



Research Article

The role of serum acute phase reactant levels in the prediction of impacted ureteral stone

 Ismet Aydin Hazar¹,  Tuncay Tas²,  Cem Tugrul Gezmis³,  Ersan Arda⁴,  Nusret Can Cilesiz¹,
 Basri Cakiroglu⁵

¹Department of Urology, University of Health Sciences Gaziosmanpasa Taksim Training and Research Hospital, Istanbul, Turkey

²Department of Urology, Esenyurt University Istanbul Cerrahi Hospital, Istanbul, Turkey

³Department of Urology, Public Hospital of Bitlis, Bitlis, Turkey

⁴Department of Urology, Trakya University School of Medicine, Edirne, Turkey

⁵Department of Urology, Hisar Intercontinental Hospital, Istanbul, Turkey

Abstract

Objectives: The aim of this study was to investigate the determination of ureteral stone impaction using acute phase reactants.

Methods: A total of 110 patients who had a single ureteral stone treated during a single month using medical expulsive therapy of tamsulosin 0.4 mg/day, diclofenac 75 mg upon analgesic requirement, and at least 3 liters fluid per day were evaluated prospectively. The patients underwent ureteroscopy and were divided into 2 groups according to the presence or absence of impaction. The preoperative white blood cell (WBC) count, red blood cell distribution width (RDW), C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), mean platelet volume (MPV), and neutrophil-to-lymphocyte ratio (NLR) in the non-impacted stone group (Group 1; n=59) and the impacted group (Group 2; n=51) were statistically compared.

Results: There was no statistically significant difference in terms of age, stone diameter, body mass index, grade of hydronephrosis, or stone localization between the 2 groups. The WBC, RDW, and MPV value differences were statistically significant between the groups ($p=0.035$, $p=0.035$, and $p=0.005$, respectively). An MPV cut-off value of 9.55 fL was defined in Group 2 with 66% sensitivity and 62% specificity for impaction. There was no statistically significant difference between the groups in CRP, ESR, or NLR values ($p=0.44$, $p=0.76$, $p=0.54$, respectively).

Conclusion: Evaluation of serum MPV with a cut-off value of 9.55 fL may predict ureteral stone impaction.

Keywords: Impacted, mean platelet volume, red blood cell distribution width, ureteral stone, white blood cell

Urolithiasis is a disease that affects between 4% and 15% of the world population and the rate continues to grow [1]. Some 86% to 97% of ureteral stones are smaller than 3 mm in size and are passed spontaneously without any symptoms or medical treatment. Larger stones, on the other hand, cause dilatation of the ureter through partial or whole acute obstruction, depending on the size and location. Furthermore, they

can cause colic pain through smooth muscle and epithelial reactions [2]. An impacted ureteral stone is defined as a case in which the stone remains in the ureter for more than 2 months in the same position and a guidewire cannot be passed endoscopically to the proximal side of the stone [3, 4].

An impacted stone can lead to local inflammatory reactions as a result of remaining in the same place in the ureter for an ex-

Address for correspondence: Ismet Aydin Hazar, MD. Department of Urology, University of Health Sciences Gaziosmanpasa Taksim Training and Research Hospital, Istanbul, Turkey

Phone: +90 532 322 41 77 **E-mail:** cetege@gmail.com **ORCID:** 0000-0001-5193-2340

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tended period of time [5]. During a ureteroscopy, an impacted stone is generally observed to be covered with an edematous and inflammatory mucosa.

Compared with patients with non-impacted stones, patients with an impacted stone are generally more resistant to medical treatment and the complication rates are also higher [6].

The complete blood cell count (CBC) is an easily accessible and inexpensive blood test. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammation index are biomarkers calculated using the CBC, and have been reported to be useful in the diagnosis and monitoring of many systemic inflammatory processes. Platelets are non-nucleated blood cells with a role in tissue repair and maintaining hemostasis [7]. Platelet indices, such as platelet count, mean platelet volume (MPV), procalcitonin level, and platelet distribution width value have also proven to be useful [8].

The red blood cell distribution width (RDW) value, a component of the CBC, illustrates the heterogeneity of red cell volume. The red blood cell count is an inexpensive measure of volume variability, is readily available, and can be repeated easily [9].

In this research, patients who were not able to spontaneously pass a ureteral stone after medical expulsive treatment and therefore underwent ureteroscopy were evaluated on the basis of whether preoperatively measured acute phase reactants successfully predicted impaction of the stone.

Materials and Methods

A total of 110 patients who presented with a ureteral stone between January 2017 and December 2017 were included in the research. Only patients with a radiopaque ureteral stone that they were not able to pass for 2 months despite medical treatment were included. Patients with multiple stones, patients who had previously undergone open surgery or an endoscopic operation for ureteral stones, patients who had received extracorporeal shock wave lithotripsy for a stone in the same ureter, and patients with stent placement, congenital abnormalities, coagulopathy, or renal impairment were excluded.

Medical expulsive therapy of tamsulosin 0.4 mg/day, diclofenac 75 mg/day administered analgesically, and at least 3 liters of

fluid per day for a month was administered to the study patients, and they were evaluated prospectively. A non-contrast computed tomography (CT) scan was performed for all of the patients. The impaction of the stone and effect on the ureteral wall were verified with direct visualization during ureteroscopy in all cases. A holmium laser was used to help with lithotripsy during retrograde rigid ureteroscopy. The patients were divided into 2 groups based on observations made during ureteroscopy to determine if the ureteral stone was impacted in the wall. Patients whose stones were not impacted in the ureteral wall were assigned to Group 1 (n=59), while those with wall impaction were classified as Group 2 (n=51). The preoperative measures of the white blood cell (WBC) count, RDW value, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), MPV, and NLR in the 2 groups were compared.

The distribution of the variables was assessed with the Kolmogorov-Smirnov test. Quantitative independent variables were analyzed using an independent samples t-test and the Mann-Whitney U test. For the analysis of qualitative independent variables, a chi-square test was used when applicable, otherwise Fisher's exact test was used. Spearman correlation analysis was used to examine the association between variables. Effect level and cut-off values were examined using a receiving operator characteristic (ROC) curve. All analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA), and a p<0.05 value was accepted for statistical significance.

Ethics committee approval was obtained from Gaziosmanpaşa Taksim Training and Research Hospital (04/2017-1) Ethics Committee and the study was conducted in accordance with Declaration of Helsinki.

Results

The data of 110 patients (21 female and 89 male) were evaluated: 59 of the participants were assigned to Group 1, and 51 were assigned to Group 2. The age of the patients varied between 21 and 67 years, with a mean of 36.57±9.34 years. The distribution of descriptive parameters such as age, gender, presence of primary/secondary stone, body mass index, and stone size are shown in Table 1. There were no significant

Table 1. Descriptive data

	Number of patients (n=110)		Group 1 (n=59)		Group 2 (n=51)		p
	Mean	SD	Mean	SD	Mean	SD	
Gender,							
Female/Male	21/89		10/49		11/40		
Primary/Secondary stone	40/70		18/41		22/29		
Age (years)	36.57	9.34	37.66	8.95	35.64	4.04	0.770
BMI (kg/m ²)	25.80	4.57	25.57	4.38	26.07	4.57	0.606
Stone size (mm ²)	39.52	19.32	34.63	19.70	47.74	19.47	0.000

BMI: Body mass index.

Table 2. Laboratory parameters

	Number of patients (n=110)		Group 1 (n=59)		Group 2 (n=51)		p
	Mean	SD	Mean	SD	Mean	SD	
WBC	9.60	2.70	10.17	2.75	9.09	2.53	0.034
RDW	14.30	1.85	13.91	2.00	14.64	1.60	0.035
NLR	2.90	1.92	2.80	2.03	3.02	1.80	0.543
MPV	9.55	1.05	9.19	0.92	9.68	0.84	0.005
Creatinin	1.00	1.01	0.87	0.26	1.08	1.44	0.299
CRP	7.79	9.56	8.43	10.65	7.05	8.15	0.446
Sedimentation	11.63	7.75	11.83	8.71	11.39	6.54	0.764

CRP: C-reactive protein; MPV: Mean platelet volume; NLR: Neutrophil-to-lymphocyte ratio; RDW: Red blood cell distribution width; WBC: White blood cell.

differences between the 2 groups in terms of body mass index ($p > 0.05$). However, there was a significant difference in the size of the stone: the mean area of the stone was $34.63 \pm 19.70 \text{ mm}^2$ in Group 1 and $47.74 \pm 19.47 \text{ mm}^2$ in Group 2.

In between-group analyses, the mean WBC, RDW, and MPV values were found to be significantly higher in Group 2 ($p < 0.05$). The most significant difference was detected in MPV, with a mean of $9.19 \pm 0.92 \text{ fL}$ in Group 1 and $9.68 \pm 0.84 \text{ fL}$ in Group 2 ($p < 0.01$). These data are displayed in detail in Table 2.

In order to examine the power of MPV in group differentiation, ROC analysis was conducted, and the area under the curve was calculated to be 0.655 ($p < 0.01$). The cut-off level determined for MPV (9.55 fL) differentiated the groups with 66% sensitivity and 62% specificity (Fig. 1). Odds ratio analysis indicated that an MPV value over 9.55 fL was 1.75 times more likely in Group 1.

Discussion

The presence an ureteral stone is the most frequent urological emergency, and is associated with pain, renal obstruction, and urinary tract infections [10].

According to the European Association of Urology and American Urological Association (AUA) guidelines, the spontaneous stone passage rate differs significantly depending on the stone's position in the ureter. According to AUA guidelines, 98% of ureteral stones smaller than 5 millimeters pass naturally with conservative management [11].

The most common treatments for ureteral stones are ureteroscopy and extracorporeal shock wave lithotripsy. However, treatment of impacted ureteral stones is a little more difficult.

Prolonged impaction of ureteral stones can lead to edema and fibrosis in the ureter mucosa. Microscopic studies have shown the formation of chronic interstitial fibrosis and ureteral hypertrophy in the area between the stone and the ureter. Long-term physical pressure or decreased blood stream due to an immunological reaction to the stone can

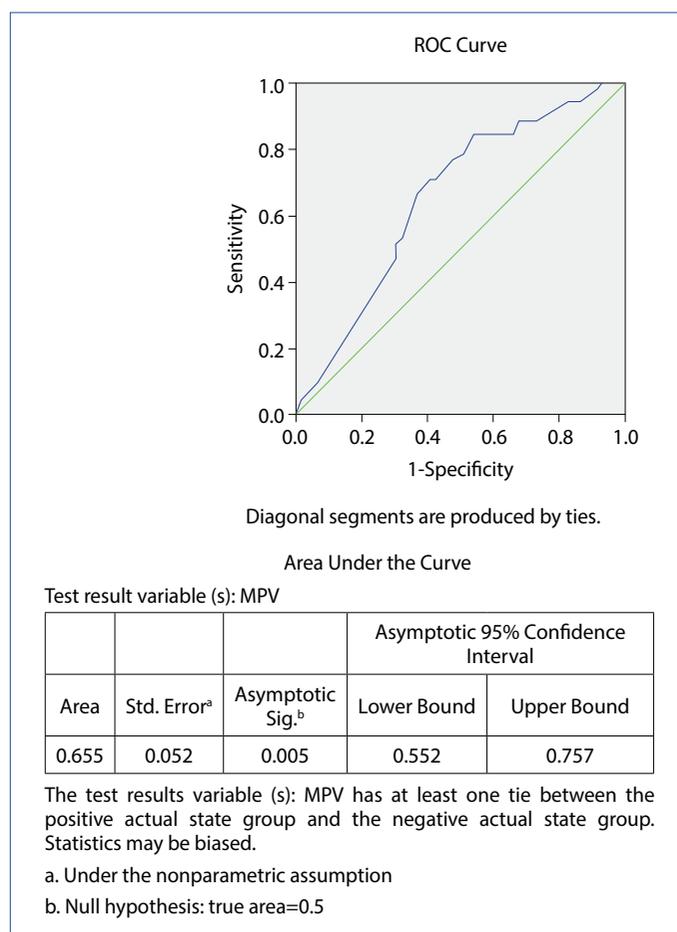


Figure 1. Receiver operating characteristic (ROC) analysis to examine the power of the mean platelet volume (MPV) in group differentiation.

cause serious and chronic inflammation in the ureter mucosa [12]. Inflammation and edema may be observed in the ureteral wall of patients with chronically impacted stones, and these changes can spread to surrounding tissues. It is well known that, depending on the duration of the stone's presence in the same part of the ureter, inflammatory and edematous changes can increase the thickness of the ureteral wall in the related area [13].

However, impaction of ureter stones can be difficult to determine. Imaging methods have been used to evaluate and measure the presence and level of an impacted stone (e.g., embedment in the ureteral wall) but they may not be able to completely reveal the impaction [14].

There is a direct relationship between the passage of the stone and its diameter; it is more difficult for larger stones to move through the ureter. Studies have also demonstrated that the transverse size of the stone affects impaction [12, 15]. Similarly, our research found impacted stones to be larger than non-impacted stones. While the average area of the stones was $34.63 \pm 19.70 \text{ mm}^2$ in Group 1, it was $47.74 \pm 19.47 \text{ mm}^2$ in Group 2.

According to the literature, the deeper stones are embedded into the ureteral wall, not only is the spontaneous passage rate affected, but also the complications of endourological stone extraction techniques increase [16, 17, 18, 19, 20].

Yamaguchi et al. [21] reported that impacted stones caused lesions, which may increase the degree of ureteral obstruction and ureteral wall inflammation. Studies of the impaction of ureteral stones in the ureteral wall are mostly based on radiological visualization methods. Other than preoperative radiological visualization studies of impacted stones, there is only 1 study examining preoperative CBC results and biochemical tests. In this research, Sarica et al. [22] reported that serum CRP and sedimentation levels were closely associated with the degree of stone impaction in the ureteral wall.

In another study, Aldaqadossi [10] reported that the level of CRP, a non-specific systemic inflammatory marker, was lower in cases of distal ureteral stones that passed spontaneously compared with those that did not pass. Our research did not reveal a significant difference in the CRP and sedimentation values between the 2 groups.

Our results indicated that the MPV was the most important marker for an impacted ureteral stone, and that the 9.55 fL cut-off value determined in ROC analysis examining MPV can be used for differentiation between groups with 66% sensitivity and 62% specificity.

Conclusion

Treatment of an impacted ureteral stone is more difficult than treatment of those that are not impacted. Radiological methods and other conventional methods can be insufficient to detect the impaction. We think that acute phase reactants can help to diagnose impacted ureteral stones. In particular, the serum MPV value can be predictive of ureteral stone impaction with a cut-off level of 9.55 fL. Further research is required to support this thesis.

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