Original Article
Özgün Araştırma

Endourol Bull. 2023;15(2):38-45. doi: 10.54233/endouroloji.20231502-1224856

In Vivo Evaluation of The Chemical Composition of Urinary Stones Using Non-Contrast Helical Computerized Tomography

İdrar Taşlarının Kimyasal Bileşiminin Kontrastsız Helikal Bilgisayarlı Tomografi ile In Vivo Değerlendirilmesi

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ÖZET

Amaç: Düşük doz helikal bilgisayarlı tomografi kullanılarak böbrek taşlarının yoğunluğunun ve kimyasal yapısının belirlenmesi.

Gereç ve Yöntemler: Çalışmamıza; böbrek taşı nedeniyle ekstrakorporeal şok dalga litotripsisi (ESWL) yapılacak veya üriner sistem taş cerrahisi geçirmesi planlanan, böbrek veya üreter taşı olan 79 hasta dahil edildi. Tüm taş yoğunlukları, Hounsfield Ünite olarak düşük doz abdominal kontrastsız helikal bilgisayarlı tomografi incelemesi ile ölçüldü. Bilgisayarlı tomografi incelemesi için 4 dedektörlü Marconi MX 8000 sistemi kullanıldı. Tüm taşların analizlerinde X-Ray difraktometri kullanıldı.

Bulgular: Taş tipi 52 hastada tek tip ve 27 hastada mikst taş olarak bulundu. Karışık taşlar içinde en büyük grubu, 17 hasta ile kalsiyum oksalat monohidrat-dihidrat taşları oluşturdu. Ürik asit taşları en düşük, kalsiyum oksalat monohidrat taşları en yüksek yoğunluğa sahip olarak bulundu. Ürik asit ve sistin taşlarının dansite değerleri ile diğer taş çeşitleri arasındaki fark istatistiksel olarak anlamlıydı.

Sonuç: Teşhiste kullanılan kontrastsız helikal bilgisayarlı tomografi, taş kompozisyonunun in vivo tayininde de kullanılabilir. Uygun terapötik alternatifler sağlamak için görüntüleme çalışmaları ile taş kompozisyonlarını tanımlamak çok yardımcı olabilir.

Anahtar Kelimeler: *taş, yoğunluk, tomografi, sarmal, hounsfield ünitesi*

Cite As: *Karabacak OR, Sandıkçı F, Saltas H, Dilli A, Zengin K, Yalçınkaya F, Ayaz ÜY. In Vivo Evaluation of The Chemıcal Composition of Urinary Stones Using Non-Contrast Helical Computerized Tomography. Endourol Bull. 2023;15(2):38-45. doi: 10.54233/endouroloji.20231502-1224856*

This study was approved by the University of Health Sciences, Ankara Yıldırım Beyazıt Dışkapı Education and Research Hospital Ethical Committee (Approval Number: 34, Date: 2009-06-30). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

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Received : December 27, 2022 ***Accepted*** : May 20, 2023

ABSTRACT

Objective: To determine the density and chemical structure of renal stones by using in vivo low dose helical computerized tomography (CT).

Material and Methods: 79 patients with urinary stones such as renal or uretheral stones were included in our study who were going to have extracorporeal shock wave lithotripsy (ESWL) or planned to go through urinary stone surgery due to renal stones. All stone densities were measured in Hounsfield Unit by low dose abdominal non-contrast helical computed tomography examination. Marconi MX 8000 CT system with 4 detectors was used for the CT examination. X-Ray diffractometry was used in the analyses of all stones.

Results: The stone type was found to be pure type in 52 patients, and mixed stone in 27 patients. The largest group among the mixed stones included whewellite stone with 17 patients. Uric acid stones had the smallest, whewellite stones had the highest density. The difference between the density values of uric acid and cystine stones and the other stone types were statistically significant.

Conclusion: Non-contrast helical computed tomography used in the diagnosis can also be used in the in vivo determination of the stone composition. It can be very helpful to define stone compositions by imaging studies to provide suitable therapeutic alternatives.

Keywords: *stone, density, tomography, helical, hounsfield unit*

INTRODUCTION

Urolithiasis is an important health problem that affects all societies. Its prevalence and incidence have been increasing worldwide (1). Thus, along with the diagnosis and treatment of urolithiasis, the prevention of recurrences should also be considered. One of the most important parameters in the assessment of the urolithiasis patients is the determination of the stone composition. Information about the chemical structure of the stone guides non-invasive, minimal treatment approaches. Stone analysis is generally performed after stone extraction. However, determination of in vivo stone composition is also important for some groups of patients, e.g. extracorporeal shock wave lithotripsy (ESWL), patient evaluation. In vivo stone composition determination has been a recent procedure, predominantly done using helical computed tomography (CT) (2). Several studies on in vitro and in vivo stone composition determination have reported that non-contrast helical CT (NCHCT), which is currently the mainstay of stone diagnosis, can be used to predict the mineral type of urinary stones on the basis of their attenuation coefficient (3). With this, it is possible to predict the stone type, and to direct the treatment to break the stone before ESWL, performing chemoprophylaxis, evaluating the patients, and managing diet. We aimed to determine in vivo chemical structure of urinary stones using NCHCT, and to correlate our results with x-ray diffractometry results.

MATERIAL AND METHODS

Between 2010 and 2013, 79 patients suffering from stone diseases with urinary stones such as renal or uretheral stones were included in the study conducted prospectively. First of all, patients were informed about the planned study. Afterwards, the study was initiated after "obtaining informed consent" from the patients. The study ethics approval was obtained from the ethics committee of the University of Health Sciences, Ankara Yıldırım Beyazıt Dışkapı Training and Research Hospital, "Ethics declarations date and number: 30.06.2009-34". The patients were planned to be treated with ESWL or percutaneous stone surgery at our clinic.

For all patients, pre-operative preparation was applied including blood count, and urine analysis, coagulation parameters, and biochemistry. Biochemistry included glucose, urea, creatinin, alanine aminotransferase, aspartate aminotransferase analyses. Metabolic evaluation was utilized in the stonelessness periods of the patients. Also, plain abdominal graphy, abdominal CT, and when necessary renal ultrasonography was performed preoperatively. Patients having renal stones of sizes ≥5 mm (5-37 mm) were included in the study. Ultrasonography and/or plain abdominal graphy were applied for stone diagnosis. Philips MX 8000, 4-detector helical CT was used for stone localization and stone density determination. Technical parameters for enhanced abdominal scan were as follows: Pitch values 1.75/1, reference tube current 80 mA, tube voltage 120 kVp, slice thickness 1.6 mm, and acquisition slice thickness 3.2 mm. The dose used in stone protocol was 5.5 mGy which is 9.3 mGy in routine abdominal CT. For each stone, Hounsfield unit (HU) measurements were taken from the largest possible area for each stone determining a region of interest. Measurements were taken in bone window from three different regions from the stone center and the adjacent regions with the cross sections increased 4 times. The HU value which was the average of the three measurements was considered as base for the study. The impact of stone size on the accuracy of the measurement of stone density was evaluated using the largest sample group, calcium oxalate monohydrate (COM) stones (n=37) which were grouped into three as 5-14 mm, 15-25 mm, and >25 mm in diameters. Stone analysis was performed with Philips PW 3710/1830 X-Ray diffractometry device at 2.5-40^{o}.

Inclusion and Exclusion Criterias

The treatment methods that we can obtain fragmented stones are ESWL and percutaneous nephrolithotomy (PCNL). Due to the necessity of stone analysis, patients who underwent ESWL and PCNL were included in our study. Stone fragments are difficult to obtain in patients undergoing RIRS, as the stone fragments are dusted. Therefore, these patients were not included in the study. Patients with contraindications for ESWL and PCNL treatment such as pregnancy, bleeding diathesis, skeletal deformity, arterial aneurysm in close proximity to the stone, and kidney tumor were excluded from the study. Stones smaller than 5 mm and bladder stones were also excluded from the study. After ESWL and PNL treatment, patients with stone analysis results were included in the study.

Statistical Analysis

Data was analyzed using SPSS 15.0 version. X-ray attenuation mean values of the stone types were compared in HU using Kruskal Wallis (test was applied due to lack of Normal distribution and common/same variance assumptions) and for comparsion aim of the results One-way ANOVA tests at 95% confidence level was also applied. And non-significant correlation between stone size and density in COM stones was found out by using Spearman test. The correlation between Maximum Density and Mean Density was evaluated using regression model.

RESULTS

Mean age of 79 patients was 44 (6-78), of whom 46 were male and 33 female, with stone diseases such as renal or ureteral stones. We classified the urinary stones obtained into two groups according to their chemical composition as pure and mixed stones (Table 1). Pure stone group included five types: COM, Calcium oxalate dihydrate (COD), cystine, struvite, and uric acid. Mixed stone group included four types: COM-CaP (COM-Calcium phosphate), COM-COD, and COM-whitlockite. In the evaluation of the stone densities, uric acid stone had the lowest density, whereas COM-whitlockite stone had the highest (Table 1).

The analysis of x-ray attenuation values revealed that the densities of cystine and uric acid stones were significantly different than the other stone types whereas there was no difference between the densities of cystine and uric acid stones. No statistically significant difference was observed between the densities of COM, COD, and struvite stones (Table 2). Since the components of the mixed stones may affect the density of the stone, they were not included in the comparison.

The effect of stone size on density was evaluated in the largest group COM stones, and no difference was found between the density values according to the stone size. There was not any significant correlation between stone size and stone density in the regression analysis. However, there was a linear correlation between maximum density and mean density which was %88.5 (Figure 1). The significance of the regression model was shown using ANOVA test (Table 3).

Table 1. Stone type and density

Pure Stone	n	Mean Density (HU)	Min.-Max. Density (HU)	Mixed Stone	Mean Density (HU)	n	Min.-Max. Density (HU)
COM	37	945	715-1420	**whewellite-Weddellite**	804	17	730-1339
COD	3	811	742-1210	**whewellite-Uric acid**	804	5	475-1117
Uric acid	5	414	359-645	**whewellite-Dahlite**	1068	3	1035-1285
Cystine	5	523	412-810	**whewellite-Whitlockite**	1247	2	830-1540
Struvite	2	915	840-1140				
Total	**52**					**27**	

HU; Hounsfield unit, ***COM;*** calcium oxalate monohydrate, ***COD;*** calcium oxalate dihydrate,

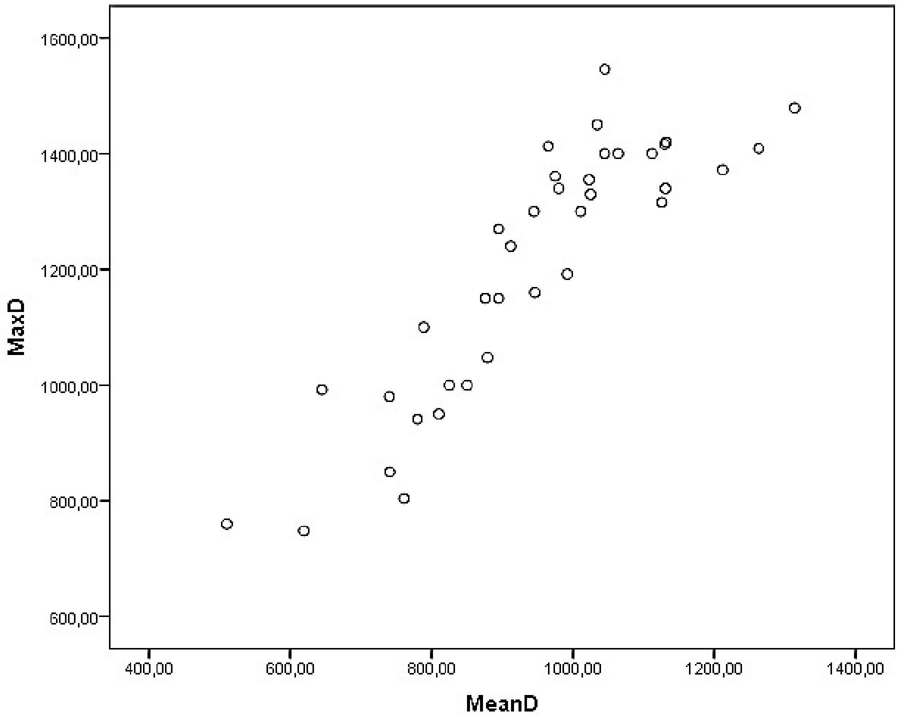
Table 2. Mean differences between stone types in Hounsfield Units

Stone Type	Stone Type Compared	Mean Difference	p
whewellite	Weddellite	134.86486	0.634
	Uric acid	531.86486	0.000
	Cystine	422.86486	0.000
	Struvite	30.86486	0.999
Weddellite	whewellite	-134.86486	0.634
	Uric acid	397.00000	0.012
	Cystine	288.00000	0.121
	Struvite	-104.00000	0.954
Uric acid	whewellite	-531.86486	0.000
	Weddellite	-397.00000	0.012
	Cystine	-109.00000	0.821
	Struvite	-501.00000	0.005
Cystine	whewellite	-422.86486	0.000
	Weddellite	-288.00000	0.121
	Uric acid	109.00000	0.821
	Struvite	-392.00000	0.042
Struvite	whewellite	-30.86486	0.999
	Weddellite	104.00000	0.954
	Uric acid	501.00000	0.005
	Cystine	392.00000	0.042

Table 3. HU density values of whewellite stones according to stone size.

Stone Size (mm)	n	Max. Density (HU)	Mean Density (HU)
5-14	16	1160.5	910.3
15-25	13	1175.8	913.1
>25	8	1353	1070
p		p=0.104	p=0.082
Total	37	1207	945.8

Figure 1. Linear correlation between maximum density and mean density values of whewellite stones



DISCUSSION

The chemical structure of the stone determines the stone fragmentation by different techniques such as ESWL and laser (4-6). COM and cystine stones are resistant to breakage whereas COD and uric acid can easily be fragmented. Until recently, the stone composition has been determined after the stone was extracted. However, knowing the stone composition before treatment would be to the benefit of both the patient (for preventing the suffering), and the clinic (for saving time and budget) (7). NCHCT has high sensitivity, it is performed in vivo with low dose radiation, and provides information about the chemical composition of the stone preoperatively (6,8). For these reasons, it replaced the excretory urography (9). It is seen in literature that the studies have been conducted both in vivo and in vitro. The studies conducted using NCHCT have continued with dual energy CT.

Demirel and Suma applied NCHCT to 160 patients with acute flank pain to clarify the presence of urinary stone, and to determine the chemical composition of the stone (10). They reported that the highest density was seen in calcium oxalate (CaOx) stones which were followed by struvite and uric acid stones. Since there were not any cystine or brushite stones in their study, they did not comment on those. They concluded that the stone compositions could be distinguished on the basis of their HU densities. In our study, the highest density was found in COM-whitlockite, a mixed stone. The highest density in pure stones was measured in COM stone. The densities of pure stones were as COM>struvite>COD>cystine >uric acid.

El-Assmy et al. (11) scanned stones obtained from patients using 80 kV and 120 kV, determined the densities for chemical composition, and fragmented the stones in vitro by shock wave lithotripsy. They evaluated the correlations between HU density and fragmentation. They found statistically significant difference between uric acid and COM, struvite and mixed stones. They did not find any significant difference between struvite and COM, and mixed stone, and concluded that dual CT did not contribute to what have already been known. In our study with in vivo NCHCT, we did not find any statistically significant difference between the density values of uric acid and cystine stones and other stones which is consistent with the results of El-Assmy et al. The advantage of our study is that since it is in vivo, it can be used in the diagnosis and programming of the treatment.

In the stone composition determination with tomography, use of dual CT different from NCHCT is quite common with a considerably large literature. Hidas et al. (12) used in vivo dual CT in their study in which they determined three pure stone types as uric acid, cystine, and CaOx. According to the x-ray diffractometry and tomography results, there was correlation in calcium and uric acid stones, whereas no correlation was found in the cystine stones. From this finding, it can be concluded that the accurate results obtained for the determination of CaOx and uric acid stones are not true for the determination of the cystine stone. Our study revealed that the densities of the uric acid and cystine stones were significantly different than the other stone types. When comparing the uric acid and cystine stones, no significant difference was found between their densities. We found the densities from the lowest to the highest HU value as uric acid<cystine<struvite<CaOx. This is similar to the results of Hidas et al. except that our method is more advantageous for the reasons that the patients are exposed to less radioactive beam, and the method has low cost because the evaluations are made using the CT which is originally used for diagnostic purposes.

Wisenbaugh et al. (13) evaluated the urinary stones using conventional and dual CT, and found that the HU values of the uric acid stones were significantly different than that of CaOx, and the HU values of cystine, struvite and CaOx stones overlapped. Thus, it could be suggested that the accurate determination of all urinary stones except uric acid may not be possible with dual CT similarly with the NCHCT used in our study. Unlike Wisenbaugh et al, Erdogan et al. (14), who also used dual-energy CT, for invivo analysis of urinary. Dual-energy CT analysis results are compared with in vitro stone analysis results, the stone types could be predictable correctly in 32 (91.4%) patients and detected incorrectly in 3 (8.6%) patients. Especially uric acid and cystine stones were predictable by 100% sensitivity, specificity, and diagnostic accuracy rate. Although it shows that dual CT is superior due to its high predictive rating, its excessive radioactive exposure and cost-effectiveness make it difficult to choose Dual CT.

Mostafavi et al. (15) reported that single-energy CT at 120 kV is efficient in differentiating the most common type of stones (struvite, cystine, and calcium oxalate) whereas dual-energy CT is needed to differentiate the stones with similar densities. They were able to determine the chemical composition of pure stones and found the attenuation values to range from 409 HU for uric acid and 1703 HU for brushite. In our study, the lowest density was 359 HU in uric acid stones, and the highest density was 1546 HU in a mixed stone composed of COM and whitlockite which is a phosphate stone. Similar to a number of studies, our study did not reveal any cystine stone with HU density value of 1000 or higher from which it could be concluded that during the evaluation of the cystine stone it should be kept in mind that its density does not exceed 1000 HU (16,17). In our study, 80% of uric acid stones and 60% of cystine stones had the attenuation values lower than 600 HU, and 20% of uric acid stones and 40% of cystine stones had the attenuation values between 600 and 900 HU.

Grosjean et al. (18) examined the attenuation values of 241 urinary stones in 4 different CT scanners and showed significant differences in CT attenuation values in different voltages in different scanners. Thus, it should be kept in mind that the data obtained at a particular center for the stone composition are the data obtained from that center's CT scanner and have similar collimation values. Our study was carried out using a single machine and same technical features (e.g. collimation and slice values), thus the HU values obtained could be considered as specific to our clinic.

Urinary stones with the same compositions may have different densities. The reason for this may be the use of different CT equipment, degree of collimation, energy setting, and stone size (4, 19). In the evaluation of stone densities using CT, stone composition and slice ranges are considered to be more important than the stone size (20). Stewart et al (21), in their study where they examined the relationship between the stone size and stone composition using HU, found that the stone size limits the determination of the stone composition. In our study, we kept the CT slice range constant, and evaluated Caox stone densities according to stone size only. We found that although there was an increase in the max and mean densities with the increase in stone sizes, the correlation between the densities of stones and stone sizes was statistically insignificant.

It is also difficult to do classification in mixed stones because of the probability of density overlap as the dominant component changes the density of the mixture. We found the density range of the mixed stones between 730 and 1546 HUs. COM-phosphate stone had the highest density, while COM-uric acid stone had the lowest density due to the influence of uric acid. Thus, the identification of the stone types in mixed stones by tomography is difficult. In the present study, there was no statistically significant difference among the densities of the mixed stones.

In these studies, the most powerful decision can be made about the uric acid stones whereas it is difficult to differentiate the other stone types. In our study conducted in vivo using 120 kV, uric acid stones were successfully differentiated from the CaOx stones. We believe that the low dose helical CT is more feasible than dual CT for the prevention of patients from higher doses of radiation. Besides, helical CT has an advantage as it can be used in both diagnosis and the programming of the treatment.

Limitations

Stone analyzes are performed by patients at a different institution upon their own application. This limits the number of patients included in the study. It is known that CT attenuation values are different at different voltages with different devices. Therefore, different devices and larger number of patients may affect the results of our study. It is also difficult to classify mixed stones as the dominant component changes the density of the mixture. Therefore, it is difficult to determine the stone types by tomography in mixed stones. In such studies, the increase in mixed type stones affects the data of the study.

CONCLUSION

Our results suggest that the NCHCT performed for diagnostic purposes can also be used for the determination of the chemical composition of the stone. For some stone types, the limitations of both methods (dual CT and helical CT) are similar in the accurate determination of the stone composition. The NCHCT, which is used for diagnostic purposes, is more advantageous as it does not put an additional cost, produce similar results with other tomography methods such as dual CT, prevents higher doses of radiation exposure, and saves time.

Abbreviations:

CT	: Computerized tomography
COM	: Calcium oxakate monohydrate
COD	: Calcium oxalate dihydrate
CaOx	: Calcium Oxalate
CaP	: Calcium phosphate
ESWL	: Extracorporeal shock wave lithotripsy
HU	: Hounsfield unit
NCHCT	: Non contrast helical computerized tomography

Conflict of Interest: The authors declare to have no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Ethical Approval: The study was approved by the Ethics Committee of University of Health Sciences, Ankara Yıldırım Beyazıt Dışkapı Education and Research Hospital (Approval Number: 34, Date: 2009-06-30). The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions: Conception and design; Karabacak OR, Sandıkçı F, Zengin K, Data acquisition; Sandıkçı F, Saltas H, Dilli A, Data analysis and interpretation; Karabacak OR , Dilli A, Zengin K, Yalçınkaya F , Drafting the manuscript; Karabacak OR, Sandıkçı F, Dilli A, Zengin K, Critical revision of the manuscript for scientific and factual content; Karabacak OR, Zengin K, Yalçınkaya F, Ayaz ÜY, Statistical analysis; Sandıkçı F, Saltas H, Dilli A, Supervision; Yalçınkaya F, Ayaz ÜY.

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