

DİSTAL ÜRETER TAŞI OLAN HASTALARDA MEDİKAL EKSPULSİF TEDAVİNİN BAŞARISINI ETKİLEYEN ÖNGÖRÜCÜ FAKTÖRLER

PREDICTIVE FACTORS AFFECTING THE SUCCESS OF MEDICAL EXPULSIVE THERAPY IN PATIENTS WITH DISTAL URETERAL STONE

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ÖZET

AMAÇ: Bu çalışmada distal üreter taşı nedeniyle medikal ekspulsif tedavi başlanan hastalarda spontan taş düşürmeyi etkileyen faktörleri araştırmayı amaçladık.

GEREÇ VE YÖNTEM: Eylül 2022 ve Ekim 2023 tarihleri arasında 4-10 mm boyutlarında distal üreter taşı olan toplam 148 hasta dahil edildi. Hastalara medikal ekspulsif tedavi olarak silodosin 4 mg başlandı ve en fazla dört hafta takip edildi. Spontan taş düşürmeyi etkileyen hasta ve taşa bağlı değişkenler değerlendirildi.

BULGULAR: Katılımcıların yaş ortalaması 42,92±12,78 yılı. Taş düşürme oranı %64,2 idi. Taş boyutu, taş yükü, üreter duvar kalınlığı, taşın üreterovesikal bileşkeye olan uzaklığı, nötrofil lenfosit oranı ve hidronefroz derecesi daha düşük olan hastalarda spontan taş düşürme oranı anlamlı olarak daha yüksekti (hepsi için p<0.05). Çok değişkenli analizde, taşın üreterovesikal bileşkeye olan mesafesi, üreter duvar kalınlığı ve nötrofil-lenfosit oranı spontan pasajın bağımsız belirleyicileriydi (sırasıyla p:0.036, p:0.001, p:0.001).

SONUÇ: Taşın üreterovesikal bileşkeye olan mesafesi, üreter duvar kalınlığı ve nötrofil-lenfosit oranı, spontan taş düşürmeyi tahmin etmede yararlı parametreler olabilir. Bu faktörler distal üreter taşlarının tedavisine yönelik karar verme sürecinde önemli bir rol oynamaktadır.

ANAHTAR KELİMELEER: Üreter taşları, Ürolitiaz, Medikal ekspulsif tedavi.

ABSTRACT

OBJECTIVE: In this study, we aimed to investigate the factors affecting spontaneous stone passing in patients who received medical expulsive therapy due to distal ureteral stones.

MATERIAL AND METHODS: From September 2022 to October 2023, a total of 148 patients with distal ureteral stones sized 4-10 mm were included. Patients received silodosin 4 mg as medical expulsive therapy and were followed up for a maximum of four weeks. The patient- and stone-related variables affecting spontaneous stone passage were evaluated.

RESULTS: The mean age of the participants was 42.92±12.78 years. The stone expulsion rate was 64.2%. The rate of spontaneous stone passage was significantly higher in patients with lower stone size, stone burden, ureteral wall thickness, distance of the stone to the ureterovesical junction, neutrophil-lymphocyte ratio and hydronephrosis grade. (all, p<0.05). The distance of the stone to the ureterovesical junction, ureteral wall thickness, and neutrophil-to-lymphocyte ratio were independent predictors of spontaneous passage (p:0.036, p:0.001, p:0.001, respectively).

CONCLUSIONS: The distance of stone to the ureterovesical junction, ureteral wall thickness, and neutrophil-to-lymphocyte ratio can be useful parameters to estimate spontaneous stone expulsion. These factors play important roles in decision-making for the management of distal ureteral stones.

KEYWORDS: Ureteral Calculi, Urolithiasis, Medical expulsive therapy.

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INTRODUCTION

Urolithiasis is a common disease worldwide, with an incidence of up to 20% (1). Twenty percent of urinary system stones are located at the ureter, and 70% of ureteral stones are distal ureteral stones (2). Although there are treatment methods such as extracorporeal shock wave lithotripsy (ESWL), endoscopic lithotripsy (EL) and surgical stone removal in the management of ureter stones, medical expulsive therapy (MET) is proposed for distal ureter stones smaller than 1 cm in the European Association of Urology guidelines (3). The success rate of spontaneous expulsion has been reported up to 70% with MET. Therefore, MET should be offered first to patients with uncomplicated distal ureter stones <1 cm to avoid the need for surgical intervention (4). The content of MET consists of plenty of fluid intake, pain palliation and medical treatment (alpha-adrenergic blocker, corticosteroid, phosphodiesterase type 5 inhibitor, antispasmodic or calcium channel blocker) for 4 weeks (5).

Studies investigating the success of MET have mostly focused on which medical treatment is more effective (6 - 8). However, the success of MET is also affected by patient and stone-related factors. The number of studies conducted on this subject is insufficient. The present study aimed to evaluate the factors affecting the success of spontaneous stone passage in adult patients with uncomplicated 4-10 mm sized distal ureter stones and in whom MET was initiated.

MATERIALS AND METHODS

The data of patients who applied with renal colic and were diagnosed as ureteral stones between 4-10 mm in the distal ureter at Department of Urology, Kemer State Hospital, and subsequently treated with MET between September 2022 and October 2023 were retrospectively examined. Exclusion criteria are listed below:

- Patients with urinary tract infection, fever >38°C or other focal infection
- Patients with bilateral or multiple ureter stones
- Patients with anamnesis of solitary kidney
- Patients with hematological, inflammatory disease or malignancy
- Patients who needed instant intervention due to renal impairment

•Patients with a history of using drugs that may change blood cell ratios (corticosteroids, oral contraceptives, etc.)

All patients were assessed by physical examination, complete blood tests, kidney function tests, urinalysis, urine culture, urinary ultrasonography (USG), and X-ray kidney, ureter, and bladder (KUB). Computed tomography (CT) was performed for all patients to confirm the diagnosis. All of the participants received silodosin 4 mg once a day as MET. Besides, 50 mg/day diclofenac sodium tablets were prescribed for episodes of renal colic. All of the patients were advised to remain active, drink 3 L of water daily, and strain their urine to search for stones. They were told to report the time they saw stones in the filtered urine. Patient follow-up was done once a week for 4 weeks with kidney function tests, urinalysis, X-ray KUB. Drugs were continued until stone expulsion or for a maximum four weeks. CT was reapplied in patients with suspicious or unsuccessful expulsions of stone at the end of the fourth week. Patients with no stone expulsion at the end of 4 weeks were advised to undergo an interventional treatment.

Demographic data of included participants (age, gender, body mass index [BMI], and neutrophil-to-lymphocyte ratio [NLR]) were noted. Stone-related parameters including stone size, stone burden, ureteral wall thickness (UWT), distance to the ureterovesical junction (UVJ), and hydronephrosis grade were also recorded using CT. The stone size was determined by calculating the widest diameter of the stone. The stone burden was calculated from CT scans and recorded in square millimeters. NLR was calculated by dividing neutrophil count by lymphocyte count before starting treatments.

Ethical Committee

Ethics committee approval was received from Antalya Training and Research Hospital. (Approval number: 2023-14/8).

Statistical Analysis

Data are presented as number (%) or mean \pm standard deviation for continuous variables, and frequency (%) for categorical data. Normality assumption was evaluated with the Shapiro Wilk test. Student's t-test was used for normal-

ly distributed continuous variables; otherwise, the Mann–Whitney U test was used. Pearson chi-square or Fisher's exact test was performed for categorical variables. All potential variables in the descriptive analysis were included in the initial univariable analysis and then only variables that were determined as significant ($p < 0.200$) were included in the final presented multivariate logistic regression models. Statistical analysis was performed by using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp.). A p -value < 0.05 was accepted as statistically significant.

RESULTS

148 patients finished the study. The mean age of the cohort was 42.92 ± 12.78 years. Most of the patients were men (83.1%). The number of patients who experienced spontaneous stone expulsion was 95 (64.2%). The average expulsion interval was 9.35 ± 4.89 days in patients who spontaneously passed the stone. The characteristic features of the patients and the comparison of patients who passed stones and those who failed to pass the stone are summarized in (Table 1). The factors affecting the spontaneous expulsion were examined by univariate and multivariate analyses. The distance of the stone to UVJ, UWT, and NLR were independent predictors of spontaneous passage (Table 2).

Table 1: Demographic data and comparison of characteristics according to stone passage status

Variables	Total n=148	SP+ n=95	SP- n=53	p value
Age, years, mean±SD	42.92±12.78	42.26±13.24	44.11±11.93	0.400
Gender, n,%				0.983
Male	123 (83.1)	79 (83.2)	44 (83)	
Female	25 (16.9)	16 (16.8)	9 (17)	
BMI, kg/m ² , mean±SD	25.45±2.79	25.26±2.66	25.81±3.01	0.250
Stone size, mm, mean±SD	6.51±1.87	5.94±1.78	7.52±1.57	<0.001
Stone burden, mm ² , mean±SD	33.84±21.68	26.95±18.92	46.18±20.97	<0.001
UWT, mm, mean±SD	1.74±0.82	1.41±0.55	2.32±0.91	<0.001
Distance to UVJ, mm, mean±SD	14.15±10.26	12.03±8.76	17.96±11.65	0.002
NLR, mean±SD	1.85±0.73	1.59±0.58	2.32±0.76	<0.001
Hydronephrosis Grade Group, n,%				<0.001
Grade 0.1	62 (41.9)	54 (56.8)	8 (15.1)	
Grade 2.3	86 (58.1)	41 (43.2)	45 (84.9)	

SP:spontaneous passage, BMI:body mass index, UWT:ureteral wall thickness, UVJ:ureterovesical junction, NLR; neutrophil-to-lymphocyte ratio

Table 2: Predictive factors for spontaneous distal ureteral stone passage

Variables	B	S.E.	P value	Odds ratio	95% C.I. for EXP(B)	
					Lower	Upper
Stone Size	-.221	.463	.633	.801	.323	1.987
Stone Burden	.038	.039	.336	1.039	.961	1.122
Distance to UVJ	.047	.022	.036	1.048	1.003	1.095
Ureteral Wall Thickness	1.314	.386	.001	3.720	1.745	7.931
NLR	1.229	.379	.001	3.416	1.625	7.183
Hydronephrosis Grade Group	.912	.544	.094	2.489	.856	7.236

UVJ; ureterovesical junction, NLR; neutrophil-to-lymphocyte ratio

DISCUSSION

Studies questioning the effectiveness of MET have mostly focused on which drug is more successful. A recent meta-analysis showed that

alpha blockers ensure prominent advantages over placebo in the management of distal ureter stones (9). Furthermore, in a meta-analysis study comparing the effectiveness of the three most commonly used alpha-adrenergic blockers as MET, silodosin was shown to be the most effective molecule (10). In a randomized prospective study, the authors concluded that silodosin 4 mg facilitated the expulsion of distal ureteral stones (11). However, patient- and stone-related factors can also affect treatment success in addition to the treatment option. So, we investigated the patient- and stone-related factors affecting spontaneous stone passing in patients who used silodosin as MET. The present study concludes that the distance of stone to the UVJ, UWT, and NLR are independent predictive factors for spontaneous stone expulsion.

The NLR is a biomarker of inflammation. It is commonly used in the prognosis of cancer patients (12). It has been shown that the stone causes ureteral mucosal edema and inflammation during its passage through the ureter (13). Excessive inflammation may reduce spontaneous stone passing by increasing mucosal impaction of the stone. For this reason, some researchers have investigated the significance of inflammation as a predictor of spontaneous stone passage. In the study by Heidar et al. (14), higher NLR was useful for predicting failure of spontaneous passage. Similarly, NLR was inversely associated with spontaneous stone expulsion (15,16). Previous studies on this topic also suggested that C-reactive protein which is another inflammation marker was correlated with the failure of MET (17,18). Our study showed that NLR independently affected the spontaneous stone passage on multivariate analysis.

Stone-related factors including stone size, stone burden, Hounsfield unit (HU), UWT, Framingham score, and presence of hydronephrosis have been investigated as predictive factors for stone passage. The results of studies on stone size and stone burden, which are the most evaluated factors, are controversial. Several investigators found that stone size and stone burden were significantly correlated with spontaneous passage on multivariate analysis (16-19). Conversely, some authors failed to identify this correlation (20-22). Bokka and Jain concluded that HU cannot be used as a

predictor of outcome (23). Nevertheless, Sahin et al. found a significant correlation between HU and spontaneous passage (24). On multivariate analysis, UWT was an independent predictor of stone passing in the majority of studies (16, 19, 20, 22). Mucosal edema and inflammation induced by the stone in the ureteral mucosa may be an important indicator of failure of spontaneous passage. UWT and inflammation markers such as NLR and CRP that show the mucosal edema and inflammation of the ureter could be promising to predict treatment success. Our data suggest that stone size, stone burden, and the degree of hydronephrosis were statistically significant predictors in the univariate analysis. However, this was not confirmed by the multivariate analysis. The distance of stone to the UVJ and UWT were significant predictors of successful passage.

There is a variety of options including conservative therapy, ESWL, or EL to treat the distal ureter stones. MET is an inexpensive and non-invasive treatment given the fact that most ureteral stones pass spontaneously. However, MET has also the risk of complications including infections, colic episodes, and renal function loss. Therefore, it becomes essential to predict situations in which MET may fail and early intervention is needed. For this purpose, a nomogram that contains ureteral mucosal edema and inflammation markers is needed to estimate spontaneous stone passage in the decision-making process.

This study had some limitations. First, it was conducted retrospectively with few patients. Second, we measured the NLR at the beginning of the treatment. Measurements taken during follow-up may be more instructive in the success of MET. Further prospective studies that evaluate patient- and stone-related factors in detail are needed to overcome these limitations. In conclusion, the distance of stone to the UVJ, UWT, and NLR can be useful parameters for spontaneous stone expulsion. These factors play a considerable role in decision-making for the management of distal ureteral stones.

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