

Correlation between Hounsfield Unit Value and Stone Composition in Nephrolithiasis

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OBJECTIVE: To examine whether the Hounsfield Unit value predicts calcium oxalate monohydrate stones in patients who are undergoing percutaneous nephrolithotomy.

METHOD: 119 patients who underwent percutaneous nephrolithotomy were prospectively evaluated between February 2012 and August 2014. Using thin cuts, the highest single-energy computed tomography attenuation value within a pixel was measured for each stone. Data regarding age and gender were assessed before surgery. The extracted stones were analyzed using infrared spectrophotometry.

RESULTS: By receiver operating characteristics analysis, a cutoff value of 1548 Hounsfield Unit and an age of 42.5 years were used to determine the likelihood of a stone being composed of calcium oxalate monohydrate. A higher Hounsfield Unit value and increased age augmented the chances of a stone being composed of calcium oxalate monohydrate. In general, females had a greater likelihood of harboring calcium oxalate monohydrate stones than males.

CONCLUSION: The maximum Hounsfield Unit value, as determined by unenhanced single-energy computed tomography in association with gender, predicts the presence of calcium oxalate monohydrate stones in patients who are undergoing percutaneous nephrolithotomy.

KEYWORDS: Urinary Calculi, Lithotripsy, Tomography, Hounsfield Unit.

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INTRODUCTION

Determining the composition of urinary stones is a fundamental step of preoperative patient evaluations. Stones that are composed of calcium oxalate monohydrate (COM) are firm and might be treated more effectively with percutaneous nephrolithotomy (PCNL).^{1,2} Uric acid stones can be treated with medical measures if their composition is known.³

Stone analysis methods are costly and time-consuming and can only be performed after the extraction of the stones. These methods offer no benefits when the treatment is planned preoperatively.⁴ Single-energy computed tomography (SECT) is the standard method for diagnosing and evaluating urinary stones and is widely used because of its safety and high sensitivity.⁵

SECT is limited in its ability to determine the stone composition. Specific attenuation values are difficult to obtain with this method, primarily because of the partial volume averaging effect (inclusion within the region-of-interest of elements distinct from the stone crystal and space between the crystals and the matrix). Previous studies used SECT that generated datasets by drawing large regions of interest, which invariably included various minerals in the single attenuation measurements.

To minimize this bias, Dretler et al. have suggested using thin slices and the highest attenuation value in a pixel.⁶ The goal of this study was to review the use of unenhanced SECT with values that have been recorded by assessing the pixel-to-pixel attenuation and to verify if the highest Hounsfield Unit (HU) value of each stone examined by multivariate analysis can preoperatively identify patients with calcium oxalate monohydrate (COM).

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MATERIALS AND METHODS

Following institutional review board approval and obtainment of written informed consent from all the participants, 119 patients who were undergoing percutaneous nephrolithotomy (PCNL) with stone burdens that were greater than 2.0 cm were prospectively assessed between February 2012 and August 2014. None of the patients had received treatment for previous stones, and all the subjects were evaluated before surgery (whole blood count, serum biochemistry, coagulation tests, urinalysis, and bacteriological analysis). Only stones with a diameter of more than 20 mm were included in the study.

All patients underwent a single-energy computed tomography (SECT) scan (General Electric Bright Speed® USA) per our hospital protocol for renal stones (1.25-mm thickness, 2.5-mm increments, 120 kVp, and 240 mA, pixel width 0,7mm). In order to assess the HU values, we used the Synapse Viewer® (Fujifilm USA) to view and evaluate the scans digitally. The highest attenuation value in a pixel for each stone was accessed by adjusting the window view with the width made equal to 1 HU (maximum contrast) and the level progressively heightened (Figure 1).

The highest HU value in a stone (PixHU); the mean HU value (mPixHU), defined as the sum of the highest HU values of a pixel in each cut divided by the total number of cuts; and the standard deviation of the mPixHU (sdmPixHU) were considered the representative SECT values of each stone.

The stones were analyzed by infrared spectrophotometry (Louis C. Herring laboratory - Orlando - Florida - US). The predominant composition of the stones defined their primary group. The stones were classified as COM, calcium oxalate dehydrate or weddellite (COD), calcium phosphate carbonate form (CPC), calcium phosphate hydroxyl form (CPH), calcium monohydrogen phosphate dehydrate (CHPD) or brushite, magnesium ammonium phosphate hexahydrate (MAPH) or struvite, and uric acid (UA); the stone classification was based on the highest mineral percentage by stone analysis (range 30% to 100%).

The statistical analyses were performed using SPSS, version 21.0, using a significance level of 5% ($p < 0.05$). The stones were divided into 2 groups: COM and others. A Mann-Whitney test was applied to verify differences in the scalar variables between the groups. A maximum likelihood test was performed to verify differences in the categorical variables between the two groups. Receiver operating characteristics (ROC) curve analysis was used to determine cutoffs for the variables that divided the groups. Multivariate analysis was performed using logistic regression to model an equation that calculated the probability of a stone belonging to the COM group.

RESULTS

The mean age of the patients was 47.2 ± 12.4 years (range 24 to 84 y); 77 patients were female (64.7%) and 42 were male (35.3%). The renal stone characteristics are

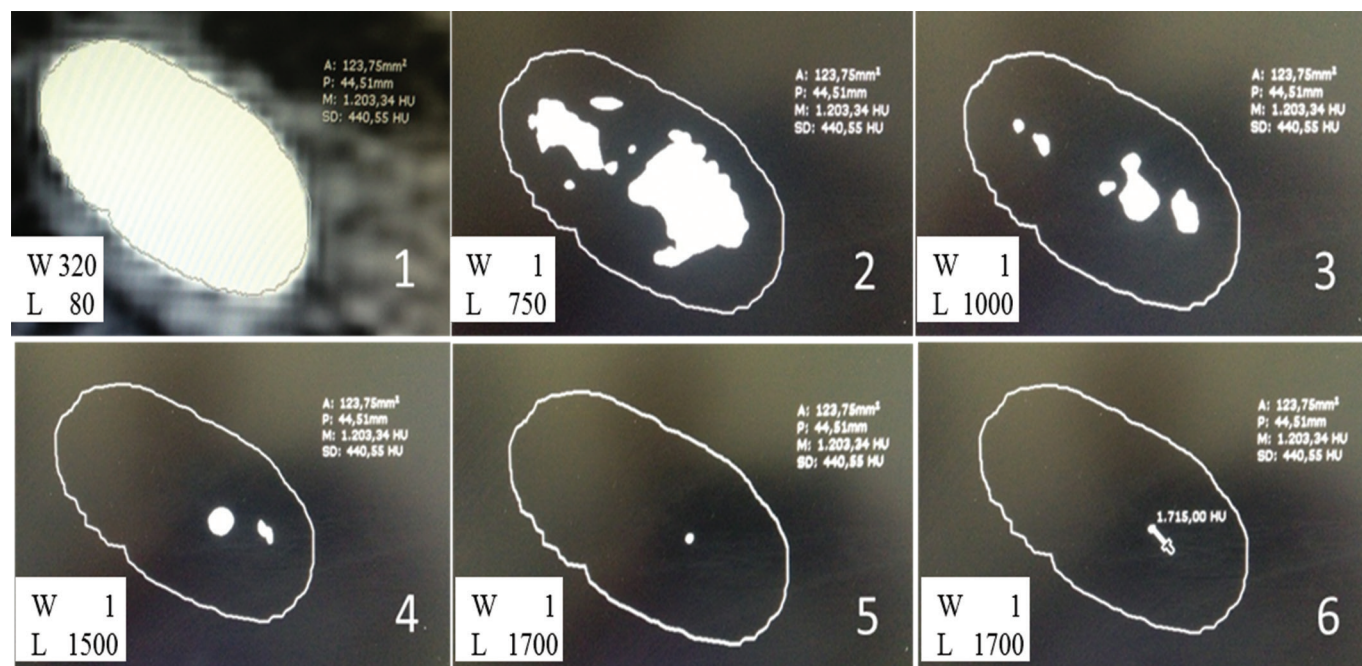


Figure 1 - Synapse Viewer: adjusting the window view (the width made equal to 1 HU and the level progressively heightened) to determine the highest SECT value in the slice for a pixel.

summarized in Table 1. Seven patients with uric acid stones were identified by presenting with the highest attenuation value for a pixel in stones less than 987 HU (all other stones types exceeded 1131 HU). The procedure of adjusting the window view (the width made equal to 1 HU and the level progressively heightened) to determine the highest SECT value in any slice for a pixel proved to be not time-consuming and easily reproducible (Figure 1).

The number of stone slices, age, PixHU, mPixHU, sdmPixHU, and gender were distinguished between the two groups ($p < 0.05$). An age above 42.5 years and a PixHU value higher than 1548 HU defined the likelihood of a stone being a COM.

A logistic regression model was generated using scalar and categorical variables that differentiated between the COM stones and "others" groups at a probability level of $p < 0.05$. Being a COM stone in the logistic regression model was a dependent variable, while age, PixHU, mPixHU, sdmPixHU, number of slices and gender were independent variables.

The regression modeling resulted in the prediction equation presented below.

$$\text{Probability of a stone being composed of COM} = 1 / (1 + \exp(- (0.001\text{PixHU} - 1.506 (\text{gender}))))$$

where gender = 1 (female) or 2 (male)

note: to calculate the probability of a stone belonging to the "others" group, it is sufficient to calculate 100% - probability of a stone being composed of COM.

Based on the application of this equation we found that lower PixHU values reflect a lower probability of a stone being composed of COM in males and females (Figure 2). In general, females had a greater likelihood of harboring COM stones than males. These are novel findings with regard to the stone composition in patients who are undergoing percutaneous nephrolithotomy. Additionally, we present these data as a working instrument for professional staff (Table 2).

Chemical analysis

As shown in Table 1 out of 119 analyzed stones, 63 (52.9%) were COM, 16 (13.4%) were struvite, 16 (13.4%) were carbonate apatite, 9 (7.6%) were calcium oxalate dehydrate, 7

(5.9%) were uric acid, 4 (3.4%) were brushite, and 4 (3.4%) were hydroxyl apatite. Seven stones (5.9%) were pure; of these, 3 (2.5%) were COM, 3 (2.5%) were uric acid and 1 (0.8%) was carbonate apatite. The remaining 112 stones were mixed (as shown in Table 3). In terms of crystals composition, 23 (19.3%) were composed of two different crystals, 48 (40.3%) of three different crystals and 41 (34.5%) of four different crystals (Table 3). The most common association encountered between two different crystals were COM and COD which occurred in 68 (57%) of the stones and MAPH and CPC in 36 (30%) of the stones. The composition of calculi from major to minor mineral components is presented in Table 3.

DISCUSSION & RECOMMENDATION

The value of Single-energy computed tomography (SECT) in making treatment decisions depends on the size, burden, and location of the stone and the degree of obstruction.^{7,8} A successful percutaneous nephrolithotomy (PCNL) requires appropriate preoperative planning and optimal percutaneous intervention. SECT has become an important imaging method in planning standard pre-PCNL interventions, inserting the guide-wires, and planning the latter stages of surgery.⁹ Higher success rates have been reported when planning PCNL access using SECT.¹⁰

Knowing the precise chemical composition of a urinary tract stone and its corresponding fragility can guide the selection of an effective clinical management program.^{8,11} Urinary calculi that consist primarily of uric acid can be treated with oral medications (urine alkalization). Cysteine-, calcium oxalate-, and brushite-based stones are less fragile than other types of calculi and are unlikely to benefit from Extracorporeal Shock Wave Lithotripsy (ESWL), which can be expensive if repeated treatments are necessary and in some cases, results in renal hemorrhage and fibrosis.¹²

Recent in vitro,¹³⁻¹⁵ and in vivo studies¹⁶⁻¹⁸ have used dual-energy CT and its x-ray attenuation properties at high and low kVs to differentiate uric acid (UA)-and calcium-containing urinary calculi, reporting sensitivities of 74%

Table 1 - Description of the renal stones

Stone Group	COM	Struvite	Carbonate apatite	COD	Hydroxyl apatite	Brushite	Uric acid
Predominant mineral range (%)	(30-100)	(40-66)	(45-100)	(34-80)	(60-80)	(50-93)	(65-100)
Mean \pm SD (%)	(68 \pm 20)	(53 \pm 7)	(59 \pm 12)	(49 \pm 11)	(74 \pm 9)	(68 \pm 13)	(85 \pm 14)
Number of Calculi	119	63	16	16	9	4	7
Pure calculi	3	-	1	-	-	-	3
Male	42	29	2	3	1	2	4
Female	77	34	14	15	6	3	3

COM: calcium oxalate monohydrate; Struvite: magnesium ammonium phosphate hexahydrate (MAPH); Carbonate apatite: calcium phosphate carbonate form (CPC); COD: calcium oxalate dehydrate; Hydroxyl apatite: calcium phosphate hydroxyl form (CPH); Brushite: calcium monohydrogen phosphate dehydrate (CHPD); Uric acid: (UA)

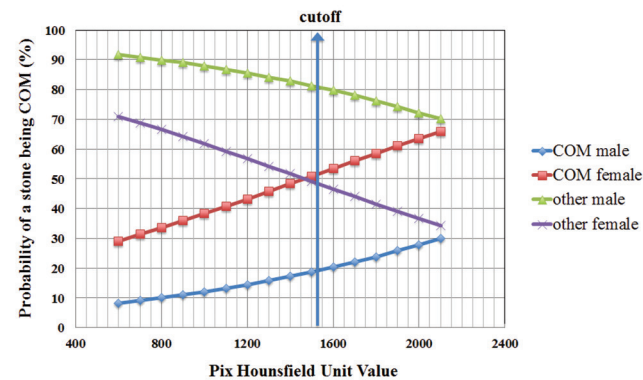


Figure 2 - Probability of a stone being predominantly composed of COM or other mineral as calculated by the prediction equation model. COM: calcium oxalate monohydrate stones; cutoff: ROC cutoff value of 1,548 Hounsfield Units.

Table 2 - Probability of a stone being predominantly composed of COM or other mineral as calculated by the prediction equation of model

PixHU (HU)	COM Stone		Other minerals Stones	
	Male (%)	Female (%)	Male (%)	Female (%)
600	8.3	29.1	91.7	70.9
700	9.2	31.3	90.8	68.7
800	10.0	33.5	89.9	66.5
900	11.0	35.9	89.0	64.1
1000	12.1	38.3	87.9	61.7
1100	13.2	40.7	86.8	59.3
1200	14.4	43.2	85.6	56.8
1300	15.8	45.8	84.2	54.2
1400	17.2	48.3	82.8	51.7
1500	18.7	50.9	81.3	49.1
1600	20.3	53.5	79.7	46.5
1700	22.0	56.0	78.0	44.0
1800	23.8	58.5	76.2	41.5
1900	25.8	61.0	74.3	39.0
2000	27.8	63.4	72.2	36.6
2100	29.9	65.8	70.1	34.2

to 100% and accuracies of 89% to 100%. There are several limitations of dual-energy CT, including the equipment cost, the high number images that are generated per study, technical learning curves, and a lack of reimbursement. Dual CT scanners are more expensive than their single-energy counterparts.¹⁹ The main drawback of dual-energy acquisition is the relatively high irradiation involved because of the simultaneous acquisitions at high and low kVs.²⁰ Early in vitro studies that used SECT attempted to characterize stones over ranges of HU values;²¹⁻²³ however, because of the overlap in these HU ranges, it was not

possible to apply single-energy spectral data to characterize stones accurately.^{11,21} Dretler and Spencer theorized that the sensitivity and accuracy of unenhanced SECT could be improved by reducing the partial volume averaging effect (the inclusion of crystal differences, the spaces between the crystals, matrix, or other stone components) in the region of interest.⁶ This result could be achieved by using tighter collimation with thinner slices and considering HU values from the unit area of density-i.e., the pixel (Figure 1). In the present study, the HU values were increased compared to in other publications.^{12,13} For example, pure uric acid stones ranged from 643 HU to 987 HU. These increased HU values are due to the exclusion from the region of interest of the spaces between crystals whose attenuation values range from -1000HU to zero. Calcium oxalate monohydrate (COM) stones are among the most prevalent and hardest urinary stones to fragment.^{24,25} In this study, COM calculi were the most frequent type (Table 2). We focused on distinguishing this resistant and predominant stone group from the others using the highest SECT values and routine preoperative parameters by multivariate analysis in patients undergoing nephrolithotomy.

We observed that it is ideal to use tighter collimation, thinner slices, and the highest pixel numbers. This method allowed us to identify all the uric acid (UA) stones (accuracy of 100%). When considering the remaining calculi, we could also distinguish the most prevalent group of COM. By ROC analysis, the highest CT value (PixHU)-1548 HU or higher-was the cutoff for a COM stone. Using logistic regression, we generated an equation to calculate the probability of such a stone being composed of COM. Calculations were not labor intensive as they were done once and converted into a data sheet for daily use in clinical practice (Table 2). The calculated formula was established by identifying the highest attenuation values using the Synapse Viewer® software, which regrettably is not available to most urologists. Nevertheless, several other commercial software programs could be applied to obtain the HU numbers from the pixel. A limitation of the present study is that the 4 brushite-based stones (which are as firm as COM stones) could not be identified using our method. Considering the decision to use the equation at the time of diagnosis (when stone analysis is not available for the urologist), we forced the inclusion in the modeling of all stones independently of their purity (range: 30 to 100). This resulted in lower specificity and area of 0.645 for the highest CT value in predicting COM stones. Most clinicians would choose PCNL for stones > 2 cm. In cases of high surgical risk, if it were possible to predict with some certainty, a non-calcium oxalate monohydrate composition, ESWL would most likely be used instead of PCNL. Stones 1 to 2 cm in size could represent a clinical dilemma. If a calcium oxalate monohydrate composition were highly predictable, we would most likely perform PCNL rather

Table 3 - The composition of calculi from major to minor crystal constituents

Group	n	%	Group	n	%
Calcium oxalate monohydrate (COM) range: 30-100% (mean: $68 \pm 20\%$)	63	52.9	Calcium oxalate dehydrate (COD) range: 34-80% (mean: $49 \pm 11\%$)	9	7.6
COM+COD+CPH+CPC	22	18.5	COD+COM+CPH+CPC	4	3.4
COM+COD+CPH	21	17.6	COD+COM+CPH	3	2.5
COM (pure)	3	2.5	COD+CPH+COM+CPC	1	0.8
COM+CPH	3	2.5	COD+CPC+COM+MAPH	1	0.8
COM+CPH+CPC	3	2.5			
COM+COD	2	1.7	Uric acid (AU) range: 65-100% (mean: $85 \pm 14\%$)	7	5.9
COM+CPH+COD	2	1.7	AU (pure)	3	2.5
COM+CPH+COD+CPC	2	1.7	AU+AAU	1	0.8
COM+COD+MAPH+CPC	2	1.7	AU+COM	1	0.8
COM+COD+CPC	1	0.8	AU+COM+AAU	1	0.8
COM+MAPH+COD+CPC	1	0.8	AAU+COM+COD	1	0.8
COM+COD+CPC+MAPH	1	0.8	Calcium phosphate hydroxyl form (CPH) range: 60-80% (mean: $74 \pm 9\%$)	4	3.4
Struvite (MAPH) Range: 40-66% (mean: $53 \pm 7\%$)	16	13.5	CPH+CPC	2	1.7
MAPH+CPC+COM	7	5.9	CPH+CPC+COM	2	1.7
MAPH+CPC	5	4.2			
MAPH+CPC+COM+COD	4	3.4	Brushite (CHPD) range: 50-93% (mean: $68 \pm 13\%$)	4	3.4
			CHPD+COM+CPH+CPC	1	0.8
Calcium phosphate carbonate form (CPC) range: 45-100% (mean: $59 \pm 12\%$)	16	13.5	CHPD+CPH+COM	1	0.8
CPC+MAPH	9	7.6	CHPD++CPH+COM+COD	1	0.8
CPC+MAPH+AAU	2	1.7	CHPD+COM+CPH	1	0.8
CPC (pure)	1	0.8			
CPC+MAPH+COM	1	0.8	Total	119	100
CPC+MAPH+COD	1	0.8			
CPC+COD+MAPH	1	0.8			
CPC+MAPH+COD+COM	1	0.8			

than ESWL or ureteroscopy. Our results in terms of stone composition, patient's age and gender are not expandable to other patient populations, but the present method could easily be applied anywhere generating specific cutoff values and equations for different populations by using less expensive easily accessible SECT. The classification of stone groups was based on the highest mineral percentage (in case of COM stones, this mineral could range from 30 to 100%, with average of $68 \pm 20\%$ for the group studied). If a stone were at a lower range (30%), a second predominant ingredient could be, for example, 29% of COD (this was the most common association encountered with COM, verified in 68 (57%) of stones (Table 3). Considering this stone to be made of COM (that is a hard calculus), we would indicate

PCNL surgical removal (the most effective for hard calculi) and would most certainly obtain the fragmentation of the COD crystals, which are more amenable to fragmentation.

Stone size limits the use of Hounsfield units for prediction of calcium oxalate stone composition.²⁶ Micro-CT for ex-vivo stone analysis has recently demonstrated spatial separation of various stone materials for slice thicknesses and pixel widths ranging from 25 to 34 μm .²⁷ SECT for in-vivo stone analysis can also be performed using a smaller pixel width. The display field of view (DFOV) determines how much of the scan field of view is reconstructed into an image. The DFOV influences the physical dimensions of image pixel. A 10-cm DFOV in a 512x512 matrix results in pixel size of approximately 0,2mm.²⁸ Through awareness of the DFOV

size and proper technologist training, patient positioning can be ensured to provide inclusion of the kidney of interest.²⁹ Further studies limiting the image reconstruction to the kidney will result in even more reduced partial volume effect allowing the present method to access the composition of small renal calculi in patients undergoing Shock Wave Lithotripsy or stone dissolution protocols.³⁰

CONCLUSION

Our study demonstrates the potential of unenhanced SECT to predict the presence of UA and COM stones in patients who are undergoing percutaneous nephrolithotomy when the stone is first encountered.

AUTHOR CONTRIBUTION

Silva, TR: conception and design of the project, acquisition of data, interpretation of data and writing the article; De Lima, ML: writing the article and final approval of the submitted Version.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

CORRELAÇÃO ENTRE OS VALORES DE UNIDADES HOUNSFIELD E A COMPOSIÇÃO CRISTALINA NA NEFROLITÍASE

OBJETIVO: verificar se as medidas de atenuação de raios-X em Unidades Hounsfield (HU) preveem os cálculos de oxalato de cálcio mono-hidratado (OCM) em pacientes tratados através de nefrolitotripsia percutânea.

MÉTODO: 119 pacientes submetidos a tratamento por nefrolitotripsia percutânea foram avaliados prospectivamente entre fevereiro de 2012 e Agosto de 2014. Utilizando cortes tomográficos finos, o maior valor de atenuação de raios-X para um pixel utilizando tomografia convencional sem contraste foi determinado para cada cálculo. Dados laboratoriais foram avaliados antes da cirurgia. Os cálculos extraídos foram analisados utilizando-se espectrofotometria no infravermelho.

RESULTADOS: Através de análise por curva ROC (*receiver operating characteristic*) um valor de corte de 1548 HU e uma idade de 42,5 anos foram utilizadas para determinar a probabilidade de um cálculo ser composto de OCM. Valores superiores de atenuação de raios-X e de idade aumentaram as chances de um cálculo ser composto de OCM. Em geral, as mulheres apresentaram uma maior probabilidade de ter cálculos de OCM do que os homens.

CONCLUSÃO: O valor da medida de atenuação máxima em Unidades Hounsfield de um cálculo, como o determinado pela tomografia computadorizada convencional sem contraste, em associação com o gênero preveem a presença de cálculos de OCM em pacientes submetidos a tratamento por nefrolitotripsia percutânea.

PALAVRAS CHAVE: Cálculo urinário, Litotripsia, Tomografia, Unidades Hounsfield.

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