Original Research Article

Prediction of chemical composition of urinary calculi in-vivo based on ct attenuation values – An analytical study

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Abstract

Introduction: Chemically, stones are of various types including calcium stones, uric acid stones, struvite stones and cystine stones among others. Each pathophysiological group has a predisposition to form certain kind of stones. Hence, knowledge of the chemical composition of the stone that a patient forms can and does direct the management of the patient. **Objectives:** To evaluate if the chemical composition of urinary stones can be predicted with mean Hounsfield Unit (HU) value on computed tomography (CT). **Methods:** This is prospective and analytical study conducted in the Department of Radiology of a tertiary care teaching hospital in India. Patients diagnosed with urinary stones who had a non-contrast CT done and had stone retrieved were included in the study. The predominant chemical composition of the stone was analysed by X-ray diffraction crystallography. **Results:** Fifty-one stones of four types were studied. Statistically significant ($p<0.001$) differences were seen in the mean HU, maximum HU and median HU values between all the four types. No significant difference was observed in the difference between periphery and core HU values. Hierarchy of density among the stone types correlated with previous studies but absolute measurements varied among different studies. **Conclusion:** Mean HU of urinary stones correlates with their chemical composition. Calcium oxalate monohydrate, calcium oxalate dihydrate, uric acid and hydroxyapatite stones can be differentiated on their CT attenuation parameters if a database of attenuation characteristics for stones of known composition is built for given scanner and protocol.

Keywords: Computed tomography, Calcium oxalate monohydrate, Calcium oxalate dihydrate, Uric acid.

Introduction

Urolithiasis is a common disease affecting both sexes and is commoner among the middle-aged[1]. It is a disease with significant economic burden and is especially so among recurrent stone formers[2].

Pathophysiologically, stone formers are a heterogeneous group and fall under different categories. It is logical that the management protocol also differs with the individual patient. The disease has well researched treatment protocols for both surgical and medical management.

Chemically, stones are of various types including calcium stones, uric acid stones, struvite stones and cystine stones among others. Each pathophysiological group has a predisposition to form certain kind of stones. Hence, knowledge of the chemical composition of the stone that a patient forms can and does direct the management of the patient[3,4].

Surgically, this knowledge can help avoid unsuccessful shock wave lithotripsy procedures. Medically, the evaluation of the patients can be more directed. This is of particular importance in recurrent stone formers who are required to undergo a barrage of investigations. If this investigation can be more directed, it can[2] reduce the economic burden on the patient and this assumes special significance in a developing country like ours where every measure to reduce medical costs without compromising efficacy of treatment is generally undertaken.

This knowledge of the chemical composition is generally limited to patients who have the stones retrieved either through spontaneous passage of the stone or more commonly through surgery. In patients who lack pointers in history, clinical examination and basic laboratory investigations, an undirected metabolic evaluation will be extensive. Unsuccessful shock wave lithotripsy procedures are also not without significant morbidities. It follows that various workers have tried to evaluate methods to predict the chemical composition of stones in-vivo.

With rapid progress in computed tomography (CT) technology, non-contrast CT is becoming the investigation of choice in patients with suspected urinary stones[5,6]. Although plain radiographs and ultrasound remain preferred initial investigations in developing countries like ours, with wider availability and better healthcare systems, CT is assuming greater importance even here. This study attempts to find out if any significant relationships exist between the CT attenuation properties of stones and their chemical composition.

Material and Methods

This was a prospective and analytical study conducted in the Department of Radiology of a tertiary care teaching hospital in India. The Institutional Medical Ethics Committee approved this study. All patients who had been diagnosed with urinary stones and had a non-contrast CT study done as part of the diagnostic workup over a period of 1 year were considered for the study. Those patients from whom

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stones were retrieved either through surgery or spontaneous passage were included. Written informed consent was obtained from all patients before their inclusion in the study. No children or healthy volunteers were included in the study. We excluded all patients for whom the protocol for the standard non-contrast CT examination of the kidneys, ureters and bladder (KUB) region had to be modified for individual reasons.

Inclusion criteria

- Adult (Age >18 years).
- Patient diagnosed with urinary stone and has a non-contrast CT examination of the KUB region as part of diagnostic workup.

Exclusion criteria

- Patient for whom the standard institutional protocol for non-contrast CT examination of the KUB region has to be modified for any reason.

All patients included in the study underwent the standard institutional protocol for a non-contrast CT study of the KUB region in our department. The mean attenuation values of all the stones were calculated from the reconstructed CT images by a single observer. The stones which were subsequently retrieved from the patient were analysed by x-ray diffraction crystallography and sorted on the basis of the predominant chemical composition. Any statistically significant correlation was sought between the mean CT attenuation values and the chemical composition of the stone.

All patients who were referred to the Department of Radiology for a non-contrast CT study of the KUB region were considered for the study. The standard protocol for a non-contrast CT study of the KUB region in our institution involved a tube potential of 120 kVp, automated tube current modulation, a pitch of 1.5:1 and a slice thickness of 3 mm. The images were acquired on a GE dual slice CT scanner.

Statistical methods

Statistical analysis was carried out using statistical software namely SPSS 25.0 versions.

Descriptive and inferential statistical analysis was carried out in the present study. Results on continuous measurements are presented on Mean ± Standard deviation (Minimum-Maximum) and results on categorical measurements are presented in Number (percentage). Significance was assessed at 5% level of significance.

The following assumptions on the data were made.

- Dependent variables are normally distributed.
- Samples drawn from the population were random.
- Cases of the samples were independent.

Analysis of variance (ANOVA) was used to find the significance of the study parameters between three or more groups. Chi-square/ Fisher Exact test were used to find the significance of study parameters on categorical scale between two or more groups.

For determination of prediction accuracy, a discriminant function analysis was performed on the five attenuation parameters namely HU mean, HU maximum, Periphery HU, Core HU and median HU. This was used to classify the stones into one of the groups.

Significant figures are as follows.

Suggestive significance – (P value: $0.05<P<0.10$)

Moderately significant – (P value: $0.01<P\leq0.05$)

Strongly significant – (P value: $P\leq0.01$)

Results

A total of 51 stones from separate patients were studied for their attenuation characteristics and chemical composition. The subjects in this study belonged primarily to the fourth and fifth decade of life, with more than 85% between 21 and 60 years of age with a mean age of 41 years. This is shown in Table 1.

Table 1: Distribution of study population by age

Age in years	No. of patients	Percentage
18-20	3	5.9
21-30	9	17.6
31-40	16	31.4
41-50	11	21.6
51-60	8	15.7
>60	4	7.8
Total	51	100.0

Table 2: Distribution of study population by gender

Gender	No. of patients	Percentage
Female	13	25.5
Male	38	74.5
Total	51	100.0

A male preponderance was seen with almost 75% of the subjects being males as seen in Table 2.

Table 3: Distribution of stones by chemical composition

Chemical composition	No. of patients	Percentage
Calcium Oxalate Monohydrate	14	27.5
Calcium Oxalate Dihydrate	17	33.3
Uric Acid	14	27.5
Hydroxyapatite	6	11.8
Total	51	100.0

The stones studied in this study fell under four types. The four types of stones observed in the study were calcium oxalate monohydrate, calcium oxalate dihydrate, uric acid and hydroxyapatite. Calcium stones as a group and uric acid stones formed 73% and 27% of the total number of stones. The distribution of stones in various groups is shown in Table 3.

Table 4: Distribution of stones by location

Location of stone	No. of patients	Percentage
Upper Ureter	26	51.0
Lower Ureter	18	35.3
Bladder	4	7.8

Kidney	3	5.9
Total	51	100.0

The majority of the stones (86 % of total stones) seen on the CT images were seen in the ureters. As demonstrated in Table 4, more than half of all the stones (51 % of total stones) were seen in the upper ureter above the level where the ureter crosses the iliac vessels.

Table 5: Distribution of location of stones by chemical composition

Location	Chemical Composition				Total
	Calcium oxalate monohydrate	Calcium oxalate dihydrate	Uric acid	Hydroxyapatite	
Kidney	2(14.3%)	0(0%)	1(7.1%)	0(0%)	3(5.9%)
Upper Ureter	8(57.1%)	9(52.9%)	6(42.9%)	3(50%)	26(51%)
Lower Ureter	2(14.3%)	7(41.2%)	7(50%)	2(33.3%)	18(35.3%)
Bladder	2(14.3%)	1(5.9%)	0(0%)	1(16.7%)	4(7.8%)
Total	14(100%)	17(100%)	14(100%)	6(100%)	51(100%)

No predilection for any location was noted for stones with regard to their chemical composition (P value=0.401). This is depicted in Table 5.

Table 6: Distribution of maximum cross-sectional diameter of the stones among the different types

Max Cross Sectional Diameter	Chemical Composition				Total
	Calcium oxalate monohydrate	Calcium oxalate dihydrate	Uric acid	Hydroxyapatite	
1-5	1(7.1%)	10(58.8%)	7(50%)	2(33.3%)	20(39.2%)
6-10	7(50%)	6(35.3%)	7(50%)	1(16.7%)	21(41.2%)
11-15	6(42.9%)	1(5.9%)	0(0%)	2(33.3%)	9(17.6%)
>15	0(0%)	0(0%)	0(0%)	1(16.7%)	1(2%)
Total	14(100%)	17(100%)	14(100%)	6(100%)	51(100%)
Mean ± SD	9.43±3.44	5.59±2.32	5.50±2.03	10.17±4.88	7.16±3.52

The mean maximal cross-sectional diameter of the stones included in the study was 7.2 mm. Calcium oxalate dihydrate stones (mean 5.6 mm) and uric acid stones (mean 5.5 mm) were smaller than the calcium oxalate monohydrate (mean 9.4 mm) and hydroxyapatite stones (mean 10.2 mm). This is shown in Table 6.

Table 7: Comparison of attenuation parameters among stones of different chemical compositions

	Chemical Composition				P value
	Calcium oxalate monohydrate	Calcium oxalate dihydrate	Uric acid	Hydroxyapatite	
HU Mean	1006.43±134.54	710.35±114.17	452.43±79.73	1274.33±55.02	<0.001**
HU Maximum	1257.93±184.15	862.18±169.54	542.36±75.54	1454.00±64.12	<0.001**
Periphery HU	984.86±142.89	662.18±127.91	438.86±77.13	1240.00±73.16	<0.001**
Core HU	1067.57±212.69	788.29±135.00	497.07±92.28	1387.83±64.70	<0.001**
Median HU	1019.07±134.86	719.12±114.54	499.36±140.58	1292.00±57.32	<0.001**
Periphery HUcoreHU	-82.71±201.72	-126.12±69.15	-58.21±41.83	-147.83±58.39	0.284

A statistically significant difference (p<0.001) was seen in the mean HU of the stones between all the four groups of stones analysed. Hydroxyapatite stones showed the greatest mean density (1274.33±55.02HU) followed in order by calcium oxalate monohydrate (1006.43±134.54HU), calcium oxalate dihydrate (710.35±114.17HU) and uric acid (452.43±79.73HU).

The median HU values were similar to the mean HU values with hydroxyapatite stones having the greatest values (1292.00±57.32 HU). These were followed in order by calcium oxalate monohydrate (1019.07±134.86 HU), calcium oxalate dihydrate (719.12±114.54 HU) and uric acid (499.36±140.58 HU) stones in the same order.

The maximum HU values observed in the stones also showed profiles similar to the mean and median HU values. The stones with the greatest to the least maximum HU values were hydroxyapatite (1454±64.12 HU), calcium oxalate monohydrate (1257.93±184.15 HU), calcium oxalate dihydrate (862.18±169.54) and uric acid (542.36±75.54) in the same order.

Analysis of the differences between the peripheral and core HU values showed no statistically significant differences (p = 0.284). Hydroxyapatite stones had the biggest difference (mean -147.83±58.39 and uric acid stones had the smallest values (mean -58.21±41.83).

For determination of the prediction accuracy, a discriminant function analysis of the five attenuation variables namely Mean HU, Maximum HU, Periphery HU, Core HU and Median HU was done. A function was developed which enabled a prediction accuracy of 84.5 %

Discussion

Urinary stones show great differences in their attenuation of x-rays due to differences in their chemical composition[7]. This difference in x-ray attenuation seen due to variations in chemical composition can be attributed to the physical principles behind x-ray attenuation. Both the physical characteristics of the object of interest and the penetrating characteristics of the incident x-ray beam have their effect on the subject contrast[8]. The physical characteristics of the object of interest that affect x-ray attenuation include thickness, physical density and effective atomic number[8]. Since stones made of different chemical compositions differ in their physical properties, it follows that they differ in their attenuation characteristics.

The attenuation characteristics of 51 urinary stones belonging to four different chemical compositions were observed in this study. The four types were calcium oxalate monohydrate, calcium oxalate dihydrate, uric acid and hydroxyapatite.

The observed mean HU values among the four types showed statistically significant differences. This finding is in agreement with the majority of previous similar studies which found statistically significant differences in mean HU values of different types of stones[10,11]. Hydroxyapatite stones formed the densest stones followed in order of decreasing density by calcium oxalate monohydrate, calcium oxalate dihydrate and uric acid. This hierarchy observed in the density of the stone is in agreement with that observed in these previous studies with hydroxyapatite forming the densest stones and uric acid the most lucent stones.

Only one study in the reviewed literature commented on inability to differentiate any type of stone based on the mean HU values[12]. The mean HU values observed in that particular study had significant overlap between values observed in different groups with no statistically significant difference observed between them. The authors had concluded that mean HU value was not useful in identifying stones in-vivo. However, this study had used a beam collimation of 5 mm which is much higher than the 3mm collimation used in the present study. The partial volume averaging effect would have been more pronounced in the 5 mm thick slices than in the 3 mm thick slices. This averaging could have resulted in the inability of those investigators to differentiate stone using only mean HU values.

Some of the studies in the literature which had classified calcium stones into separate subtypes have experienced difficulties in differentiating between the different types of calcium stones. The mean HU values observed in the calcium stones in this study showed differences with statistical significance between the groups. This finding is in agreement with more recent studies which show non overlapping attenuation values for calcium stones of different subtypes[13]. In this study, hydroxyapatite stones had mean HU values of 1274.33±55.02. Within the calcium oxalate subtype, calcium oxalate monohydrate stones were denser with mean HU values of 1006.43±134.54 compared to calcium oxalate dihydrate stones which had mean HU values of 710.35±114.17.

The statistically significant differences seen in the mean HU and maximum HU values of the stones are also reflected in the measurements of periphery and core HU values. But the reasoning behind measuring these individually was to measure the difference between the core and periphery HU values which could possibly aid in quantifying the heterogeneity observed in many urinary stones. No statistically significant differences were seen in this study variable among the different groups. Uric acid stones had the smallest differences agreeing with previous observations that they are more homogeneous[14]. Most stones had a denser core and a relatively lucent periphery. This was also in agreement with the literature[14].

Although the current study shows significant differences in the CT attenuation parameters of chemically different stones, comparison of the absolute attenuation values observed in previous studies show differences. Although the hierarchy maintained by the different types of stones with regard to their density is similar in previous studies, the differences in absolute HU values observed in various studies cannot be neglected as it has significant implications. Comparisons of the attenuation values of stones of various compositions observed in different studies have been made in the past[15,16]. From such comparisons, it is evident that although confident estimates could possibly be established with data from a particular study, the estimates would differ between studies with possible overlap of values between different stone types. It has been observed that the study by Gupta et al[17] described the mean attenuations of calcium oxalate monohydrate and calcium oxalate dihydrate stones as being 1008 HU and 748 HU respectively while Zarse et al[18] describe the same as within a range of 1707-1925 HU and 1416-1938 HU respectively and Patel et al[13] describe them as 879±230 HU and 517±203 HU respectively. This is probably attributable to the fact that the studies were performed on different machines and under different protocols. Studies suggest that stone size and scan collimation have their influences on the measured density of the stone[19].

Literature also suggests that attenuation measurements are affected by the x-ray tube potential and that they vary from manufacturer to manufacturer. Previous studies have also demonstrated the inter-scanner differences in attenuation measurements with various phantoms[20]. The importance of this fact is that although this study suggests that the chemical compositions of stones can be predicted on the basis of CT attenuation values on a given machine, it is questionable whether the stone compositions identified with attenuation data from one machine can be extrapolated to data obtained on another machine. This important issue has been raised in one of the earliest studies about the topic in the literature[7].

This study was limited in the aspects that the sample size was small and that not all stone types were evaluated. Stones like brushite and cystine stones were not evaluated since none of the patients included in the study had such stones.

Conclusion

Based on the results and the methodology employed, we have concluded that there is a significant relationship between the chemical composition of a urinary stone and its CT attenuation values. Calcium oxalate monohydrate, calcium oxalate dihydrate, hydroxyapatite and uric acid stones show differences in mean, median and maximum HU values that are statistically significant ($p<0.001$). If a database of attenuation characteristics is built for a given CT machine and a specific protocol with stones of known chemical composition, subsequent stones of the above-mentioned types can be predicted in the future.

References

1. Saigal CS, Joyce G, Timilsina AR, Urologic Diseases in America Project. Direct and indirect costs of nephrolithiasis in an employed population: opportunity for disease management? Kidney Int. 2005 Oct;68(4):1808–14.
2. Lotan Y. Economics and cost of care of stone disease. Adv Chronic Kidney Dis. 2009 Jan;16(1):5–10.
3. Moe OW. Kidney stones: pathophysiology and medical management. Lancet. 2006 Jan 28;367(9507):333–44.
4. Xu H, Zisman AL, Coe FL, Worcester EM. Kidney stones: an update on current pharmacological management and future directions. Expert Opin Pharmacother. 2013 Mar;14(4):435–47.
5. Westphalen AC, Hsia RY, Maselli JH, Wang R, Gonzales R. Radiological imaging of patients with suspected urinary tract stones: national trends, diagnoses, and predictors. Acad Emerg Med Off J Soc Acad Emerg Med. 2011 Jul;18(7):699–707.
6. Wang J-H, Shen S-H, Huang S-S, Chang C-Y. Prospective comparison of unenhanced spiral computed tomography and intravenous urography in the evaluation of acute renal colic. J Chin Med Assoc JCMA. 2008 Jan;71(1):30–6.
7. Hillman BJ, Drach GW, Tracey P, Gaines JA. Computed tomographic analysis of renal calculi. AJR Am J Roentgenol. 1984 Mar;142(3):549–52.
8. Schueler BA. Clinical applications of basic x-ray physics principles. Radiogr Rev Publ Radiol Soc N Am Inc. 1998 Jun;18(3):731–744; quiz 729.
9. Flannigan R, Choy WH, Chew B, Lange D. Renal struvite stones--pathogenesis, microbiology, and management strategies. Nat Rev Urol. 2014 Jun;11(6):333–41.
10. Nakada SY, Hoff DG, Attai S, Heisey D, Blankenbaker D, Pozniak M. Determination of stone composition by noncontrast spiral computed tomography in the clinical setting. Urology. 2000 Jun;55(6):816–9.
11. Tiscione D, Ruggera L, Beltrami P, Cerruto MA, Cielo A, Gigli F, et al. [Using computed tomography to predict in vivo stone chemical composition.]. Urologia. 2009 Jun;76(2):107–11.
12. Motley G, Dalrymple N, Keesling C, Fischer J, Harmon W. Hounsfield unit density in the determination of urinary stone composition. Urology. 2001 Aug;58(2):170–3.
13. Patel SR, Haleblian G, Zabbo A, Pareek G. Hounsfield units on computed tomography predict calcium stone subtype composition. Urol Int. 2009;83(2):175–80.
14. Marchini GS, Remer EM, Gebreselassie S, Liu X, Pynadath C, Snyder G, et al. Stone characteristics on noncontrast computed tomography: establishing definitive patterns to discriminate calcium and uric acid compositions. Urology. 2013 Sep;82(3):539–46.
15. Grosjean R, Sauer B, Guerra RM, Daudon M, Blum A, Felblinger J, et al. Characterization of human renal stones with MDCT: advantage of dual energy and limitations due to

respiratory motion. AJR Am J Roentgenol. 2008 Mar;190(3):720–8.

16. García Marchiñena P, Billordo Peres N, Liyo J, Ocantos J, Gonzalez M, Jurado A, et al. [CT SCAN as a predictor of composition and fragility of urinary lithiasis treated with extracorporeal shock wave lithotripsy in vitro]. Arch Esp Urol. 2009 Apr;62(3):215–222.
17. Gupta NP, Ansari MS, Kesarvani P, Kapoor A, Mukhopadhyay S. Role of computed tomography with no contrast medium enhancement in predicting the outcome of extracorporeal shock wave lithotripsy for urinary calculi. BJU Int. 2005 Jun;95(9):1285–8.
18. Zarse CA, Hameed TA, Jackson ME, Pishchalnikov YA, Lingeman JE, McAteer JA, et al. CT visible internal stone structure, but not Hounsfield unit value, of calcium oxalate monohydrate (COM) calculi predicts lithotripsy fragility in vitro. Urol Res. 2007 Aug;35(4):201–6.
19. Saw KC, McAteer JA, Monga AG, Chua GT, Lingeman JE, Williams JC. Helical CT of urinary calculi: effect of stone composition, stone size, and scan collimation. AJR Am J Roentgenol. 2000 Aug;175(2):329–32.
20. Grosjean R, Daudon M, Chammas MF, Claudon M, Eschwege P, Felblinger J, et al. Pitfalls in urinary stone identification using CT attenuation values: are we getting the same information on different scanner models? Eur J Radiol. 2013 Aug;82(8):1201–6.

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