

# Is it possible to predict spontaneous passage of a ureteral stone? An up-to-date comment on the current problem with new concepts concerning the patient and the stone

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**Introduction** The aim of this article was to determine a predictive factor by examining the patient's characteristics and the stone to predict the ureteral stone spontaneous passage.

**Material and methods** A total of 200 patients aged 18–55 who were referred with middle and distal ureter ureteral stones between 5–7 mm were analyzed retrospectively. Patients were randomized as 50 spontaneous stone passage positive (SSPP) and 50 negative patients. Body mass index (BMI), waist-to-hip ratio (WHR), stone size, ureter length, ureter diameter, stone Hounsfield unit value (SHU), ureteral wall thickness (UWT), kidney parenchymal thickness (KPT), kidney parenchymal density, neutrophil-lymphocyte ratio (NLR) and thrombocyte-lymphocyte ratio (TLR) values were recorded.

**Results** The average SHU of the SSPP group was 579 and 970 in the negative group ( $p: 0.000$ ). While the mean was 1.7 mm in the UWT SSPP group, it was 2.4 mm in the negative group ( $p: 0.000$ ). SHU and UWT were statistically significantly different in univariate and multivariate logistic regression analyses. WHR values were 39.6 and 29.3 for SSPP and the negative group, respectively ( $p: 0.032$ ). The ureter diameter was 7.6 mm for the SSPP group and 8.9 mm in the negative group ( $p: 0.01$ ).

**Conclusions** Low SHU value is related to the ureteral stone's positive spontaneous passage, and the increase of UWT is inversely related to the spontaneous passage. WHR is higher in people who can passage ureteral stones. A narrow ureter diameter is correlated with spontaneous stone passage. Ureter length, KPT, and kidney parenchymal density were not associated with spontaneous passage.

**Key Words:** passage ↔ stone ↔ ureter

## INTRODUCTION

Ureteral stone treatment can be diverse depending on its stone size and location in the ureter and kidney function. It is crucial to have a septic condition in this treatment selection, mainly due to the kidney's obstruction [1]. Ureterorenoscopy (URS), shock wave lithotripsy (SWL), and medical expulsive treatment (MET) are well-known and preferred treatment methods [2].

Spontaneous passage of ureteral stones remains a problem to this day. Studies show that 95%

of ureteral stones with a diameter of up to 4 mm pass spontaneously [3, 4]. In the literature, some criteria for spontaneous passage have been defined, generally based on the stone size [5, 6]. The most identified advantageous treatment method regarding spontaneous passage is medical expulsive treatment (MET). According to the European Association of Urology (EAU), MET may be preferred for stones larger than 5 mm in the distal ureter. However, MET is not recommended due to the low probability of spontaneous passage of ureteral stones >10 mm in diameter [3]. To predict spontaneous passage, determining

specific criteria other than the stone's size will help manage the disease. Based on this idea, we conducted a retrospective randomized study to find one or more determinants of both the patient and the stone in the process of spontaneous passage.

## MATERIAL AND METHODS

After obtaining institutional review board approval at our institution between January 2019 and February 2021, 200 patients aged 18–55 years had a single ureteric stone between 5–7 mm in the distal and middle ureter confirmed by non-contrast computed tomography were reviewed retrospectively. Distal and middle ureteral stones were defined as located under the iliac cross.

Exclusion criteria:

- Presence of pyelonephritis or complicated urinary tract infection
- Having multiple comorbidities
- Previous endourological surgery history
- Solitary kidney
- Renal dysfunction
- Previous treatment with MET

As it was forecast that the cases who underwent MET would change the outcomes; 55 patients were excluded from the study. Also, 22 patients with pyelonephritis, 13 patients with multiple comorbidities, and 10 patients who had undergone previous endourological surgery were excluded from the study; as it was thought that previous endourological surgery may lead to ureteral stenosis and affect the results (Figure 1).

After applying the exclusion criteria, a total of 100 patients were included in the study, 50 who were spontaneous stone passage positive (SSPP) and 50 who underwent ureterorenoscopy (URS) or shock wave lithotripsy (SWL) due to lack of spontaneous stone passage. Also, it was confirmed with non-contrast computed tomography that all patients in the SSPP group passed their stones.

Patient's demographic properties, body mass index (BMI), waist-to-hip ratio (WHR), right or left side, stone size, ureter length, ureter wall thickness (UWT), ureter diameter above the stone, Hounsfield unit of the stone, neutrophil-lymphocyte ratio (NLR), thrombocyte-lymphocyte ratio (TLR), kidney parenchyma thickness (KPT), and kidney parenchyma density were measured.

Ureter length was measured considering the number of transverse lines in non-contrast tomography between the ureteropelvic and ureterovesical junction. NLR and TLR were proportioned according to the patients' hemogram values at first examination. KPT was calculated by taking the average

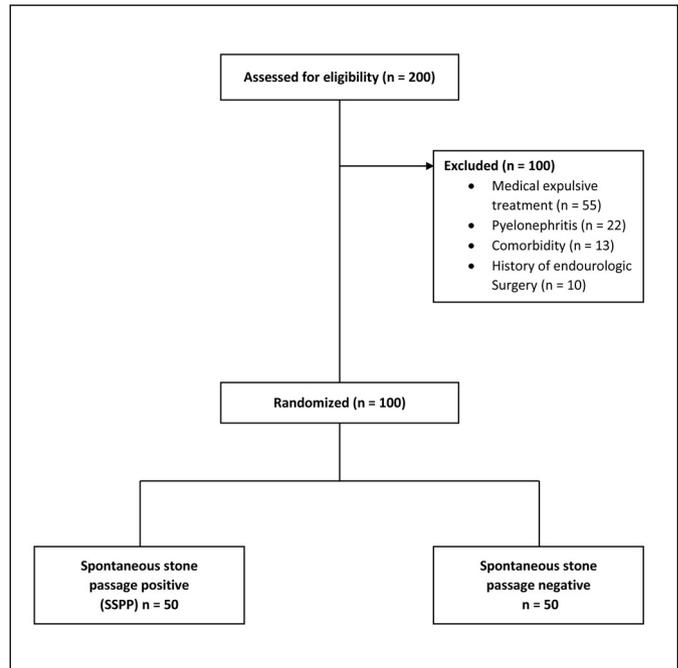


Figure 1. Flowchart showing exclusion criteria and numbers.

thickness in the transverse scans of the tomography of the kidney's upper, middle, and lower poles.

We established ureter wall thickness (UWT) by looking at the stone's line non-contrast tomography. We assigned the diameter of the ureter in the non-contrast tomography at the proximal section taken as the baseline. We accounted for a value for kidney parenchyma density unit by averaging the upper middle and lower pole of the kidney parenchyma Hounsfield unit values in non-contrast tomography. Since there is no standard term in this regard, we used the expression of kidney parenchyma density.

## Statistical analysis

Patients were divided into two groups by the simple randomization method. Pearson chi-Square test, Student t-test, Mann-Whitney U test was employed. All data were transferred to the SPSS IBM 25 program. Additionally, we established univariate and multivariate logistic regression analyses to determine the factors affecting spontaneous passage.

## RESULTS

There was no statistical difference between the mean ages of the groups ( $p: 0.131$ ). In both groups, 25 patients were male, and 25 patients were female. Of the SSPP group, 29 were right ureteral stones, and 21 were left ureteral stones. In the negative group, there were 26 right sides and 24 left sides.

**Table 1.** *The properties of groups*

	SSPP	SPN	Total	p
Female gender	25	25	50	1.000*
Male gender	25	25	50	
Right ureter	29	26	55	0.627*
Left ureter	21	24	45	
Stone size	6.3	6.8		0.14**
Age (mean)	44	39		0.131**

SSPP – spontaneous stone passage positive; SPN – spontaneous passage negative

\*Pearson Chi Square; \*\*Student t test

**Table 2.** *Statistical differences of variables between groups*

Variables	SSPP	SPN	p
Ureter diameter (mm)	7.6	8.9	0.01*
NLR	33.6	35.3	0.736**
TLR	125.3	143.3	0.145
SHU	579	970	0.000
WHR	39.6	29.3	0.032**
BMI (kg/m <sup>2</sup> )	28.4	27.4	0.35*
UWT (mm)	1.7	2.4	0.000*
KPT (mm)	20.1	21.6	0.067*
Kidney parenchyma density	31.1	33.9	0.26*
Ureter length (mm)	197	199	0.78*

SSPP – spontaneous stone passage positive; SPN – spontaneous passage negative; NLR – neutrophil-lymphocyte ratio; TLR – thrombocyte-lymphocyte ratio; SHU – stone Hounsfield unit; WHR – waist-to-hip ratio; BMI – body mass index, UWT – ureteral wall thickness; KPT – kidney parenchymal thickness

\*Student t test; \*\* Mann-Whitney U test

There was no statistical difference between the sides and the groups (p: 0.627). Furthermore, there was no significant difference between the groups in mean stone size; it was 6.3 and 6.8 for SSPP and the negative group, respectively (Table 1).

BMI, ureter length, TLR, NLR, KPT, and kidney parenchyma density values did not significantly differ between groups and logistic regression models. The mean stone Hounsfield unit value (SHU) was 579 in the SSPP group, and it was 970 in the negative group (p: 0.000). We observed that the mean UWT was 1.7 mm in the SSPP group and 2.4 mm in the negative group (p: 0.000). Another variable that we calculated the statistical difference between the two groups is the ureter diameter. This value was 7.6 mm in the SSPP group; we found it 8.9 in the negative group (p: 0.01). We evaluated the WHR value and found SSPP and the negative group to be 39.6 mm and 29.3 mm, respectively (p: 0.032). The distribution of variables by groups is summarized in Table 2.

SHU and UWT showed significant differences in both univariate and multivariate logistic regression analyses. In so much that it was reached, a one-unit increase in UWT reduces the spontaneous passage probability of the stone by 7.4 times. However, the ureter diameter, which showed a statistically significant difference between the groups, yielded significant results in the univariate logistic regression model, however not in the multivariate model. Similarly, WHR showed a statistical difference between the two groups, but we could not obtain these significant results in univariate and multivariate logistic regression models (Table 3).

**Table 3.** *Univariate and multivariate logistic regression models*

Variables	Univariate				Multivariate			
	P	Odds ratio	95%CI		P	Odds ratio	95%CI	
			Lower	Upper			Lower	Upper
Ureter diameter (mm)	0.016	1.376	1.060	1.786	0.697	0.920	0.605	1.399
NLR	0.571	1.084	0.820	1.434	0.038	0.535	0.297	0.966
TLR	0.148	1.007	0.997	1.017	0.068	1.021	0.998	1.044
SHU	0.000	1.004	1.002	1.006	0.001	1.006	1.003	1.010
WHR	0.617	1.069	0.822	1.391	0.969	0.994	0.736	1.342
BMI (kg/m <sup>2</sup> )	0.346	0.945	0.839	1.064	0.335	0.911	0.755	1.101
UWT (mm)	0.002	4.113	1.7	9.950	0.006	7.405	1.785	30.726
KPT (mm)	0.073	1.154	0.987	1.348	0.552	1.091	0.820	1.451
Kidney parenchyma density	0.265	1.028	0.979	1.079	0.607	1.021	0.944	1.104
Ureter length (mm)	0.784	1.003	0.983	1.022	0.665	0.992	0.958	1.028

NLR – neutrophil-lymphocyte ratio; TLR – thrombocyte-lymphocyte ratio; SHU – stone Hounsfield unit; WHR – waist-to-hip ratio; BMI – body mass index; UWT – ureteral wall thickness; KPT – kidney parenchymal thickness

## DISCUSSION

Ureteral stones mostly have to be treated more urgently than kidney stones due to renal failure, severe pain, and secondary urinary system infections caused by obstruction. Significant improvement has been made in treating ureteral stones with SWL and endourological surgery advancements [7]. However, it should be kept in mind that even these minimally invasive treatments may have some complications. Therefore, spontaneous passage of the stone remains the most sought after circumstance.

Spontaneous passage of ureteral stones has long been an issue of discussion for clinicians. In this regard, we can state that the underlying studies in the literature concentrate on the stone size and location [3, 8, 9]. Hydronephrosis, pyuria, and perinephric fat stranding in non-contrast tomography have been a matter of previous studies. It is possible to say that there is a positive correlation between the findings obtained and the distal part of the stone and the reduction in stone size and the spontaneous passage [5, 10, 11]. We excluded patients with pyuria or complicated urinary infections to obtain a homogeneous population. Furthermore, since it was foreseen that proximal stones might have longer spontaneous passage time, only patients with distal and middle ureteral stones were included in the study.

The principal component of MET, which is the primary treatment method for spontaneous stone passage, is alpha-blockers; also, calcium channel blockers, phosphodiesterase (PDE) inhibitors, and spasmolytics may be clinically effective [12]. Moreover, MET can be applied to increase the success of SWL and help symptoms caused by ureteral stents [13, 14]. Since we aimed to find a different variable for spontaneous passage in our study, we excluded patients who received MET. Some studies have been carried out by presenting different parameters in the literature to predict spontaneous passage of ureteral stones. In studies conducted on white cell count, neutrophil count, and C-reactive protein (CRP), the level of inflammatory markers has been associated with impacted ureteric stones [15–18].

Apart from these inflammatory markers, it has been investigated whether neutrophil-to-lymphocyte ratio (NLR) and the thrombocyte-to-lymphocyte ratio (TLR) increased in cases of various cancers and infections associated with spontaneous passage. In the study conducted by Heidar et al., it is emphasized that both NLR and TIR values for spontaneous passage are inversely correlated [18]. Similarly, Lee et al. found that low NLR (<2.3) increased the spontaneous passage in patients with ureteral stone size <1.0 cm [19]. However, we did not observe a sig-

nificant difference between the groups in both NLR and TLR values.

Another variable that has been researched regarding its relationship with spontaneous passage is body mass index (BMI). In a study conducted in 2015, BMI was significantly lower in people with spontaneous passage [20]. On the other hand, we did not see a significant relationship between BMI and spontaneous passage.

Waist-to-hip ratio (WHR) is used for similar purposes as BMI. It is stated in epidemiological studies that it is particularly associated with cardiovascular diseases [21]. Considering that this measurement is generally a marker for metabolic syndrome and obesity, it can be thought that there is a possibility of increasing urinary system stone disease. Studies in the literature show that waist-to-hip ratio, waist circumference, and waist stature are related to the stone's composition and supersaturation status [22, 23]. However, there is no study on whether a relationship exists between WHR and spontaneous passage. We found the waist-to-hip ratio rate to be significantly higher in the SSPP group. In this respect, we can signify that our study constitutes a first in these terms. However, we cannot say that we observed a significant difference in univariate and multivariate logistic regression analyses.

Hounsfield unit is a parameter customarily associated with the success of SWL [24]. Balci et al. examined the spontaneous passage success of patients who underwent MET in 2014, and the Hounsfield Unit values of the groups with and without spontaneous passage were found to be 507 and 625, respectively, and no statistical difference was observed [25]. After logistic regression analysis, we obtained statistically significant results between the stone's low Hounsfield unit value and the spontaneous passage between the groups and after logistic regression analysis. Thus, we can state that our findings are the first in the literature.

Ureter wall thickness (UWT) has been previously examined in the literature, and its low level was found to be significant for spontaneous stone passage [26]. For this parameter, our results support the literature.

Another variable that we anticipate to gain a different outcome for is ureter length. With the opinion that spontaneous passage would be difficult if the ureter length increased, the ureter lengths of all patients were calculated according to the number of sections between the ureteropelvic junction and the ureterovesical junction in non-contrast tomography. However, ureter length was 197 mm and 199 mm in SSPP and the other groups, respectively. These results were not statistically significant ( $p: 0.78$ ). We know that there is no standard concept such as 'ureter length'.

We used this concept, thinking that we would see a difference between groups; however, we did not see a statistically significant difference. In this respect, although our study is open to criticism, we claim that the concept of 'ureter length' was first stated here.

We have knowledge that kidney parenchymal thickness (KPT) is a predictive factor for kidney functions [27]. Although patients with renal dysfunction were not included in our study, we thought that the parenchyma's thickness with ureteral stones might influence spontaneous passage. However, according to our outcomes, there was no significant difference in renal parenchymal thickness between groups.

A concept such as the Hounsfield unit of the renal parenchyma does not exist in the literature yet. Inspired by the 'relationship between kidney Hounsfield unit and kidney failure' study conducted by our clinic, this expression was introduced here. The findings we have obtained in this study support the idea that 'there is a relationship between high renal parenchyma Hounsfield unit value and renal failure' for now. In this study, we used the concept of 'kidney parenchyma density'. However, we did not obtain a statistically significant result.

Again, we obtained results considering that the kidney parenchyma with ureter stones may affect the spontaneous passage in practical terms. Unfortunately, our data did not give us meaningful results for spontaneous passage.

Our study's limitations are that it is retrospective, single-centered, and has a low number of patients. The uncertainty of the spontaneous passage times of the patients is also a matter of criticism. Also, we acknowledge that the study results will be enriched by the inclusion of proximal ureteral stones in the study.

## CONCLUSIONS

The estimation of the spontaneous passage of the ureteral stone is still controversial. In this study, which we conducted to obtain several parameters for managing the disease, the low Hounsfield unit of the stone facilitates spontaneous passage. The increase in the thickness of the ureter wall makes spontaneous passage difficult. Furthermore, we believe that people with a high waist-to-hip ratio will pass their stones more easily. We also concluded that new concepts such as ureter length, renal parenchymal thickness, and renal parenchymal density are not associated with spontaneous passage. We think that our current results will be supported, and new information will be presented to the literature with multi-center, prospective studies which include control groups.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## References

1. Türk C, Petřík A, Sarica K, et al. EAU Guidelines on Diagnosis and Conservative Management of Urolithiasis. *Eur Urol*. 2016; 69: 468-474.
2. Bader MJ, Eisner B, Porpiglia F, Preminger GM, Tiselius H-G. Contemporary management of ureteral stones. *Eur Urol*. 2012; 61: 764-772.
3. Preminger GM, Tiselius H-G, Assimos DG, et al. Guideline for the management of ureteral calculi. *Eur Urol*. 2007; 52: 1610-1631.
4. Tzelves L, Mourmouris P, Skolarikos A. Comparison of current guidelines on medical management of stone disease. *Arch Esp Urol*. 2021; 74: 171-182.
5. Ibrahim AI, Shetty SD, Awad RM, Patel KP. Prognostic factors in the conservative treatment of ureteric stones. *Br J Urol*. 1991; 67: 358-361.
6. Hubner WA, Irby P, Stoller ML. Natural history and current concepts for the treatment of small ureteral calculi. *Eur Urol*. 1993; 24: 172-176
7. Miller OF, Kane CJ. Time to stone passage for observed ureteral calculi: a guide for patient education *J Urol*. 1999; 162 (3 Pt 1): 688-690.
8. Segura JW, Preminger GM, Assimos DG, et al. Ureteral stones clinical guidelines panel summary report on the management of ureteral calculi. *The American Urological Association*. *J Urol*. 1997; 158: 1915-1921.
9. Ueno A, Kawamura T, Ogawa A, Takayasu H. Relation of spontaneous passage of ureteral calculi to size. *Urology*. 1977; 10: 544-546.
10. Takahashi N, Kawashima A, Ernst RD, et al. Ureterolithiasis: can clinical outcome be predicted with unenhanced helical CT? *Radiology*. 1998; 208: 97-102.
11. Jendeborg J, Geijer H, Alshamari M, Cierznak B, Lidén M. Size matters: The width and location of a ureteral stone accurately predict the chance of spontaneous passage. *Eur Radiol*. 2017; 27: 4775-4785.
12. Türk C, Knoll T, Seitz C, et al. Medical expulsive therapy for ureterolithiasis: The EAU recommendations in 2016. *Eur Urol*. 2017; 71: 504-507.
13. Krocak T, Scotland KB, Chew B, Pace KT. Shockwave lithotripsy: techniques for improving outcomes. *World J Urol*. 2017; 35: 1341-1346.
14. Lim KT, Kim YT, Lee TY, Park SY. Effects of tamsulosin, solifenacin, and combination therapy for the treatment of ureteral stent related discomforts. *Korean J Urol*. 2011; 52: 485-488.

15. Sfoungaristos S, Kavouras A, Katafgiotis I, Perimenis P. Role of white blood cell and neutrophil counts in predicting spontaneous stone passage in patients with renal colic. *BJU Int.* 2012; 110 (8 Pt B): 339-345.
16. Ozcan C, Aydogdu O, Senocak C, et al. Predictive factors for spontaneous stone passage and the potential role of serum C-reactive protein in patients with 4 to 10 mm distal ureteral stones: a prospective clinical study. *J Urol.* 2015; 194: 1009-1013.
17. Park CH, Ha JY, Park CH, Kim CI, Kim KS, Kim BH. Relationship between spontaneous passage rates of ureteral stones less than 8 mm and serum C-reactive protein levels and neutrophil percentages. *Korean J Urol.* 2013; 54: 615-618.
18. Abou Heidar N, Labban M, Bustros G, Nasr R. Inflammatory serum markers predicting spontaneous ureteral stone passage. *Clin Exp Nephrol.* 2020; 24: 277-283.
19. Lee KS, Ha JS, Koo KC. Significance of Neutrophil-to-Lymphocyte Ratio as a Novel Indicator of Spontaneous Ureter Stone Passage. *Yonsei Med J.* 2017; 58: 988-993.
20. Ahmed AF, Gabr AH, Emara AA, Ali M, Abdel-Aziz AS, Alshahrani S. Factors predicting the spontaneous passage of a ureteric calculus of 10 mm. *Arab J Urol.* 2015; 13: 84-90.
21. Huxley R, Mendis S, Zheleznyakov E, Reddy S, Chan J. Body mass index, waist circumference and waist: hip ratio as predictors of cardiovascular risk – a review of the literature *Eur J Clin Nutr.* 2010; 64: 16-22.
22. Kadlec AO, Greco K, Fridirici ZC, Hart ST, Velloso T, Turk TM. Metabolic Syndrome and Urinary Stone Composition: What Factors Matter Most? *Urology.* 2012; 80: 805-810.
23. Tavasoli S, Taheri M, Khoshdel A, Basiri A. Association of Body Mass Index, Waist Circumference, and Waist-Stature Ratio With Urine Composition in Patients With Urolithiasis. *Iran J Kidney Dis.* 2017; 11: 371-378.
24. Nakasato T, Morita J, Ogawa Y. Evaluation of Hounsfield Units as a predictive factor for the outcome of extracorporeal shock wave lithotripsy and stone composition Urolithiasis. 2015; 43: 69-75.
25. Balci M, Tuncel A, Aydin O, et al. Tamsulosin versus nifedipin in medical expulsive therapy for distal ureteral stones and the predictive value of Hounsfield unit in stone expulsion. *Ren Fail.* 2014; 36: 1541-1544.
26. Yoshida T, Inoue T, Taguchi M, Omura N, Kinoshita H, Matsuda T. Ureteral wall thickness as a significant factor in predicting spontaneous passage of ureteral stones of  $\leq 10$  mm: a preliminary report. *World J Urol.* 2019; 37: 913-919.
27. Jovanović D, Gasic B, Pavlovic S, Naumovic R. Correlation of kidney size with kidney function and anthropometric parameters in healthy subjects and patients with chronic kidney diseases. *Ren Fail.* 2013; 35: 896-900. ■