ORIGINAL RESEARCH

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The Value of a Single Measurement of Calculus Density by Computed Tomography in Predicting the Composition of Stones and Its Use in Practice in Patients with Urolithiasis

Ürolitiazisli Hastalarda Bilgisayarlı Tomografiyle Kalkül Dansitesinin Tek Bir Ölçümünün Taş Bileşimi Öngörüsündeki Değeri ve Pratikte Kullanımı

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Abstract

Objective: Urinary tract stones consist of many subtypes. Prior knowledge of the chemical composition of stones is a key factor in determining the fragility of the stone and determining the treatment and prophylactic approach to be applied to the patient. In this way, the group of patients who can receive medical treatment can be determined, this group of patients can be kept away from repetitive imaging procedures and the cost to be made by reimbursement institutions can be reduced. In this study, it is aimed to predict the stone type according to Hounsfield unite (HU) values.

Method: One hundred-six patients between the ages of 18-70 who were diagnosed with urolithiasis and underwent biochemical analysis for these stones between 2013 and 2017 were included in the study. Non-contrast computed tomography images of the patients were analyzed retrospectively. While measuring the density of the stones, 3 region of interest (ROIs) were placed in different parts of the stones. The value with the highest Hounsfield unite (HU) value was determined as the density of the stone.

Results: According to the stone analysis results, 11 calcium phosphate, 18 calcium oxalate monohydrate-dihydrate, 42 calcium oxalate monohydrate, 10 cystine, 12 struvite, 13 uric acid stones were found. According to the measurement results, the density difference between the 6 stone groups was statistically significant (p=0.0001). No statistically significant difference was observed between the mean age of the stone type groups and the distribution of the sides (right-left) (p=0.284,

Öz

Amaç: Üriner sistem taşları pek çok subtipten oluşmaktadır. Taşların kimyasal bileşiminin önceden bilinmesi, taşın kırılganlığının saptanması ve hastaya uygulanacak tedavinin ve profilaktik yaklaşımın belirlenmesinde anahtar faktördür. Bu sayede medikal tedavi alabilecek hasta grubu belirlenebilmekte ve bu hasta grubunun tekrarlayan görüntüleme işlemlerinden uzak durması ve geri ödeme kurumları tarafından yapılacak maliyetin azaltılması sağlanabilmektedir. Bu çalışma ile Hounsfield unite değerlerine göre taş tipinin öngürülmesi amaçlanmaktadır.

Yöntem: 2013-2017 yılları arasında ürolitiazis saptanan ve bu taşlara yönelik biyokimyasal analiz geçiren 18-70 yaşları arasında 106 hasta çalışmaya dahil edildi. Hastaların kontrastsız bilgisayarlı tomografi görüntüleri retrospektif olarak incelendi. İş istasyonunda bilgisayarlı tomografi görüntülerindeki kalküllerin dansite ölçümleri, kemik pencere ön ayarında, standart büyütme altında, kalkülün en dens yerinden yapıldı. Dansite ölçümü dışında, taş lokalizasyonu, en büyük çapı da belirlendi. Ölçülen değerler ile kalkülün kimyasal analiz sonuçları karşılaştırıldı.

Bulgular: Taş analizi sonuçlarına göre 11 kalsiyum fosfat, 18 kalsiyum oksalat monohidrat-dihidrat, 42 kalsiyum oksalat monohidrat, 10 sistin, 12 strüvit, 13 ürik asit taşı bulundu. Ölçüm sonuçlarına göre 6 taş grubu arasında dansite farkı istatistiksel olarak anlamlı anlamlıydı (p=0,0001). Taş tipi gruplarının yaş ortalamaları ve taraf dağılımları (sağ-sol) arasında istatistiksel olarak anlamlı farklılık gözlenmedi (p=0,284, p=0,747). Taş tipi gruplarının cinsiyet dağılımları arasında istatistiksel olarak anlamlı farklılık

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Abstract

p=0.747). A statistically significant difference was observed between the gender distributions of the stone type groups (p=0.037). There was a statistically significant difference between the distribution of stone sizes and types (p=0.0001).

Conclusion: Density measurements of urinary tract stones in non-contrast computed tomography are useful in recognizing their subtypes. Thus, uric acid stones can be determined and the patient can be referred to oral chemolysis treatment. This may enable the patient to avoid repetitive imaging procedures and interventional treatments.

Keywords: Computed tomography, kidney, oral chemolysis, uric acid stone, urolithiasis

Öz

saptandı (p=0,037). Taş boyutlarının ve tiplerinin dağılımları arasında istatistiksel olarak anlamlı farklılık gözlendi (p=0,0001).

Sonuç: Kontrastsız bilgisayarlı tomografide üriner sistem taşlarının dansite ölçümlerinin yapılması subtiplerinin tanınmasında faydalıdır. Bu sayede ürik asit taşları belirlenebilir ve hasta oral kemoliz tedavisine yönlendirilebilir. Bu da hastanın tekrarlayan görüntüleme işlemlerinden ve girişimsel tedavilerden kaçınmasını sağlayabilir.

Anahtar kelimeler: Bilgisayarlı tomografi, böbrek, oral kemoliz, ürik asit taşı, ürolitiazis

Introduction

In addition to being a common disease, urinary system stone disease is an important reason for admission to the emergency department. According to a study conducted in the United States of America, although it varies according to age, race and gender, it is seen at a rate of 12% in men and 6% in women. A moderate increase of prevalence was observed in the second half of the twentieth century (1). Especially people with chronic stone disease receive various medical and surgical treatments in the long term. The choice of treatment methods is made by looking at factors such as the size of the stone, its localization, and its location, and its chemical composition is also very important at this stage. Oral chemolysis is a treatment method based on the medical dissolution of the stone and can only be applied to uric acid stones (1). Predicting that the stone is a uric acid stone allows the urologist to try medical treatment for the patient before surgical treatment methods.

Our aim in this study was to predict the chemical composition of the stones in the non-contrast computed tomography (CT) examination taken in almost all patients with suspected urolithiasis, to identify uric acid stones and to indicate this in our report, to guide the clinician in treatment, and as a result, to reduce the morbidity caused by surgical treatments in patients with chronic kidney stones. The aim is to reduce the radiation exposure and the financial burden on the health system as a result of repetitive imaging methods.

Materials and Methods

General Data

In this retrospective study, 106 urolithiasis patients (47 F, 59 M) aged between 18 and 70 years, who applied to the Urology Clinic of University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital between 2013 and 2017, were included. Stone composition analysis was performed on the calculi obtained as a result of percutaneous nephrolithotomy or ureterorenoscopy in all patients. Patients younger than 18 years of age, with mixed type calculi and calculi smaller than 5 mm in size were excluded from the study.

Ethics committee approval dated 08/12/2017 and numbered 2017.12.1.08.024 was obtained from University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Ethics Committee before the study.

CT Protocol and Evaluation of Images

The non-contrast CT images were obtained on the 64 detector Philips Brilliance device using the following parameters: Fixed noise index of 30.9; 0.625-mm collimation; reconstruction slice thickness of 2 mm 120 kVp; variable milliamperage determined by x-, y-, and z-axis dose modulation; gantry rotation time of 0.5 seconds; and 40% adaptive statistical iterative reconstruction (ASIR). All scans were applied spirally from the upper poles of the kidney to the base of the bladder in the urinary system for stone disease. While measuring the density of the stones, 3 region of interest (ROIs) were placed in different parts of the stones. The value with the highest Hounsfield unite (HU) value was determined as the density of the stone.

Statistical Analysis

In the evaluation of the data, in addition to descriptive statistical methods (mean, standard deviation), One-Way analysis of variance was used in intergroup comparisons, the Tukey multiple comparison test was used in subgroup comparisons, and the chi-square test was used in comparisons of qualitative data. The results were evaluated at the significance level of p<0.05.

Results

Applications for screening were evaluated due to the presence of flank pain, dysuria, and a family history of stones. All patients included in the study had laboratory stone composition analyses of calculi obtained as a result of percutaneous nephrolithotomy or ureterorenoscopy. The sizes of the stones varied between 3 and 50 mm, with an average of 20.6 mm. The distribution of stones according to their sizes is shown in Table 1.

A statistically significant difference was observed between the sizes of calcium phosphate, calcium oxalate monohydrate-dihydrate, calcium oxalate monohydrate, cystine, struvite and uric acid stone types (p=0.0001). While calcium oxalate monohydrate-dihydrate and calcium oxalate monohydrate were high in the group smaller than 10 mm, calcium oxalate monohydrate was found to be higher in the 10-30 mm group, and calcium phosphate and struvite were found to be higher in the group larger than 30 mm (Table 1).

A statistically significant difference was observed between the gender distributions and stone types (p=0.037). While struvite and uric acid were found to be high in women, calcium phosphate, calcium oxalate monohydrate-dihydrate and calcium oxalate monohydrate were found to be high in men (Table 2).

A statistically significant difference was observed between the appearances of calcium phosphate, calcium oxalate monohydrate-dihydrate, calcium oxalate monohydrate, cystine, struvite and uric acid stone types groups (p=0.0001). Calcium oxalate monohydrate-dihydrate, calcium oxalate monohydrate, cystine and uric acid were higher in the homogeneous group, while calcium phosphate and struvite were higher in the heterogeneous group (Table 3).

A statistically significant difference was observed between the mean density of calcium phosphate, calcium oxalate monohydrate-dihydrate, calcium oxalate monohydrate, cystine, struvite and uric acid stone subtypes (p=0.0001). The mean density of the uric acid stone subtype was statistically significantly lower than the other stone subtypes (p=0.0001). A statistical relationship between the densities of stone subtypes is shown in detail in Tables 4 and 5.

The appearance of uric acid and calcium phosphate stones and HU measurement are shown in the CT images below (Figures 1 and 2).

Discussion

Urinary system stone disease is the third most common pathology after urinary infections and prostate pathologies (2). The approach to stone disease begins with a detailed medical history and continues with physical examination, laboratory and imaging tests. Laboratory tests consist of blood and urine analysis and chemical analysis of the extracted stone. Laboratory analysis of stone composition cannot be performed in many centers, and it is an expensive and time-consuming method (3).

Table 2. Comparison of stone type groups by gender

	Gender			
	Male		Female	
Calcium phosphate	8	13.56%	3	6.38%
Calcium oxalate monohydrate-dihydrate	12	20.34%	6	12.77%
Calcium oxalate monohydrate	26	44.07%	16	34.04%
Cystine	6	10.17%	4	8.51%
Struvite	2	3.39%	10	21.28%
Uric acid	5	8.47%	8	17.02%
	p=0.037			

chi-square test

Table 1. Distribution of stone type groups by size

	Stone size					
	<10 mm		10-30 mm		>30 mm	
Calcium phosphate	0	0.00%	4	5.56%	7	36.84%
Calcium oxalate monohydrate-dihydrate	5	33.33%	13	18.06%	0	0.00%
Calcium oxalate monohydrate	6	40.00%	32	44.44%	4	21.05%
Cystine	0	0.00%	9	12.50%	1	5.26%
Struvite	0	0.00%	6	8.33%	6	31.58%
Uric acid	4	26.67%	8	11.11%	1	5.26%
	p=0.0001					

chi-square test

Table 3. Comparison of stone type groups by appearance

	Stone appearance			
	Homogeneous		Heterogenous	
Calcium phosphate	0	0.00%	11	28.21%
Calcium oxalate monohydrate-dihydrate	14	20.90%	4	10.26%
Calcium oxalate monohydrate	30	44.78%	12	30.77%
Cystine	9	13.43%	1	2.56%
Struvite	3	4.48%	9	23.08%
Uric acid	11	16.42%	2	5.13%
	p=0.0001			

chi-square test

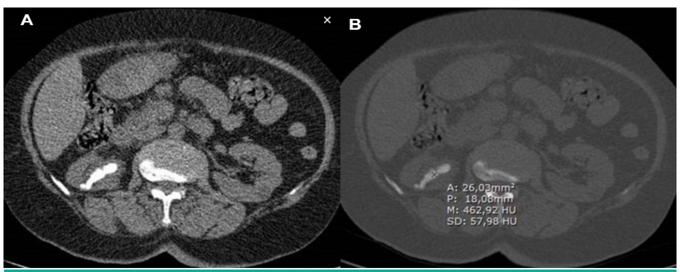

Figure 1. A 42-year-old female patient has calculus in the lower pole of the right kidney (A). Stone analysis was reported as uric acid. The average HU value taken from the densest region of the calculus is 462.92 HU (B)

HU: Hounsfield unite

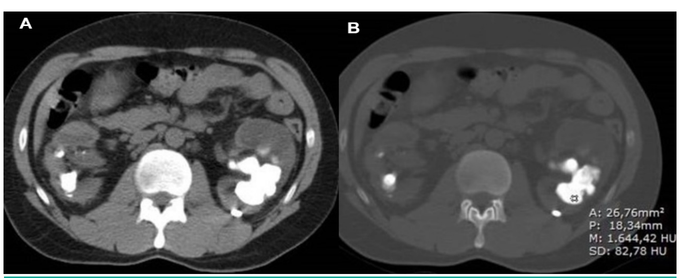

Figure 2. A 33-year-old male patient has calculi in the bilateral pelvicalyceal system (A). Stone analysis for calculus in the left kidney pelvicalyceal system was reported as calcium phosphate. The mean HU value taken from the densest region of the calculus is 1644.42 HU (B)

HU: Hounsfield unite

Imaging methods are the best problem solvers in stone disease. The location of the stone, its dimensions, whether it is single or more than one, whether there are underlying factors that may cause stone formation, whether the stone obstructs the urinary tract, and the condition of the other kidney are important in planning the treatment. Non-contrast CT plays an important role in detecting urinary system calculus, distinguishing calculus from other anomalies (such as stricture, neoplasia), and determining non-urological causes of flank pain (4).

Table 4. Comparison of densities of stone subtypes

	n	Stone density
Calcium phosphate	11	1406.45±187.71
Calcium oxalate monohydrate-dihydrate	18	1224.94±213.33
Calcium oxalate monohydrate	42	1313.31±210.53
Cystine	10	762.00±66.97
Struvite	12	749.00±126.57
Uric acid	13	413.00±60.27
		p=0.0001

One-Way Analysis of Variance

Table 5. Comparison of densities of stone subtypes

Tukey multiple comparison test	p
Calcium phosphate/calcium oxalate monohydrate-dihydrate	0.095
Calcium phosphate/calcium oxalate monohydrate	0.642
Calcium phosphate/cystine	**0.0001**
Calcium phosphate/struvite	**0.0001**
Calcium phosphate/uric acid	**0.0001**
Calcium oxalate monohydrate-dihydrate/calcium oxalate monohydrate	0.501
Calcium oxalate monohydrate-dihydrate/cystine	**0.0001**
Calcium oxalate monohydrate-dihydrate/struvite	**0.0001**
Calcium oxalate monohydrate-dihydrate/uric acid	**0.0001**
Calcium oxalate monohydrate/cystine	**0.0001**
Calcium oxalate monohydrate/struvite	**0.0001**
Calcium oxalate monohydrate/uric acid	**0.0001**
Cystine/struvite	0.999
Cystine/uric acid	**0.0001**
Struvite/uric acid	**0.0001**

Singh et al. (5), in their study with 100 patients in 2020, found high sensitivity and specificity in the detection of stone subgroups by dual-energy CT. The sensitivity and specificity of dual-energy computed tomography (DECT) for hydroxyapatite, uric acid, cysteine, oxalic acid, and mixed types were 89.6% and 88.5%, 82.6% and 97.5%, 86.7% and 96.5%, 80% and 98.9%, and 88.9% and 98.9%, respectively (5). Erdogan et al. (6), on the other hand, conducted a study involving 373 patients using dual-energy CT in 2019. *In vitro* analysis of stones was performed in 35 patients, and 8 hydroxyapatite, 18 calcium oxalate, 6 uric acid and 3 cystine stones were detected. In DECT analysis results compared with the results of *in vitro* analysis, the correct type of stone was detected in 32 (91.4%) patients and the wrong type of stone in 3 (8.6%) patients. All uric acid and cystine stones were detected correctly, especially with DECT (6). With advanced post-procedure analysis methods, DECT can analyze urinary stones. DECT has been found to be superior, especially in the detection of uric acid and cystine stones. It also has a high success rate in detecting hydroxyapatite and calcium oxalate stones.

There are *in vivo* and *in vitro* studies on stone analysis in the literature. From *in vitro* studies, Mostafavi et al. (7) distinguished the chemical content of pure stones as uric acid, struvite and calcium oxalate stones in CT taken with 120 kV. They also stated in their studies that stones of similar density such as cystine, brushite and calcium oxalate could be distinguished by using dual energy (7). Saw et al. (8) scanned 127 stones using 1 mm, 3 mm, and 10 mm collimation and stated that they could distinguish stones other than brushite from hydroxyapatite at 1 mm collimation. From *in vivo* studies, Nakada et al. (9) showed that there was a statistically significant difference between the densities of stones containing uric acid and calcium in a study on 129 patients.

In the results of our study, a statistical difference was observed in terms of the average density of stone subtypes (p=0.0001). The mean density of calcium phosphate and calcium oxalate monohydrate-dihydrate subtypes was statistically significantly higher than the mean density of cystine, struvite and uric acid stone subtypes (p=0.0001). In addition, the mean density of the uric acid subtype was found to be statistically significantly lower than the mean density of cystine and struvite stone type groups (p=0.0001). In our study, it was concluded that the density values of the calcium-containing stones were found to be significantly higher than the other groups, but they could not be distinguished between themselves only by the non-contrast CT method.

In the study of Patel et al. (10), 100 stones were analyzed. Considering HUs, calcium phosphate stones (brushite and apatite) have the highest density (1.123±254, 844±346 HU). There is a significant difference between HU values of all calcium stones and HU values of uric acid stones (10). Similarly, there was a significant difference in HU values between calcium stone groups and uric acid, cystine and struvite stones in our study. However, in our study, there was no significant difference between the calcium-containing stone subtypes in terms of HU values.

In the study of Spettel et al. (11), 235 stone analyses were performed. The average density of uric acid stones was 484±44 HU, the average density of calcium-weighted stones was 890±20, and the difference between them was statistically significant. When these results were evaluated together with the urine pH results, the sensitivity of detecting uric acid stones was 100% and the specificity was 80% (11).

When we compare the *in vivo* and *in vitro* studies in the literature, it is seen that the density of stone types in *in vivo* studies is lower than those stated in *in vitro* studies. This is most likely due to the volume average effect of adjacent soft tissue and the use of smaller collimation size in *in vitro* studies. As the collimation decreases, the volume average artifacts will decrease and thus the attenuation-size measurement will be better.

Study Limitations

Our study had some limitations. Urinary system stones can be better shown using dual-energy tomography. In the following years, images obtained using dual-energy CT can be studied in a larger patient group.

Conclusion

Our main goal in our study is to show the detectability of uric acid stones, one of the urinary system stones, by non-contrast tomography, as well as to draw attention to its use in clinical practice. When we examined the patient histories retrospectively, it was seen that repetitive CT, IVP and anterograde pyelography examinations were applied to the patients more than once. This means unnecessary radiation dose is given to patients with a history of chronic kidney stones. In the treatment of urinary system stones, oral chemolysis treatment, other than interventional procedures, is a method that can only be applied to uric acid stones, with a lower cost and less patient morbidity. Indicating the localization and size of the stone as well as the calculus density value in radiology reports may save the patient from unnecessary interventional treatment methods and reduce morbidity.

Ethics

Ethics Committee Approval: Ethics committee approval dated 08/12/2017 and numbered 2017.12.1.08.024 was obtained from University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Ethics Committee before the study.

Informed Consent: The study was conducted retrospectively, because of that we did not obtain consent of patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: E.S., M.Ö., Design: E.S., M.Ö., Data Collection or Processing: S.Ö., A.T.C., Analysis or Interpretation: E.S., S.Ö., Drafting Manuscript: E.S., S.Ö., Critical Revisation of Manuscript: M.Ö., A.T.C., Final Approval and Accountability: E.S., S.Ö., M.Ö., A.T.C.

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