1 Flowchart of the study design

Framingham risk score

This score predicts the 10 year risk of cardiovascular disease development [8]. The parameters used in the risk score include age, gender, BMI, systolic blood pressure, total cholesterol, high density lipoprotein levels, presence of smoking and diabetes mellitus (DM). Scoring is performed for each parameter and the total score is calculated. According to the scores, patients were divided into three risk groups: low risk (< 10%), intermediate risk (10–19%) and high risk (≥ 20%) [8]. All parameters mentioned above were measured at the time of presentation. After the Framingham score was calculated, all patients were classified according to this risk score.

Observation protocol

After a detailed medical history and physical examination, urinary ultrasonography or kidney–ureter–bladder radiographs (KUB) were generally used as the primary diagnostic imaging tools. CT was initially performed only for patients who were very likely to have suspected ureteral stones due to physical examination findings and presence of stone history. Subsequently, CT was performed for all patients with higher probability of having ureteral stones after KUB or ultrasonography to determine suitable patients to include the study. Patients with unilateral ureteral stones ≤ 10 mm diameter were included in the observation protocol. Within the scope of the MET protocol, all patients received a daily dose of 0.4 mg tamsulosin and a maximum dose of diclofenac sodium 150 mg/day. Abundant hydration (drinking at least two liters of water daily) was recommended to all patients. They were re-evaluated weekly during a 4 week follow-up. A control CT was performed for patients who had SP during this period. Stone and HN status were evaluated by weekly ultrasonography for patients who did not have SP. If stone-related complications occurred or the patients did not pass their stones within 4 weeks, a control CT was performed for final evaluation and active interventions (URS or ESWL) were recommended.

In our study, patients were divided into two groups according to whether SP was observed (Group I) or not observed (Group II). SP was observed in 176 (62.9%) patients (Group I). Group II consisted of 104 (37.1%) patients who had failure in SP. Patients with sufficient stone fragment for post-intervention stone analysis were included in Group II. Analysis of stone composition by infrared

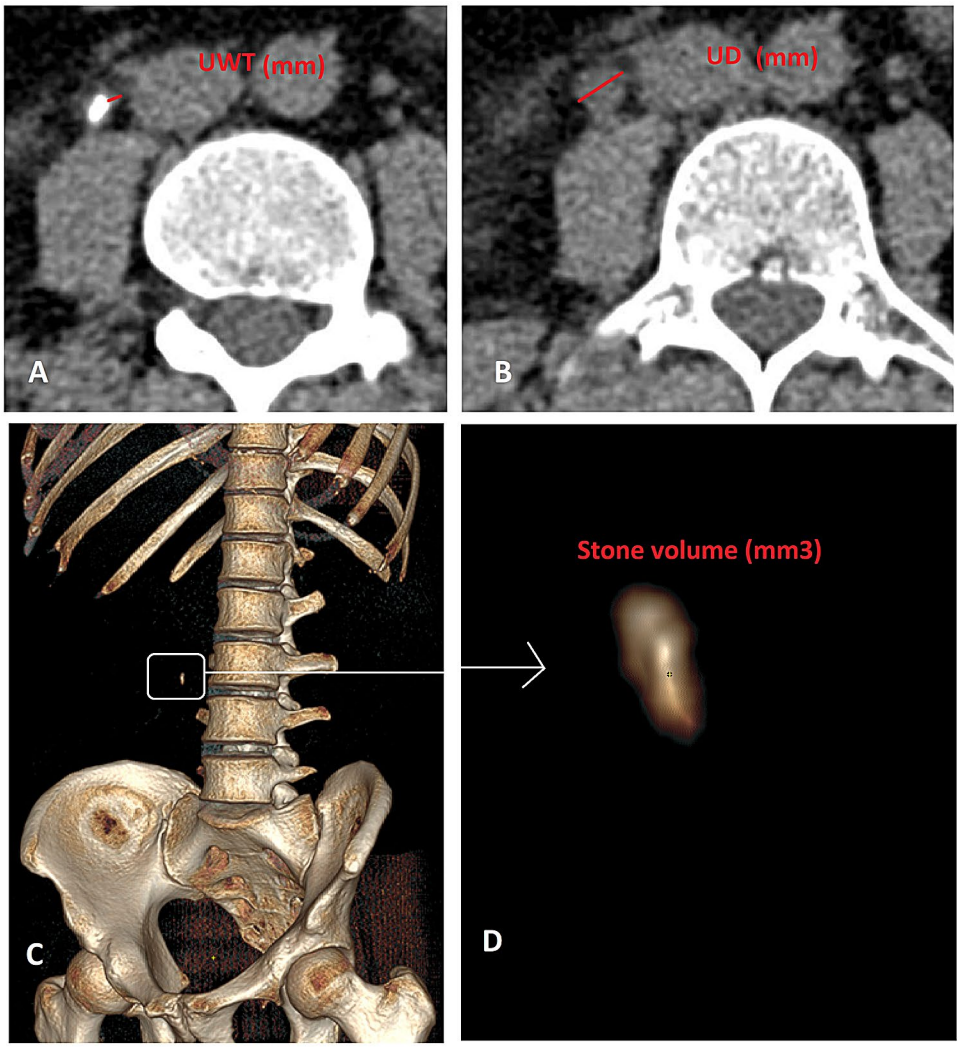

Fig. 2 Measurement of non-contrast computed tomography related stone parameters. **a** Ureteral wall thickness (UWT) measurement on the axial CT image. **b** Ureteral diameter (UD) measurement at the level of 3 mm proximal to the stone on the axial CT image. **c** The view of ureter stone on the three dimensional CT image. **d** Automatic measurement of stone volume with the GE Centricity PACS program (GE Healthcare, UK)

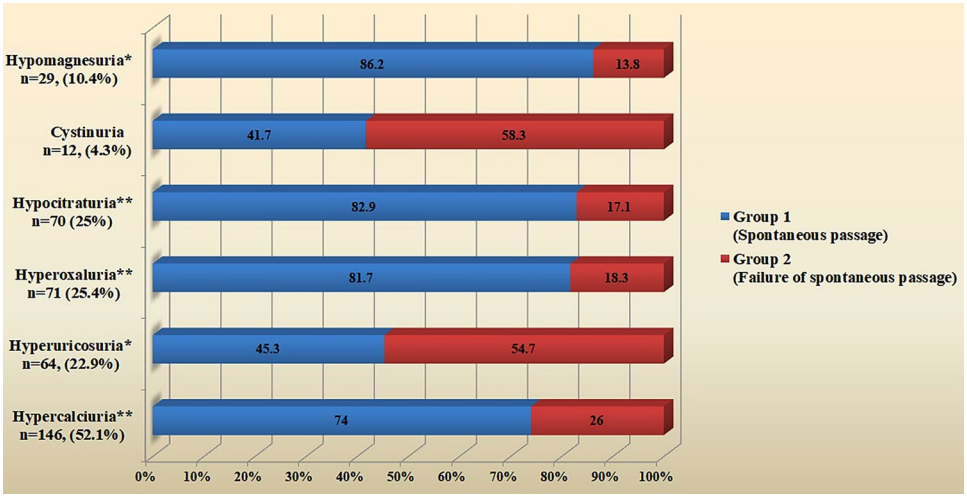

Fig. 3 Metabolic urine analysis of the patients according to the presence of spontaneous stone passage (* shows $p < 0.05$ and ** shows $p < 0.001$. Parameters on the *Y* axis show the distribution of metabolic abnormalities in all 280 patients. Each bar gives the percentage of metabolic abnormalities seen in the two groups).

spectroscopy was performed in both groups. Metabolic urine analysis was also performed for all patients after being stone-free [11] (Fig. 3).

Statistical analysis

G*Power (G*Power Ver. 3.0.10, Franz Faul, University Kiel, Germany, https://www.psycho.uni-duesseldorf.de/aap/projects/gpower) package program was used for determining sample size. The sample size was calculated as at least 100 individuals in each group to obtain a test power of 80.4%, confidence interval of 90% and Type I error (alpha) of 0.05.

The normality status was evaluated by Kolmogorov–Smirnov and Shapiro–Wilk tests to compare differences between two groups. Mann Whitney-*U* test was performed between two groups for non-normal distribution, while Kruskal–Wallis test was done for three non-normally distributed groups. Chi-square analysis was done to evaluate categorical variables. Spearman test was used for correlation analysis. Univariate and multivariate logistic regression analysis was used for defining predictor factors for SP. Receiver operating characteristic (ROC) curve analysis was performed to determine cut-off values for additional parameters. Analyses were performed using IBM SPSS Statistics 23 (IBM, Armonk, NY USA) software. $p < 0.05$ was considered statistically significant.

Results

Patient clinical data and stone characteristics are listed in Table 1. During four weeks of observation, SP was observed in 176 (62.9%) patients whereas 104 (37.1%) patients failed in SP. When the patients having SP were divided into two subgroups as TSD ≤ 5 mm and TSD > 5 mm, the median time to SP was 8 days (range 5–19) and 14 days (range 9–23), respectively ($p < 0.002$). In the subgroup analysis in terms of lower and upper stones, the median time to SP was 9 days (7–13) and 12 days (9–14), respectively ($p = 0.002$). In the follow-up of 280 patients, 6 (2.1%) had febrile urinary tract infection, 41 (14.6%) had persistent renal colic and 12 (4.2%) had impaired renal function tests or an increase in hydronephrosis. Active treatment was decided in these patients without completing the 4 weeks of observation.

Significantly lower values of BMI, sagittal stone diameter, stone volume, UD, USD, UWT, systolic blood pressure, total cholesterol, Framingham score, NLR, and lower rates of HN grade and DM, and higher values of HDL were seen in patients with SP (Table 1). In the subgroup analysis done according to stone localization, outcomes were consistent with the findings mentioned above, except for BMI levels with upper stones (Table 2). According to multivariate analysis and ROC analysis, the SP rate was 13.3 times greater with UWT < 1.88 mm, 4.4 times greater with USD < 1.24, 3.4 times greater with Framingham score < 11.5%, 2 times greater with NLR < 1.96, 1.9 times greater with UD < 6.33 mm and 1.5 times greater with stone volume < 38.54 mm^3 (Tables 3, 4). The correlations between Framingham score and CT-related parameters are listed in Table 5. The differences between stone volume and Framingham score according to stone composition are shown in Table 6. Table 7 shows the relationship between duration until stone passage and predictive factors for spontaneous passage.

Discussion

The most well known factors to predict SP are stone size and ureteral stone location [4, 12–14]. In contrast, Sfoungaristos et al. [12] did not find stone location to be as a significant predictor as stone size. An underestimation rate of 13–20% for stone burden was shown in axial CT evaluation, so an accurate method of stone size measurement is still controversial [15]. Although TSD and LSD were found to be equal in predicting SP by Yoshida et al. [1], Lee et al. [5] showed LSD to be a better predictor. Longer LSD forms a wider contact surface between stone and the ureteral mucosa, so inflammation and ureteral mucosal edema can be seen at higher rates and the possibility of SP decreases. By adjusting TSD, LSD and stone localization between the two groups so that there was no significant difference, we actually tried to more clearly evaluate other predictive factors for SP. Similar to the findings of Zorba et al. [16], stone volume was found to be more significant than TSD and LSD in our study.

In the past few years, new CT parameters have been investigated in various studies. Among them, UWT, UD and USD were shown to be more reliable markers for predicting SP than stone size and location [1, 5, 6]. According to the hypothesis of Yoshida et al. [1], stone impaction triggers inflammation and causes mucosal ischemia, and ureteral and peri-ureteral edema. As a result, they used higher UWT levels as a predictor for stone impaction, failure in SP and stone-related complications. In their opinion, UWT and stone size had a significantly higher accuracy than stone location. UD and USD were defined as indicators for severe ureteral obstruction due to the stone. Since USD is a ratio in which UD is adjusted by ureteral stone size, there is a consideration that USD would better indicate ureteral obstruction than UD [15, 17]. However, there are controversial results indicating that UD and USD are not useful predictors [5, 18]. According to our findings, UWT and USD were more significant predictors than UD. Additionally, we did not observe the effect of stone density on SP, as indicated in various studies [6, 18].

Table 1 Demographic, clinical data and stone characteristics of all patients

Parameters	Group I spontaneous passage ($n=176$, 62.9%)	Group II failure of spontaneous passage ($n=104$, 37.1%)	p
Age (years)	45 (36–51)	44 (35–54)	†0.634
Gender (n, %)			
Male	89 (50.6)	63 (60.6)	‡0.104*
Female	87 (49.4)	41 (39.4)	
Body mass index (kg/m^2)	22.9 (22.1–24.6)	24.4 (22.3–26.9)	†0.002*
Longitudinal stone diameter (mm)	5 (4–6)	5 (4–7)	†0.084
Transverse stone diameter (mm)	5 (4–6)	5 (4–6)	†0.116
Sagittal stone diameter (mm)	3 (2–3)	3 (3–4)	† < 0.001*
Stone volume (mm^3)	37.75 (26.21–46.40)	53.74 (31.46–72.75)	† < 0.001*
Ureteral diameter (mm)	5.64 (5.01–6.87)	8.65 (6.58–9.42)	† < 0.001*
Ureter-to-stone diameter ratio	1.18 (1.04–1.33)	1.46 (1.23–1.83)	† < 0.001*
Ureteral wall thickness (mm)	1.36 (1.17–1.97)	2.78 (2.07–3.13)	† < 0.001*
Stone localization (n, %)			
Upper	68 (38.6)	50 (48.1)	‡0.122
Lower	108 (61.4)	54 (51.9)	
Stone side (n, %)			
Left	91 (51.7)	55 (52.9)	‡0.849
Right	85 (48.3)	49 (47.1)	
Hydronephrosis grade (n, %)			
No	124 (70.5)	53 (51.0)	‡ < 0.001*
Mild	32 (18.2)	21 (20.2)	
Moderate	20 (11.4)	30 (28.8)	
Presence of stone history (n, %)			
Presence	95 (54.0)	62 (59.6)	‡0.358
Absence	81 (46.0)	42 (40.4)	
Stone density (hounsfield unit)	1039 (879–1455)	1036 (634–1453)	†0.055
Smoking (n, %)			
Yes	100 (56.8)	64 (61.5)	‡0.438
No	76 (43.2)	40 (38.5)	
Diabetes mellitus (n, %)			
Yes	30 (17.0)	33 (31.7)	‡0.004*
No	146 (83.0)	71 (68.3)	
Total cholesterol (mg/dl)	163 (155–180)	170 (163–190)	† < 0.001*
High density lipoprotein cholesterol (mg/dl)	46 (40–52)	39 (36–46)	† < 0.001*
Systolic blood pressure (mmHg)	128 (120–135)	134 (126–144)	† < 0.001*
Framingham risk score (%)	8 (5–13)	17 (8–21)	† < 0.001*
Framingham risk group (n, %)			
Low	109 (61.9)	29 (27.9)	ᵇ < 0.001‡
Intermediate	56 (31.8)	34 (32.7)	
High	11 (6.3)	41 (39.4)	
Neutrophil/lymphocyte ratio (NLR)	1.59 (1.12–2.09)	2.29 (1.76–2.78)	† < 0.001*
Stone composition (n, %)			
Calcium oxalate	130 (73.9)	28 (26.9)	‡ < 0.001*
Calcium phosphate	30 (17.0)	20 (19.2)	
Uric acid	7 (4.0)	31 (29.8)	
Magnesium ammonium phosphate	8 (4.5)	19 (18.3)	
Cystine	1 (0.6)	6 (5.8)	

†*Mann–Whitney U test* data are shown as "median, (25th–75th percentile)"

‡*Chi-square test* data are shown as "number (percentage)"

*$p < 0.05$ asterisk (*) indicates statistical significance

Table 2 Demographic, clinical data and stone characteristics in the patients with upper and lower ureteral stones

Parameters	Upper ureteral stones			Lower ureteral stones		
	Spontaneous passage ($n=68$, 57.6%)	Failure of spontaneous passage ($n=50$, 42.4%)	p	Spontaneous passage ($n=108$, 66.7%)	Failure of spontaneous passage ($n=54$, 33.3%)	p
Age (years)	45 (36–49)	43 (33–54)	†0.426	45 (36–51)	45 (36–53)	†0.916
Body mass index (kg/m^2)	23.5 (22.4–24.6)	24.6 (22.7–26.9)	†0.100	22.6 (21.3–24.6)	23.7 (22.1–27.2)	†0. 010*
Longitudinal stone diameter (mm)	6 (4–7)	6 (5–7)	†0.388	5 (4–6)	5 (4–6)	†0.234
Transverse stone diameter (mm)	5 (4–6)	5 (4.75–6)	†0.077	5 (4–6)	5 (4–7)	†0.381
Stone depth (mm)	3 (2–3)	3 (3–4)	†< 0.001*	3 (2–3)	3 (3–4)	†< 0.001*
Stone volume (mm^3)	37.75 (28.31–47.19)	55.05 (31.46–76.03)	†< 0.001*	36.70 (25.17–44.04)	49.81 (31.46–67.12)	†< 0.001*
Ureteral diameter (mm)	5.64 (5.01–6.52)	8.84 (6.52–9.23)	†< 0.001*	5.65 (5.02–6.96)	8.64 (6.63–9.65)	†< 0.001*
Ureter-to-stone diameter ratio	1.20 (1.08–1.38)	1.56 (1.20–1.82)	†< 0.001*	1.13 (1.03–1.32)	1.43 (1.24–1.84)	†< 0.001*
Ureteral wall thickness (mm)	1.35 (1.18–1.97)	2.81 (2.12–3.08)	†< 0.001*	1.37 (1.16–1.91)	2.78 (2.02–3.16)	†< 0.001*
Hydronephrosis grade (n,%)						
No	49 (72.1)	26 (52.0)	‡< 0.030*	75 (69.4)	27 (50.0)	‡< 0.015*
Mild	12 (17.6)	10 (20.0)		20 (18.5)	11 (20.4)	
Moderate	7 (10.3)	14 (28.0)		13 (12.1)	16 (29.6)	
Framingham risk score (%)	7 (6–13)	17 (8–24)	†< 0.001*	8 (4–13)	17 (8–20)	†< 0.001*
Neutrophil/lymphocyte ratio	1.62 (1.08–2.08)	2.29 (1.85–2.78)	†< 0.001*	1.58 (1.12–2.09)	2.29 (1.58–2.79)	†< 0.001*
Stone composition (n, %)						
Calcium oxalate	51 (75.0)	11 (22.0)	‡< 0.001*	79 (73.2)	17 (31.4)	‡< 0.001*
Calcium phosphate	10 (14.7)	11 (22.0)		20 (18.5)	9 (16.7)	
Uric acid	3 (4.4)	16 (32.0)		4 (3.7)	15 (27.8)	
Magnesium ammonium phosphate	4 (5.9)	10 (20.0)		4 (3.7)	9 (16.7)	
Cystine	0 (0.0)	2 (4.0)		1 (0.9)	4 (7.4)	

†*Mann–Whitney U test* data are shown as "median, (25th–75th percentile)"

‡*Chi-square test* data are shown as "number (percentage)"

*$p < 0.05$ Asterisk (*) indicates statistical significance

Although HN grade is another known predictor for SP, there are contraversial views. Most studies found HN to be a negative predictor [6, 12], whereas it facilitates SP according to Ozcan et al. [19]. In the present study, HN grade was found to be a negative predictor of SP.

Obstruction and ureteral trauma due to an impacted stone may give rise to a systemic inflammatory response. Some studies found that significant increases in white blood cell (WBC) count, neutrophil count, NLR and C-reactive protein were associated with impacted stones and failure in SP [18–20]. In contrast, Sfoungaristos et al. [12] claimed that movable ureteral stones can produce a local inflammatory response due to minor trauma in the ureteral epithelium. Stones that are more likely to pass spontaneously stimulate WBC production. Differently, we observed that higher NLR levels were associated with failure in SP.

In current studies, the effects of metabolic syndrome, its components and predisposing factors such as smoking on the etiology of urolithiasis were specified [3, 21, 22]. Various metabolic disturbances can cause stone formation with different mechanisms. High levels of low density lipoprotein, glucose and insulin resistance may stimulate chronic inflammation and ureteral smooth muscle cell dysfunction through interfering with ureteral interstitial cells [3, 23, 24]. This may increase susceptibility to the development of stone formation and functional impairment of ureteral peristalsis may increase the possibility of failure in SP [7]. Kohjimoto et al. [7] observed that as the number of metabolic syndrome components increased, the incidence of recurrent and/or multiple

Table 3 Predictive factors for spontaneous ureteral stone passage

Spontaneous stone passage	Univariate model				Multivariate model			
	OR	95% CI		*p*	OR	95% CI		*p*
		Lower	Upper			Lower	Upper	
Age (years)	1.004	0.980	1.028	*0.726*				
Gender (female vs. male)	1.501	0.918	2.457	*0.105*				
Body mass index (kg/m^2)	1.144	1.049	1.247	*0.002**	1.012	1.000	1.023	*0.042**
Stone volume (mm^3)	2.170	1.918	3.118	*< 0.001**	1.553	1.025	1.882	*< 0.001**
Ureteral diameter (mm)	2.225	1.841	2.690	*< 0.001**	1.953	1.548	2.217	*< 0.001**
The ratio of ureter to stone diameter	7.813	5.630	21.586	*< 0.001**	4.452	3.591	7.357	*< 0.001**
Ureteral wall thickness (mm)	13.326	7.318	24.265	*< 0.001**	13.326	7.318	24.265	*< 0.001**
Stone localization (Lower vs. upper)	1.470	0.900	2.398	*0.123*				
Stone side (left vs. right)	1.048	0.645	1.703	*0.849*				
Presence of stone history	1.259	0.770	2.057	*0.359*				
Presence of hydronephrosis	1.825	1.334	2.496	*< 0.001**	1.504	1.391	2.605	*< 0.001**
Stone density (HU)	1.001	1.000	1.001	*0.065*				
Framingham score (%)	4.134	2.476	6.900	*< 0.001**	3.424	2.381	4.923	*< 0.001**
Neutrophil / lymphocyte ratio	3.696	2.443	5.592	*< 0.001**	2.022	1.077	3.169	*< 0.001**
Stone composition (non-calcium stones vs. calcium stones)	1.821	1.498	2.213	*< 0.001**	1.362	1.103	1.963	0.006*

HU Hounsfield unit

Logistic regression analysis

*$p < 0.05$ Asterisk (*) indicates statistical significance

Table 4 Cut-off values of additional parameters for predicting failure in spontaneous ureteral stone passage

	UD (mm)	USD	UWT (mm)	NLR	Framingham score (%)	Stone volume (mm^3)
Cut-off value	6.33	1.24	1.88	1.96	11.5	38.54
Sensitivity (%)	80.8	75.0	88.5	69.2	71.2	71.2
Specificity (%)	66.5	60.8	70.5	64.2	65.3	60.2
PPV (%)	70.7	65.7	75.0	65.9	67.2	64.1
NPV (%)	77.6	70.9	85.9	67.6	69.4	67.6
AUC	0.826	0.764	0.880	0.729	0.768	0.698
p	< 0.001*	< 0.001*	< 0.001*	0.030*	< 0.001*	0.001*

PPV positive predictive value, *NPV* negative predictive value, *AUC* Area under curve, *UD* ureteral diameter, *USD* the ratio of ureter to stone diameter, *UWT* ureteral wall thickness, *NLR* Neutrophil/lymphocyte ratio

*$p < 0.05$ Asterisk (*) indicates statistical significance

stones increased. A significant correlation was also observed between the number of metabolic syndrome components and the detection rate of hypercalciuria, hyperuricosuria, hyperoxaluria and hypocitraturia in other studies [7, 25]. Valente et al. [23] observed that the presence of metabolic syndrome increased the incidence of uric acid and struvite stones. Keller et al. [13] observed that calcium oxalate stones had lower stone diameters and volumes, whereas the highest values were observed with struvite stones. 90% of calcium oxalate monohydrate stones and 75% of calcium oxalate dihydrate stones were < 6 mm in size, and they form the majority of spontaneously passed stones [13]. The majority of cystine, struvite and uric acid stones were ≥ 6 mm and their SP ratios were very low. In accordance with Valente et al. [23], we found that the rate of uric acid and struvite stones was significantly higher in Group II. Hyperuricosuria was the most common abnormality in the metabolic urine analysis of this group.

Table 5 Correlations between Framingham score and other parameters

	UD	USD	UWT	Stone volume	NLR
Framingham score					
rho	0.437	0.225	0.528	0.559	0.195
p	*< 0.001**	*< 0.001**	*< 0.001**	*< 0.001**	*0.001**

UD ureteral diameter, *USD* the ratio of ureter to stone diameter, *UWT* ureteral wall thickness, *NLR* Neutrophil/lymphocyte ratio

Spearman correlation

*$p < 0.05$ Asterisk (*) indicates statistical significance

To our knowledge, this is the first study to demonstrate the clinical significance of the Framingham score for predicting SP. In addition, we have not found a study evaluating all three parameters of UWT, USD and UD in the same study design. We used an automated measurement system to provide a more accurate calculation for CT assessment. We think that this system strengthens our study compared to similar studies in the literature [1, 5, 6, 11]. In our study, we reached a conclusion parallel to the findings of Valente [23] and Keller [13]. The higher Framingham score, showing increased cardiovascular morbidity, indirectly indicates a higher rate of metabolic syndrome because of similar components. The higher Framingham scores were associated with a decreased probability of SP. With these higher values we observed more uric acid and struvite stones. We attributed the probability of a reduction in SP to the relatively larger size of these stone types. However, we cannot explain the effect of higher Framingham score on reducing SP rates only with the differences in stone composition and stone volume. If so, the odds ratio of the Framingham score would not be higher than stone composition and stone volume in our multivariate analysis. As stated in various studies, we think that some outcomes triggered by metabolic disturbances, such as chronic inflammation and functional impairment of ureteral peristalsis, may have played a role in these results as well [3, 7, 23]. We can also show a positive correlation between Framingham score and UWT, USD, UD, NLR as support to this inference.

However, we have some limitations. Our main limitation was the non-randomized design with a relatively small number of patients, although sample size was determined based on statistical power analysis. Secondly, although we determined ureteral stones via CT after the first episode of renal colic, there was also the possibility that the stone passed into the ureter in a previous period. This may have prevented us from evaluating the exact time of SP. In addition, we are aware that the analysis of many parameters related to Framingham score such as an extended chemistry panel and cardiological evaluation are not easy to evaluate in daily practice. They seem to be impractical for all patients with renal colic. Additionally, we hypothesized according to the above-mentioned studies and our findings that the Framingham score may be associated with non-calcium stones, which have higher stone volumes, and functional impairment of ureteral peristalsis. We tried to explain the predictive value of Framingham score on SP based on these mechanisms. On the other hand, we are aware of the need for experimental studies on interstitial cells and neuronal tissue in the ureter to further strengthen our hypothesis.

Conclusion

In our study, which consisted of ureteral stone patients who did not have any significant difference in terms of stone size and localization, we observed lower levels of UWT, USD, Framingham score, NLR, UD, stone volume and absence of HN to be more successful predictors of SP. We consider that radiologists providing information on these values using an automatic measurement system may help the urologist's approach to stone patients, in that the success rate of MET can be increased by appropriate patient selection according

Table 6 Differences between stone volume and Framingham risk score in terms of stone composition

	Calcium oxalate (*n*:185)	Calcium phosphate (*n*:31)	Uric acid (*n*:38)	Magnesium ammonium phosphate (*n*:27)	Cystine (*n*:7)	*p* value
Stone volume	36.72 (25.18–44.07)[a]	37.75 (25.18–41.95)[a]	66.61 (55.08–77.61)[b]	66.07 (55.05–83.94)[b]	67.15 (55.05–83.94)[b]	[c] *< 0.001**
Framingham risk score	8 (6–13)[a]	8 (5–11)[a]	20 (16–24)[b]	18 (15–20)[b]	20 (20–25)[b]	[c] *< 0.001**

[a],[b]Statistically significant groups are shown in different letters. If the groups are labeled by the same letter, it means that there is no statistical difference

[c]*Kruskal–Wallis test* data are shown as "median, (25th–75th percentile)"

*$p < 0.05$ Asterisk (*) indicates statistical significance

Table 7 Relationships between duration until stone passage and predictive factors for spontaneous passage

		UD	USD	UWT	Stone volume	NLR	Framingham score	Presence of hydronephrosis	BMI	Presence of non-calcium stones
Duration until stone passage	*rho*	0.453	0.505	0.611	0.477	0.326	0.590	0.418	0.139	0.249
	p	*0.001**	*0.003**	*0.005**	*< 0.001**	*0.028**	*< 0.001**	*0.013**	*0.065*	*0.042*

UD ureteral diameter, *USD* the ratio of ureter to stone diameter, *UWT* ureteral wall thickness, *NLR* Neutrophil/lymphocyte ratio, *BMI* Body mass index

Spearman correlation

*$p < 0.05$ Asterisk (*) indicates statistical significance

to these predictors. Although more comprehensive studies are needed to validate our results, we think that our findings as "Preliminary Results" may be a step toward further studies.

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Compliance with ethical standards

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Ethical approval for research involving human participants. The study was approved by the local ethics committee (the protocol number: 77192459–050.99-E.10736, 6/13; the date of approval: October 7, 2019) at Karabük University Training and Research Hospital. All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent A formal written informed consent was obtained from all individual participants included in the study. The data of patients who did not consent was not used.

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