

External validation of the medical expulsive therapy stone score (METSS) for predicting spontaneous passage in proximal and mid-ureteral stones

Proksimal ve orta üreter taşlarında medikal ekspulsif terapi taş skoru (METSS) sisteminin dış validasyonu

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Abstract

Purpose: The medical expulsive therapy stone score (METSS) was developed to assess the success of MET in distal ureteral stones. In this study, we aimed to perform an external validation of the METSS to estimate spontaneous passage in patients with proximal and mid-ureteral stones.

Materials and methods: We retrospectively analyzed 62 adult patients with 4-10 mm proximal or mid-ureteral stones treated with medical expulsive therapy (MET) between September 2022 and June 2024. MET consisted of silodosin (4 mg) once daily. Patients were followed weekly for up to four weeks to assess stone passage. METSS scores were calculated, and treatment outcomes were compared.

Results: Spontaneous stone passage occurred in 53.7% of the 54 patients who completed the study. Stone size, stone burden, and the METSS score were significantly associated with treatment outcomes. Patients with lower METSSs had higher stone passage rates. The area under the ROC curve (AUROC) for the METSS was 0.674 ($p=0.029$). The METSS score demonstrated a sensitivity of 76% and specificity of 56%, indicating moderate predictive performance.

Conclusion: The METSS scoring system has a moderate ability to predict the spontaneous passage of proximal and mid-ureteral stones. Nevertheless, it may assist clinicians in making informed decisions between conservative and interventional treatment strategies.

Keywords: Ureteral stone, METSS, silodosin, scoring system, ureterolithiasis.

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Öz

Amaç: Medikal Ekspulsif Terapi Taş Skoru (METSS), distal üreter taşlarında medikal ekspulsif tedavinin (MET) başarısını değerlendirmek amacıyla geliştirilmiştir. Bu çalışmada, METSS sisteminin proksimal ve orta üreter taşlarına sahip hastalarda spontan geçişi öngörme açısından dış doğrulamasını yapmayı amaçladık.

Gereç ve yöntem: Eylül 2022-Haziran 2024 arasında, 4-10 mm boyutlarında proksimal veya orta üreter taşı olan 62 erişkin hastanın verileri retrospektif olarak incelendi. Hastalara günlük 4 mg silodosin içeren medikal ekspulsif tedavi (MET) uygulandı. Taş geçişi açısından hastalar 4 hafta boyunca takip edildi. METSS skorları hesaplanarak tedavi sonuçlarıyla karşılaştırıldı.

Bulgular: Çalışmayı tamamlayan 54 hastanın %53,7'sinde spontan taş geçişi sağlandı. Taş boyutu, taş yükü ve METSS skorları ile tedavi başarısı arasında anlamlı ilişki bulundu. Düşük METSS skoru olan hastalarda taş geçiş oranı daha yüksekti. METSS için ROC eğrisi altında kalan alan 0,674 idi ($p=0,029$). METSS skoru %76 duyarlılık (sensitivite) ve %56 özgüllük (spesifite) ile orta düzeyde bir prediktif performans sergilemiştir.

Sonuç: METSS skora sistemi, proksimal ve orta üreter taşlarının spontan geçişini öngörmeye orta düzeyde prediktif güce sahiptir. Buna rağmen, konservatif ve girişimsel tedavi seçenekleri arasında karar verme sürecinde klinisyenlere rehberlik edebilir.

Anahtar kelimeler: Üreter taşı, METSS, silodosin, skora sistemi, üreterolityazis.

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Introduction

Urolithiasis is a highly prevalent disease with a rising incidence worldwide [1]. The prevalence of ureteral stones in the entire urinary tract is 22% [2]. It is the third most commonly encountered condition in urological practice [3]. Current treatment options for ureteral stones include conservative (observation, medical expulsive therapy [MET]) or interventional approaches (endoscopic lithotripsy, extracorporeal shock wave lithotripsy (ESWL), ureterolithotomy) [4]. MET is a treatment modality used to increase spontaneous stone expulsion and reduce renal colic episodes through relaxation of smooth muscles and a reduction in peristaltic activity. The medications used for MET include alpha blockers, calcium channel blockers, and phosphodiesterase type 5 inhibitors [5]. According to the European Association of Urology (EAU) guidelines, MET facilitates the spontaneous passage of ureteral stones and reduces the need for analgesics [6]. Although the success rate of MET is higher in distal ureteral stones [7], a meta-analysis suggested that alpha blocker treatment accelerates spontaneous passage throughout the ureter [8].

It is crucial to identify which patients would benefit from conservative treatment and which would likely need intervention. With respect to noninvasive ureteral stone treatment, some authors have aimed to devise a scoring system for predicting stone clearance and selecting the best treatment. The medical expulsive therapy stone score (METSS) was developed to assess the success of MET in distal ureteral stones [9]. The authors concluded that a higher METSS indicated lower treatment success. Although several predictive models have been proposed for distal ureteral stones, evidence is limited for stones located in the middle and proximal ureters, which may behave differently due to anatomical and physiological variations. In this study, we hypothesized that the METSS would predict spontaneous passage in proximal/mid-ureteral stones with comparable accuracy to that of distal stones.

Materials and methods

Between September 2022 and June 2024, the data of 62 adult patients presenting with uncomplicated proximal or mid-ureteral stones sized 4 to 10 mm in the largest dimension

and subsequently treated with MET were retrospectively analyzed. This study received ethical approval from the Institutional Review Board of Adnan Menderes University, with reference number 2025/66. Patients who opted for early interventional approaches (n=3), patients with impaired renal function (n=1), multiple or bilateral stones (n=1), a solitary kidney (n=1), urinary tract infections (n=1), or urinary tract anomalies (n=1) were excluded.

The medical history, physical examination, urine analysis, urine culture, blood urea nitrogen and serum creatinine levels, urinary ultrasonography, and X-ray of the kidney, ureter, and bladder (KUB) were carried out for all participants. The diagnosis of ureteral stones was performed via a computerized tomography (CT) scan without intravenous contrast. Patients received silodosin (4 mg) once a day and diclofenac (50 mg) on demand until stone expulsion or a maximum of 4 weeks. All of the patients were advised to filter their urine to capture the stone that passed and drink 2.5 to 3 liters of water daily. They were also warned to report the period of stone expulsion. Patients were monitored on a weekly basis through clinical evaluation, serum creatinine measurements, urinalysis, and X-ray at KUB until either spontaneous stone passage occurred or a maximum follow-up period of four weeks was completed. In cases where stone expulsion remained uncertain or was not achieved by the end of this period, a follow-up CT scan was performed. Treatment failure was defined as radiological evidence of persistent stone presence after four weeks, at which point interventional procedures were recommended.

The demographic data of the patients, including age, sex, comorbidities, and body mass index (BMI), were recorded. Stone-related parameters, such as stone size (SS), stone density using Hounsfield units (HU), ureteral wall thickness (UWT), and ureteral diameter (UD), were measured. A clinician, blinded to the clinical outcomes, evaluated all the CTs separately and calculated the METSS according to the protocol [9]. The METSS is a 10-point predictive tool designed to estimate the likelihood of spontaneous stone passage. Points are assigned on the basis of five radiological parameters: stone size ≥ 6.5 mm (1 point), stone density >1078 Hounsfield units (2 points), ureteral wall thickness (UWT) >2.31

mm (2 points), ureteral diameter (UD) >9.24 mm (3 points), and the presence of periureteral stranding (1 point). Patients are stratified into three risk groups: low (0-3 points), intermediate (4-5 points), and high (6-10 points). The reported MET success rates are 92.8% for the low-risk group, 60.4% for the intermediate-risk group, and 8.3% for the high-risk group. On the basis of these scores, MET is recommended for low-risk patients, with caution and patient counseling for intermediate-risk patients, and active intervention is advised for high-risk patients [9]. Stone locations were classified as the proximal ureter (between the ureteropelvic junction and the sacroiliac joint) or the middle ureter (above the bifurcation of the iliac vessels).

Statistical analysis

Descriptive statistics for continuous variables are presented as the means \pm standard deviations, whereas categorical variables are expressed as frequencies and percentages (n, %). The normality of distribution for continuous variables was assessed via the Shapiro–Wilk test. If the assumption of normality was met, comparisons between groups were performed via Student's *t* test; otherwise, the Mann–

Whitney U test was applied. Differences in categorical variables between groups were analyzed via the chi-square test or Fisher's exact test, as appropriate. All the statistical analyses were conducted via SPSS version 27.0 (IBM Corp., Armonk, NY, USA). A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 54 patients successfully completed the treatment and follow-up period, while 8 patients were lost to follow-up. The mean age of the study population was 42.15 ± 12.19 years. The demographic characteristics and comparisons of patient variables based on stone expulsion status are presented in Table 1. The majority of the included patients were males (94.4%). Treatment success was achieved in 29 out of 54 patients (53.7%). There were no statistically significant differences in age, sex, BMI, or stone location between the groups (Table 1). The stone size and stone burden were significantly associated with stone expulsion success ($p=0.006$ and $p=0.001$, respectively). In patients who achieved spontaneous stone passage, the average time to expulsion was 22 ± 5.7 days.

Table 1. Comparison of patient characteristics based on stone passage status

Variables	Total (n=54)	Spontaneous Passage + (n=29)	Spontaneous Passage - (n=25)	<i>p</i>
Age, years, mean\pmSD	42.15 \pm 12.19	40.28 \pm 10.24	44.32 \pm 14.03	0.228 ^t (t=-1.221)
Sex, n (%)				
Female	3 (5.6%)	2 (3.7%)	1 (1.9%)	0.643 ^x (x ² =0.215)
Male	51 (94.4%)	27 (50.0%)	24 (44.4%)	
Stone location, n (%)				
Proximal Ureter	31 (57.4%)	19 (35.2%)	12 (22.2%)	0.194 ^x (x ² =1.685)
Mid Ureter	23 (42.6%)	10 (18.5%)	13 (24.1%)	
Stone size, mm, mean\pmSD	6.63 \pm 1.75	6.03 \pm 1.61	7.32 \pm 1.67	0.006 ^{t*} (t=-2.867)
Stone burden, mm², mean\pmSD	15.94 \pm 8.38	12.55 \pm 6.29	19.88 \pm 8.87	0.001 ^{t*} (t=-3.535)
METSS, mean\pmSD	3.37 \pm 2.21	2.76 \pm 2.08	4.08 \pm 2.18	0.027 ^{t*} (t=-2.277)
METSS Risk Group, n (%)				
Low	30 (55.5%)	19 (35.2%)	11 (20.4%)	0.122 ^x (x ² =4.210)
Moderate	13 (24.1%)	7 (13.0%)	6 (11.1%)	
High	11 (29.4%)	3 (5.6%)	8 (14.8%)	

METSS: Medical Expulsive Therapy Stone score, SD: standard deviation, t: Student's *t* test, x: Chi-square test (categorical variables)
**p*<0.05 (statistically significant)

The METSS score was significantly higher among patients in the treatment failure group ($p=0.027$). As illustrated in Figure 1, the area under the receiver operating characteristic (AUROC) curve for the METSS score in predicting spontaneous stone passage was 0.674 (95% CI:0.530-0.818; $p=0.029$), indicating modest discriminatory ability. On the

basis of the sensitivity and specificity analysis, a METSS cutoff value of 2.5 yielded a sensitivity of 76% and a specificity of 56%. In terms of drug-related adverse events, headache in 5 patients (9.3%), dizziness in 6 patients (11.1%), orthostatic hypotension in 10 patients (18.5%), and retrograde ejaculation in 12 patients (22.2%) occurred during the study.

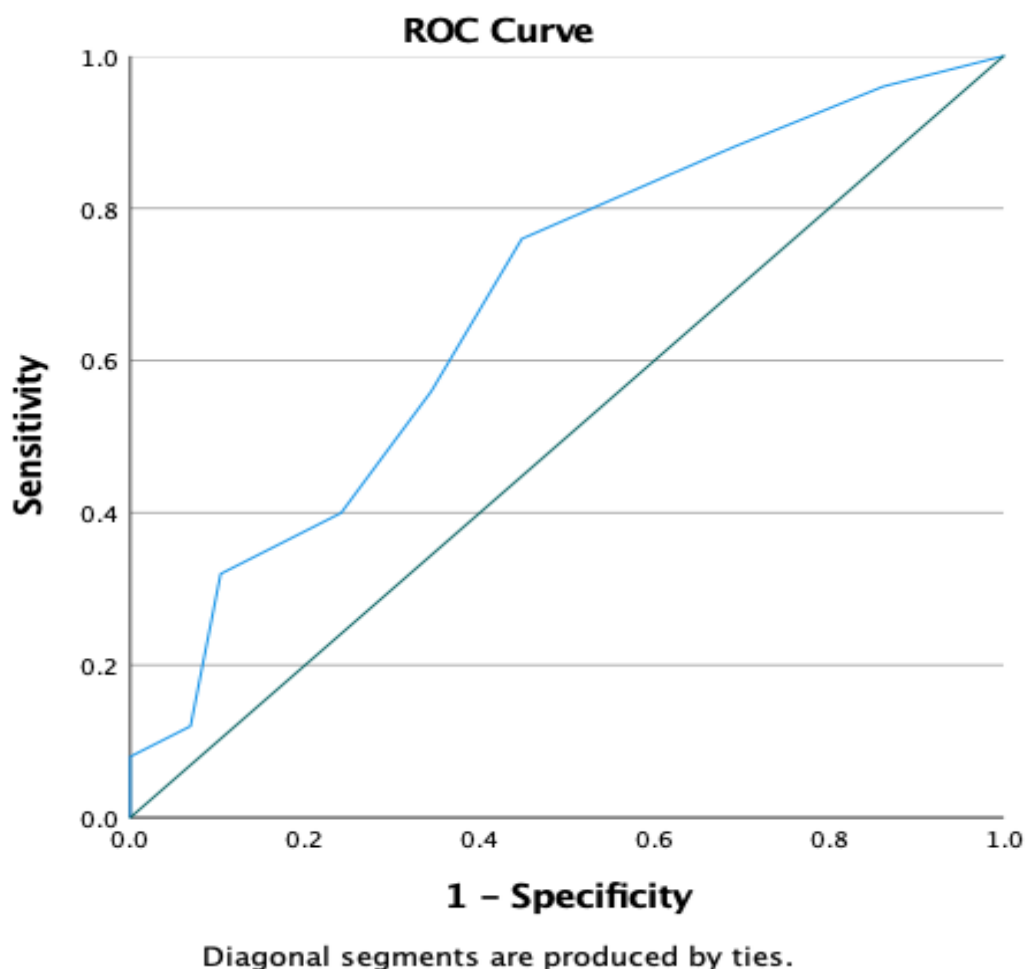


Figure 1. Receiver operating characteristic (ROC) curve illustrating the predictive performance of the METSS score for spontaneous passage of mid- and proximal ureteral stones

Discussion

Medical expulsive therapy is a treatment method that has been shown to facilitate spontaneous stone passage through ureteral stones without the need for invasive procedures. MET includes the use of agents that provide relaxation in the ureter, such as alpha blockers, phosphodiesterase type 5 inhibitors and calcium channel blockers, as well as plenty of fluid

consumption and pain palliation. In the EAU guidelines, alpha blockers are recommended as METs for 5-10 mm distal ureteral stones. Many studies have investigated which treatment is most effective among alpha blockers. Although conflicting results have been reported, a recent meta-analysis revealed that silodosin has greater treatment success [10]. In this study, we prescribed silodosin 4 mg as MET and achieved a stone-free rate (SFR) of 53.7%.

Seventy percent of ureteral stones are detected in the distal ureter [2]. For this reason, most of the studies evaluating the effectiveness of MET have been conducted on distal ureteral stones. SFRs ranging from 51.4% to 95% have been reported [11-14]. However, the success rates of MET for proximal and middle-ureteral stones are promising. In a prospective study, 68 (57.6%) of 118 patients with upper ureteral stones smaller than 10 mm passed spontaneously [14]. In another study, the SFR for proximal and mid-ureteral stones was found to be 50% [15]. In the study of Shah et al. [16], the rate of spontaneous stone passage was 52% in the proximal ureter and 70% in the middle ureter. In a prospective randomized controlled study comparing the effectiveness of tamsulosin and alfuzosin, the spontaneous passage rate for proximal and mid-ureteral stones was reported to be 71.4% in the tamsulosin group and 57.1% in the alfuzosin group [17]. Similarly, a success rate of up to 54.5% has been reported for proximal and mid-ureteral stones, although there are lower rates of stone passage than for distal ureter stones [18]. In a study investigating the location of the ureter stone at the time of diagnosis and the reasons for MET failure, the upper ureter and ureterovesical junction were found to be the most common locations. Although the expulsion rate was greater for distal ureteral stones, binary logistic regression analysis revealed that stone location was not a significant factor in predicting treatment failure [19]. The satisfactory results obtained with MET in upper ureter stones can be explained by the fact that alpha adrenergic receptors are located not only in the distal ureter but also throughout the ureter. Itoh et al. [20] reported that alpha adrenergic receptors were located throughout the entire ureter in patients who underwent nephroureterectomy.

The most important point in the decision-making process is whether to choose conservative or interventional treatment for ureteral stones. Although patients pass their stones at satisfactory rates with MET, predictive factors for treatment failure are needed. At this point, many researchers have investigated predictive factors. While some authors have evaluated stone-related factors such as stone size, stone density, and ureteral wall thickness, others have investigated inflammation markers [15, 16, 22]. Gao et al. [23] developed a

nomogram to predict spontaneous passage. Similarly, Uzun et al. [9] devised the METSS scoring system to predict treatment success in 4-10 mm distal ureteral stones. The authors reported that the SFR was 92.8% in low-risk patients with a METSS score of 0-3. They concluded that MET should be recommended for patients in low-risk groups. Additionally, the authors reported an SFR of 8.3% in the high-risk group with a METSS score of 6-10 and concluded that an interventional method should be recommended for this group. In this study, we performed external validation of the METSS scoring system for 4-10 mm proximal and mid-ureteral stones. The METSS was significantly lower in patients who passed the stone spontaneously. The success rate was 63.3% in low-risk patients, with a METSS ranging from 0 to 3. Although treatment failure is more common in proximal and mid-ureteral stones than in distal ureter stones, MET should be offered to patients in the low-risk group with a METSS. Gao et al. [23] reported a predictive accuracy of 77% in their study. In contrast, our study demonstrated a predictive accuracy of 67%. The lower predictive performance observed in our cohort than in the two previous studies may be attributed to the smaller sample size and the inclusion of patients with proximal and mid-ureteral stones. These factors could have influenced the discriminative power of the METSS score in our population.

This study has several limitations, including the relatively small number of patients, its retrospective nature, and its single-center design, which may limit the generalizability of the findings.

In conclusion, our study demonstrated that the METSS scoring system has a moderate predictive ability in patients with proximal and mid-ureteral stones. While these findings are preliminary, they are nonetheless promising and suggest that the METSS may hold clinical value in this subset of patients. Therefore, further external validation with larger sample sizes and diverse clinical populations is necessary to confirm its broader applicability and reliability.

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