# Can the Hounsfield unit predict the success of medically expulsive therapy?

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## Abstract

**Background:** We investigate the predictability of medical expulsive therapy (MET) success with alpha blockers based on Hounsfield unit (HU) values and Hounsfield density (HD) values measured by computed tomography (CT) for distal ureteral stones.

**Methods:** Between July 2011 and May 2012, 44 patients (19 female and 25 male) with 5- to 10-mm stones in the distal ureters were included in this randomized prospective study. Non-contrast CT examinations were performed in these patients. HU and HD values of stones were calculated. Doxazosine, 4 mg/day orally, was administered as a single dose to all patients for MET.

**Results:** Patients were divided into 2 groups. Group 1 included 18 patients (43.9%) with dropped stones with MET. Group 2 included 23 patients (56.1%) with no stone passage with MET. In Group 1, the mean stone size was 7.7 mm, the mean HU was 507, and the HD was 53.04/mm. In Group 2, the mean stone size was 8.25 mm, the mean HU was 625, and the mean HD was 61.54/mm. The HU and HD values in Group 2 were higher than in Group 1. However, there was no statistically significant difference (p = 0.85 and 0.93 for HU and HD, respectively).

**Interpretation:** We found that HU and HD values cannot be used to predict the chances of success for MET. Although the sample size is appropriate for the study, further comparative studies involving more patients are warranted.

## Introduction

Ureteral stones may cause the ureterohydronephrosis and acute pyelonephritis with pain; patients may need immediate and rapid medical intervention. The size, localization and composition of the stone, severity of the obstruction, symptoms and the anatomy of the urinary system are all involved in determining the proper treatment approach.[1] In this situation with multiple variables, the goal is to achieve stone removal with minimal morbidity. In numerous studies, the size of the ureter stones was the most important factor for spontaneous passage.[2] According to the results of a meta-analysis, the rate of spontaneous passage was 68% for stones with a size <5 mm, while it was 47% for stones with a size >5 mm.[2] These observations justify the use of conservative treatments for stone <5 mm.

Medical expulsive therapy (MET) administered with calcium channel blockers (nifedipine) or alpha blockers increase the chance of spontaneous passage in over 80% of cases for ureteral stones.[3,4] In the review by Hollingsworth and colleagues, the results of MET administered with calcium channel blockers and alpha blockers were evaluated in 9 randomized, controlled studies. When compared with the control groups, these agents caused 65% more spontaneous passage of stones.[5]

In computerized tomography (CT), the Hounsfield unit (HU) is used to assess tissue of body fluid density. According to these density measurements, the density of water is 0, the density of air is (-) 1000, the density of compact bone is (+) 1000, the density of solid organs and soft tissues varies between 10 and 90.[6] In urinary system calculus, HU is useful in assessing the compactness of individual stone. Previous studies conducted on this subject have demonstrated a reverse correlation between the HU and extra corporeal shock wave lithotripsy (ESWL) for stone breakability.[7,8] In addition, it has been shown that the Hounsfield density (HD) value, obtained by dividing the HU value of the stone with its dimensions, can determine the composition of the stones.[9,10]

In our study, we investigate the predictability of MET success with alpha blockers based on the HU and HD values measured by CT for distal ureteral stones.

## Methods

Following approval of the study by the local ethics committee, we prospectively randomized 44 patients (19 female and 25 male) between July 2011 and May 2012 and included

them in the study. We performed a detailed physical examination and medical history in patients with 5- to 10-mm stones in the distal ureters. We performed serum urea-creatinine, sodium, potassium, chlorine, calcium and uric acid measurements, along with urinalysis and urine culture.

Within the context of the study, plain x-ray and non-contrast CT (NCCT) examinations were performed with a 64-MDCT unit (LightSpeed VCT XTe, GE Electric Company). Transverse images were obtained with a slice thickness of 1.25 mm and an interval of 1.5 mm at 120 kV. The longest stone size by measurement on NCCT was used, and we measured stone density (HU) and location by using NCCT images in the bone window. Three transverse planes were defined in each stone (near the top, in the middle, and near the bottom). One region of interest (ROI) was obtained in each plane and absolute HU value was determined by calculating the mean of the 3 ROI. In addition, we examined the HD of the stones (the value obtained for the longest transverse section of the calculi with the HU), the thickness of renal parenchyma and the severity of hydronephrosis.

We excluded patients with urinary system infections, history of ureter or bladder surgeries, anatomical urinary system anomalies or solitary kidneys, vesicoureteral reflux, neurogenic or non-neurogenic bladder diseases, bilateral ureter stones or additional kidney stones, severe hydronephrosis, usage of diuretics and/or calcium channel blockers and previously identified hypersensitivity to doxazosine.

Doxazosine, 4 mg/day orally, was administered as a single dose to all patients in the study. In cases of accompanying pain, patients were recommended to take diclofenac, 25 mg orally 3 times a day, with 8-hour intervals at most after meals. Patients were requested to maintain their daily fluid intake between 1500 and 2000 cc. The study period was 4 weeks maximum. Within these 4 weeks, the termination criteria were defined as dropping the stone, the occurrence of side effects associated with the medication (hypertension, vertigo, allergic reactions, etc.), increases in the symptoms of patients and the occurrence of urinary tract infections.

During the study period, patients came for weekly visits. During these control visits, the possible side effects of medication, the symptoms, quantity of analgesics usage and the arterial blood pressure measurements were noted. Serum urea-creatinine, urinalysis, urine culture and plain X-ray graphy were performed again.

Statistical evaluation of the differences between the 2 groups was performed using the Wilcoxon rank test, and values with a $p < 0.05$ were considered statistically significant.

## Results

During the study period, 2 female patients (due to increase in symptoms and hypotension) and 1 male patient (due to the urinary tract infection) were excluded from the study. The mean age was 47.8 (range: 24-66) years. Eighteen patients (43.9%) with dropped stones formed Group 1, and 23 patients (56.1%) with no stone passage formed Group 2. Between these 2 groups, no statistically significant difference was identified ($p > 0.05$) with regards to age, sex, and average calculus size.

In Group 1, the mean stone size was 7.7 mm, the mean HU was 507, and the HD was 53.04/mm. The mean time to stone passage was 8.44 (6-14) days. In Group 2, the mean stone size was 8.25 mm, the mean HU was 625, and the mean HD was 61.54/mm. In Group 2, the stone was removed by ureteroscopic lithotrophy and/or ESWL. The HU and HD values in Group 2 were higher than in Group 1. However, no statistically significant difference was identified ($p = 0.85$ and 0.93 for HU and HD, respectively). The quantity of analgesics usage was 33 mg/day in Group 1, and 41 mg/day in Group 2 ($p = 0.65$). We tallied study, demographic and clinical data (Table 1).

## Discussion

The conservative treatment approach for ureter stones may be used in the absence of infection, severe obstruction, and acute severe cholic pain. Previous studies have demonstrated a 71% to 98% probability of spontaneous passage for distal ureter stones with a size <5 mm. The size and localization of the stones are the two most significant determinant factors for spontaneous passage.[2,11,12]

When reviewing the literature, we found that hormones (glucagon and prostoglandines), calcium channel blockers, nonsteroidal anti-inflammatory drugs, corticosteroids and alpha adrenergic blockers are used for MET. However, among the medications used for MET, calcium channel blockers and alpha blockers are now generally preferred. In fact, many randomized clinical studies have demonstrated safe and effective use of these medications.[3-5,13]

However, there is no standard regarding the length of time for which MET should be continued. An average period of 4 weeks (range: 1-7 weeks) was described in studies involving alpha blockers. During the 4-week follow-up, the following side effects may occur: cholic episodes, side effects associated with used medications (i.e., hypotension, vertigo, somnolence) increase in severe hydronephrosis and acute pyelonephritis.[14] In a prospective, randomized and controlled study, Chau and colleagues evaluated 79 patients; in 4 patients they found an urgent need for urinary diversion; in 2 patients an alpha blocker (alfuzosine) intolerance; and 6 patients withdrew from the study due to non-attendance in follow-up visits.[15] In Ye and colleagues' multicentered, prospective and randomized study, tamsulosine and nifedipine usage in MET were compared; a 5.62% and 6.16% rate of side effects were reported for both medications, respectively.[16] In our study, 3 patients (6.8%) had

**Table 1. Patient demographics and clinical data**

| | Group 1 (n=18) | Group 2 (n=23) | *p* value |
|---|---|---|---|
| Age, mean (range), years | 39.3 (31–49) | 53.12 (24–61) | |
| Male/female | 11/7 | 13/10 | |
| Mean stone size, mm (range) | 7.7 (5–10) | 8.25 (5–10) | 0.31 |
| Mean Hounsfield unit | 507 (340–650) | 625 (270–1180) | 0.85 |
| Mean Hounsfield unit density (HU/mm) | 53.04 (36.12–90) | 61.54 (34–137.5) | 0.93 |
| Mean analgesic dosage (mg/day) | 33 | 41 | 0.65 |

their treatments interrupted and were withdrawn from the study due to complications or side effects associated with medications. In our study, the HU and HD values for ureter stones were evaluated to determine whether these could be used to predict, prior to treatment, the chances of success with MET. The intention was to protect patients from potential side effects, by preventing treatment if chances of success with MET were determined as low. However, no statistically significant difference was identified between the stones HU and HD values and stone expulsion.

Previous studies have demonstrated the use of HU in predicting the breakability of kidney and ureter stones by ESWL. In the study by Wiesenthal and colleagues, the HU and HD values were 766.7 and 19.3/mm$^2$, respectively, for the group with stones broken by ESWL, while the HU and HD values were 862.7 and 14.1/mm$^2$, respectively, for the groups with no stones broken ($p = 0.02$ and $p < 0.01$, respectively). In this study, it was emphasized that the HU value along with the measurement of the skin-stone distance were 2 strong predictors in demonstrating breakability of kidney and ureter stones by ESWL.[17] In the study by Perks and colleagues, the rates of breaking by ESWL were compared for urinary stones between 5 and 20 mm. The authors found that stones were broken in 46% of patients with a HU value <1000, and in 17% of patients with a HU value of >1000. Hence, an inverse correlation between the HU value (which measures the compactness of the stones) and the ESWL success rate was demonstrated.[18]

An interesting area of use for the HU value is in predicting the composition of calculus in urinary systems. In Demirel and Suma's study on this topic, the calculus of 87 patients were assessed. They found that the highest HU values belonged to calcium oxalate (Ca-Ox) stones (812±135), that the second highest values belonged to stuvite stones (614±121) and that the lowest values belonged to uric acid stones (413±143). This difference was statistically significant ($p < 0.05$).[10] Moreover, with either pure or mixed calculus, higher HU values were observed for stones with higher calcium content (Ca-Ox monohydrate having the highest HU value among them).[10] For the other substances, the sequence with decreasing HU value was as follows: cystine stones, struvite, and uric acid stones.[19]

MET is performed with alpha blockers and calcium channel blockers to fasten the spontaneous passage of ureteral stones. It has become the standard approach for patients with no indications for active stone expulsion and for stones of with a size <10 mm. Furthermore, it has been demonstrated that MET can assist with removing stones following ESWL, or with cleaning residues following ureteroscopy. It has also been shown to decrease the need for analgesics and the frequency of cholic episodes.[20,21] In addition to the size of the stones, factors that can predict the chances of success of MET are: the condition of the renal reserve, the severity of mucosal odema-inflammation and the anatomic structure of the urinary system.[20,21]

In our study, the usability of the HU value in predicting MET success was investigated. Our expectation prior to conducting the study was that calculus with higher HU values would be more compact. We expected that such compact calculus would advance more slowly and with greater difficulty from the ureter lumen to the ureteral peristaltism. Based on our data, the HU and HD values of Group 2 was higher than the HU and HD values of Group 1 (for group 2 and 1 respectively: HU: 625 and HD: 61.54/mm, and HU: 507 and 53.04/mm). However, the differences between the 2 groups were not statistically significant.

The limitations of our study included the lack of analysis of the composition of expulsed stones and stones, which could not be passed by MET and were removed endoscopically. The literature mentions that a mixture in calculus composition can affect HU values.[19] When considered from this perspective, it may be possible to identify a statistically significant difference between the HU value and MET with calculus of pure composition. Although the sample size is appropriate for this study, future studies with more patients are needed.

## Conclusion

Our results indicate that HU and HD values cannot be used to predict the chances of success with MET. There is a need to performed further comparative studies involving more patient groups and the chemical analysis of the expulsed stone.

**Competing interests:** Dr. Erturhan, Dr. Bayrak, Dr. Mete, Dr. Seckiner, Dr. Urgun and Dr. Sarica declare no competing financial or personal interests.

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## References


1. Lingeman JE, Matlaga BR, Evan AP. Surgical Managemen: *Campbell's Urology*, 9th ed. Philadelphia, WB Saunders; 2007:2661-733.
2. Preminger GM, Tiselius HG, Assimos DG, et al. American Urological Association Education and Research, Inc; European Association of Urology. 2007 Guideline for the management of ureteral calculi. *Eur Urol* 2007;52:1610-31. http://dx.doi.org/10.1016/j.eururo.2007.09.039
3. Saita A, Bonaccorsi A, Marchese F, et al. Our experience with nifedipine and prednisolone as expulsive therapy for ureteral stones. *Urol Int* 2004;72:43-5. http://dx.doi.org/10.1159/000076591
4. Porpiglia F, Ghignone G, Fiori C, et al. Nifedipine versus tamsulosin for the management of lower ureteral stones. *J Urol* 2004;172:568-71. http://dx.doi.org/10.1097/01.ju.0000132390.61756.ff
5. Hollingsworth JM, Rogers MA, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet* 2006;368:1171-9. http://dx.doi.org/10.1016/S0140-6736(06)69474-9
6. Hoffer M. *CT Teaching Manuel.* Verlag, Berlin: Springer; 2007.
7. Pareek G, Armenakas NA, Fracchia JA. Hounsfield units on computerized tomography predict stone-free rates after extracorporeal shock wave lithotripsy. *J Urol* 2003;169:1679-81. http://dx.doi.org/10.1097/01.ju.0000055608.92069.3a
8. Weld KJ, Montiglio C, Morris MS, et al. Shock wave lithotripsy success for renal stones based on patient and stone computed tomography characteristics. *Urology* 2007;70:1043-6. http://dx.doi.org/10.1016/j.urology.2007.07.074
9. Motley G, Dalrymple N, Keesling C, et al. Hounsfield unit density in the determination of urinary stone composition. *Urology* 2001;58:170-3. http://dx.doi.org/10.1016/S0090-4295(01)01115-3
10. Demirel A, Suma S. The efficacy of non-contrast helical computed tomography in the prediction of urinary stone composition in vivo. *J Int Med Res* 2003;31:1-5. http://dx.doi.org/10.1177/147323000303100101
11. Ibrahim AI, Shetty SD, Awad RM, et al. Prognostic factors in the conservative treatment of ureteric stones. *Br J Urol* 1991;67:358-61. http://dx.doi.org/10.1111/j.1464-410X.1991.tb15161.x
12. Miller OF, Kane CJ. Time to stone passage for observed ureteral calculi:a guide for patient education. *J Urol* 1999;162:688-90. http://dx.doi.org/10.1097/00005392-199909010-00014
13. Dellabella M, Milanese G, Muzzonigro G. Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. *J Urol* 2003;170:2202-5. http://dx.doi.org/10.1097/01.ju.0000096050.22281.a7
14. Singh A, Alter HJ, Littlepage A. A systematic review of medical therapy to facilitate passage of ureteral calculi. *Ann Emerg Med* 2007;50:552-63. http://dx.doi.org/10.1016/j.annemergmed.2007.05.015
15. Chau LH, Tai DC, Fung BT, et al. Medical expulsive therapy using alfuzosin for patient presenting with ureteral stone less than 10mm: a prospective randomized controlled trial. *Int J Urol* 2011;18:510-4. http://dx.doi.org/10.1111/j.1442-2042.2011.02780.x
16. Ye Z, Yang H, Li H, et al. A multicentre, prospective, randomized trial: comparative efficacy of tamsulosin and nifedipine in medical expulsive therapy for distal ureteric stones with renal colic. *BJU Int* 2011;108:276-9. http://dx.doi.org/10.1111/j.1464-410X.2010.09801.x
17. Wiesenthal JD, Ghiculete D, D'A Honey RJ, et al. Evaluating the importance of mean stone density and skin-to-stone distance in predicting successful shock wave lithotripsy of renal and ureteric calculi. *Urol Res* 2012;38:307-13. http://dx.doi.org/10.1007/s00240-010-0295-0
18. Perks AE, Gotto G, Teichman JM. Shock wave lithotripsy correlates with stone density on preoperative computerized tomography. *J Urol* 2007;178:912-5. http://dx.doi.org/10.1016/j.juro.2007.05.043
19. Deveci S, Coşkun M, Tekin MI, et al. Spiral computed tomography: role in determination of chemical compositions of pure and mixed urinary stones–an in vitro study. *Urology* 2004;64:237-40. http://dx.doi.org/10.1016/j.urology.2004.03.029
20. Naja V, Agarwal MM, Mandal AK, et al. Tamsulosin facilitates earlier clearance of stone fragments and reduces pain after shockwave lithotripsy for renal calculi; results from an open-label randomized study. *Urology* 2008;72:1006-11. http://dx.doi.org/10.1016/j.urology.2008.05.035
21. John TT, Razdan S. Adjunctive tamsulosin improves stone free rate after ureteroscopic lithotripsy of large renal and ureteric calculi: a prospective randomized study. *Urology* 2010;75:1040-2. http://dx.doi.org/10.1016/j.urology.2009.07.1257


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