Dual Energy Computed Tomography (DECT) for Determination of Renal Calculi Composition - In-Vivo Analysis and In-Vitro Comparison with Qualitative Chemical Analysis - A Prospective Comparative Study at a Single Centre at SDM Medical College and Hospital – Dharwad, Karnataka

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ABSTRACT

BACKGROUND

Dual energy computed tomography (DECT) is a new method of computed tomography (CT) imaging which allows to determine stone composition in addition to assessing stone morphology. The purpose of this study was to evaluate the role of dual energy CT (DECT) preoperatively to assess the composition of urinary stones and to compare it with post-operative in vitro qualitative chemical analysis as reference standard.

METHODS

Forty patients (18 male and 22 female) who presented with symptoms of renal stones in the department of urology were included in the study. All 40 patients who were diagnosed to have renal stones clinically and by ultrasonography (USG) kidney, ureter and bladder (KUB) region were subjected to dual energy CT. The stone composition assessed in vivo using DECT preoperatively and in vitro by chemical analysis post operatively after stone extraction by surgical procedure. The results were compared by statistical analysis. Sensitivity, specificity and positive predictive value (PPV) were calculated and descriptive study done using Statistical Package for Social Sciences (SPSS) 20.00 version. Data was analysed by comparing it with correlative qualitative chemical analysis.

RESULTS

In our study, in vivo analysis using DECT showed most common type of stone was calcium oxalate seen in 20 cases compromising 50 % of total cases. Next common stone type was uric acid stone (22.5 %) followed by cysteine (17.5 %) and calcium hydroxyapatite (10 %) respectively. When the same stones were subjected to ex vivo chemical analysis, one of the calcium oxalate stone came out to be calcium phosphate and one of the cysteine stone came out to be mixed stone. Thus, out of 40 stones, 38 stones were found to have the same result in ex vivo chemical analysis as that of in vivo analysis by dual energy CT. Hence, accuracy of dual energy CT in diagnosis of renal stones was found to be 100 % with CI 91.19 % - 100 %.

CONCLUSIONS

With dual energy CT, it is possible to determine the composition of renal calculi in vivo non-invasively (with specificity of 100 % in our present study). Therefore, this helps in deciding the modality of treatment pre-operatively whether the stone is amenable to medical management (e.g., Uric acid stones) or requires extracorporeal shock wave lithotripsy (ESWL) or surgical intervention can be determined preoperatively. This helps to reduce the unnecessary financial burden and is found to be time saving.

KEYWORDS

Renal Calculus, Dual Energy CT, Stone Composition, Uric Acid Stones, Non-Uric Acid Stones, Attenuation, Hounsfield Units HU, Chemical Analysis of Stones.

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BACKGROUND

The renal stone disease is a common clinical problem representing about 10 – 14 % of the population, with the probability of having a stone varying according to age, gender, race, and geographic location. Men are affected 2 - 3 times more often than women. However, there is some evidence that the difference in incidence between men and women is narrowing. Whites have the highest incidence of stones compared to Asians, Hispanics, and African-Americans. Prevalence of stone disease is highest in southeast. The risk of stone disease correlates with weight and body mass index (BMI). Stone disease has been correlated with a number of systemic disorders, including diabetes, metabolic syndrome, and cardiovascular disease.[1] Stone occurrence is relatively uncommon before age 20 but peaks in incidence in the fourth to sixth decades of life. There are different types of renal stones; they are about sixteen in number, most of these are rare. Calcium oxalate accounts for 60 % of stones; mixed calcium oxalate and hydroxyapatite, 20 %; brushite, 2 %; uric acid, 10 %; struvite, 10 %; and cystine, 1 %. Hypercalciuria is the most common abnormality identified in calcium stone formation.[1]

The main complaint of the renal stone disease is intermittent flank pain accompanied by urinary urgency, haematuria, nausea, and vomiting.[2] If untreated, obstructed urinary stone may lead to infection of the obstructed urinary tract, that may predispose to urosepsis as well as pyelonephritis and ureteric strictures. Long standing urinary obstruction may also cause renal insufficiency and end-stage renal disease.[3] Knowing the composition of renal stones is an important part of the preoperative patient evaluation, and this influences treatment plans and recurrence prevention. For example, stones composed of cystine or calcium oxalate monohydrate have a firm composition and are resistant to treat with ESWL modality of treatment. These stones may be more effectively treated with percutaneous nephrolithotomy (PCNL).[4] Systemic and familial metabolic stone disease may be suspected in patients with some stone compositions, and specific dietary and medical measures to reduce the risk of recurrence can be offered if the stone type is known.[5]

The most common techniques for stone analysis are chemical analysis, thermogravimetry, in vitro x-ray diffraction, infrared spectroscopy, and polarization microscopy. These techniques are costly and time consuming and also analysis of stones can be done only after stone is extracted. Thus, they offer no benefit during preoperative treatment planning. Non-enhanced computed tomography (CT) of the abdomen and pelvis is currently the reference-standard examination for the diagnosis and evaluation of urinary stones, and it is widely used owing to its safety and reported high sensitivity (96 %).[6]

Dual energy CT was first developed by ALVAREZ and MACOVSKI (1976). This technique uses two separate x ray photon energy spectra, which allows interrogation of materials with different attenuation properties at different energies. Dual energy CT with post processing techniques rely on chemical characterizations of renal stone in addition to assessment of the anatomical data as site, size and character of the stone surface (smooth or rough). During image acquisition, perfect breath-hold has to be performed for in vivo use of attenuation value to assess stone chemical type because the values obtained with slight motion become significantly different from those obtained with no motion.[7,8] There are three different commercially available concepts of dual energy CT , the first concept is based on the technology of two X-ray tubes (dual source imaging) working simultaneously in 64 or 128-row detector scanners. The second method is based on the use of a dual-layer multi-detector scanner configuration with one X-ray tube performing acquisition at high energy, the top layer of detectors absorbs most of the low-energy spectrum (approximately 50 % of the beam), while the bottom detector layer absorbs higher energy photons. The third concept is based on the use of a single X-ray source with fast switching between two kilovoltage settings (80 and 140 kVp) at intervals of 0.5 ms during a single gantry rotation to generate high- and low-energy X-ray spectra.[9,10]

The dual energy CT has been reported as having a near 100 % sensitivity and specificity for characterizing the chemical composition of renal stones more than 3 mm.[9] Most researches in the past focused only on distinguishing uric acid from non-uric acid, but it was reported recently that calcium oxalate, calcium phosphate and cystine stones could be marginally differentiated.[11,12] A reliable determination of the chemical type of the stone helps the clinician to better satisfy treatment options for the patient, such as those composed of uric acid, may be treated medically and may not require surgery.[13]

The main limitation of dual-energy acquisition is related to its relatively high irradiation which does not match with the recent concepts of lower-dose CT protocols for the study of patients with acute flank pain.[14] Dual energy CT is expected to replace conventional single energy CT (SECT) as an important imaging modality in evaluating patients with suspected urinary calculi, as it provides images that pinpoint the same anatomical information as well as stone composition but with increasing patient radiation exposure.[15] DECT is not well established to be used in clinical practice as routine study for evaluation of renal stones, the aim of our study was to evaluate role of dual energy computed tomography determining composition of renal stones and its correlation with in vitro chemical analysis as a standard reference.

Aims and Objectives

To evaluate the role of dual energy CT preoperatively to assess the composition of urinary stones and to compare it with postoperative in vitro qualitative chemical analysis as reference standard.

METHODS

The prospective comparative study was conducted in the Department of Urology and Department of Radiodiagnosis at SDM Medical College and Hospital, Sattur-Dharwad district, Karnataka. Forty patients who presented with symptoms of renal stones in the department of urology were included in the study. All 40 patients who were diagnosed to have renal stones clinically and by USG KUB region were subjected to dual energy CT. The study period was for a period of one year from January 2019 to December 2019. Research Ethics Committee (REC) and informed written consent was obtained from all participants in the study after full explanation of the benefits and risks of the procedure.

Inclusion Criteria

Patients with clinical suspicion/clinical diagnosis of renal calculi who underwent PCNL procedure for stone removal, irrespective of the age and gender were included.

Exclusion Criteria

Patients with ureteric calculi.
Pregnant women with urolithiasis
Patients who did not give consent for the study.

Sample

Sample collected during the study period was 40, for a period of 12 months from January 2019 to December 2019. All 40 patients underwent 128 slice single source dual energy CT of Siemens Somatom definition AS, with fast switching between two kilovoltage settings (80 and 140 kVp) at intervals of 0.5 ms during a single gantry rotation to generate high and low-energy X-ray spectra. The complete data is collected from the patients in a specially designed case record form (CRF) by taking history of illness and by doing detailed clinical examination. After obtaining a written and informed consent they were subjected to dual energy CT evaluation of kidney urinary bladder (T12 –L3) with slice thickness of 5.0 mm with reconstructed image thickness of 0.75 mm and care dose 4D technique (where kVp and mAS automatically adjusted according to the patients). After the investigation, the images are processed on the Siemens syngovia work station choosing a dual energy protocol on the software. Images were acquired in dual energy CT protocol (Figure 1) The calculi was colour coded as red/orange for uric acid, blue for calcium containing renal calculi yellow for cysteine calculi. The stones were marked using the kidney stone marker on the protocol which helps to display the composition in terms of Hounsfield units, volume of calculi. The standard reference values were built in the post processing software, where it evaluates the composition and displays on a colour coded graph chart of Hounsfield on low energy KVp to high energy KVp making it easy for clinician to find out the composition of calculi effortlessly and objectively (Figure 2). Once the investigation was performed, the patients were divided into patients who had renal calcium containing calculi, patients who had uric acid calculi, patients who had renal cysteine calculi and patients who had renal struvite calculi. Post surgically, the extracted renal calculi were sent to biochemistry department for chemical analysis where it's physical and biochemical composition was confirmed by adding appropriate chemicals.

(A) Uric Acid Stone (Red)

(B) Calcium Oxalate Stone(Blue)

(C) Cysteine Stone (Yellow)

Figure 1. Dual Energy CT Showing Uric Acid Stone, Calcium Oxalate Stone, Cysteine Stone

Statistical Analysis

The descriptive statistics were expressed in frequency and percentage. The sensitivity, specificity and positive predictive value were calculated between in-vivo analysis and ex-vivo chemical analysis. The weighted Kappa statistic was used for assessment of agreement between dual energy CT in in-vivo analysis and ex-vivo chemical analysis in identifying the types of stones. The data were analysed by using statistical software i.e., SPSS 20.00 version. The statistical significance was set at 5 % level of significance ($p < 0.05$).

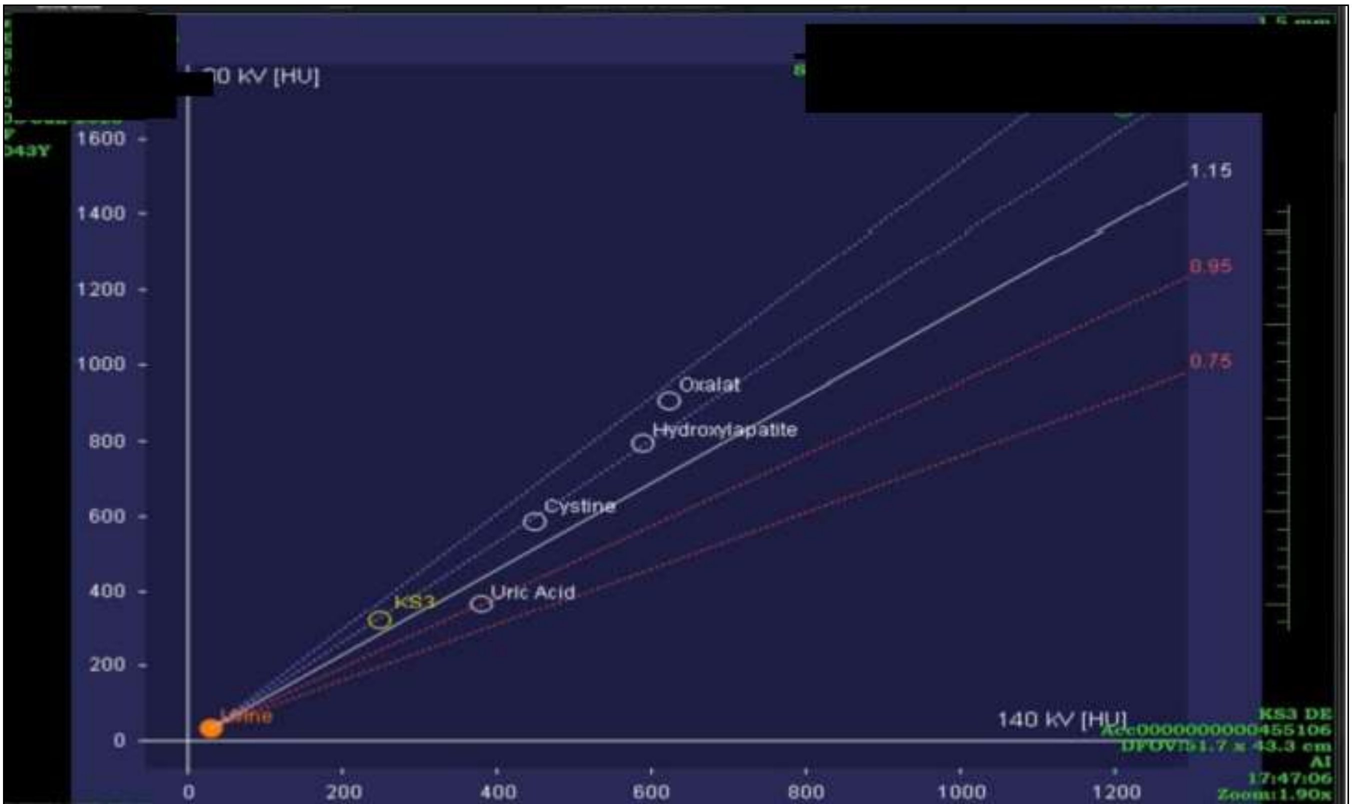

Figure 2. Dual Energy Attenuation for Different Types of Renal Stones in a DECT

RESULTS

Nephrolithiasis in our study were more common in females (55 %) than males (45 %). Most of the patients with renal stones were found in middle age group (30 years to 50 years) i.e. 67.5 %. Mean age of occurrence of renal stone was found to be 44.8 years. (Table 1)

Age in Years	Frequency	Percentage %
30 - 40	16	40.0
40 - 50	11	27.5
50 - 60	10	25.0
Above 60	3	7.5
Total	**40**	**100**
Gender	**Frequency**	**Percentage %**
Male	18	45.0
Female	22	55.0
Total	**40**	**100**

Table 1. Age and Gender Distribution

In our study, in vivo analysis using DECT showed most common type of stone was calcium oxalate seen in 20 cases 88 compromising 50 % of total cases. Next common type was uric acid stone (22.5 %) followed by cysteine (17.5 %) and calcium hydroxyapatite (10 %) respectively. When the same stones were subjected to ex vivo chemical analysis, one of the calcium oxalate stone came to be calcium phosphate and one of the cysteine stone came out to be mixed stone. Thus, out of 40 stones, 38 stones were found to have the same result in ex vivo chemical analysis as that of in vivo analysis by dual energy CT. Thus, accuracy of dual energy CT in diagnosis of renal stones was found to be 95 %. (Table 2)

Type of Stones	Ex-vivo		In-vivo	
	Number	Percent	Number	Percent
Calcium hydroxyapatite	4	10.00	4	10.00
Calcium oxalate	19	47.50	20	50.00
Cysteine	6	15.00	7	17.50
Uric acid	9	22.50	9	22.50
Calcium phosphate	1	2.50	0	0.00
Mixed stone	1	2.50	0	0.00
Total	40	100.00	40	100.00

Table 2. Distribution of Type of Stones Identified by Dual Energy CT in In-Vivo Analysis and Type of Stones Identified by Ex-Vivo Chemical Analysis

Agreement	Expected Agreement	Kappa	Std. Err.	Z-value	P - Value
97.00 %	77.67 %	0.8656	0.1093	7.9200	0.0001, HS

Table 3. Agreement between Dual Energy CT in In-Vivo Analysis and Ex-Vivo Chemical Analysis in Identifying the Types of Stones by Weighted Kappa Statistic

Validity Measures	Value	95% CI
Sensitivity	100.00 %	69.15 % to 100.00 %
Specificity	100.00 %	88.43 % to 100.00 %
Positive predictive value	100.00 %	-
Negative predictive value	100.00 %	-
Accuracy	100.00 %	91.19 % to 100.00 %

Table 4. Sensitivity and Specificity NPV and Accuracy

Ex-vivo	In-vivo		
	Uric Acid	Non-Uric Acid	Grand Total
Uric acid	10	0	10
Non-Uric acid	0	30	30
Grand Total	**10**	**30**	**40**

Table 5. Distribution of Non-Uric Acid and Uric Acid Stones in-Vivo and Ex-Vivo

DISCUSSION

Multi-detector computed tomography (MDCT) is now most commonly used in the evaluation of renal stones. MDCT has high sensitivity which permits evaluation of the size and site of stones but cannot evaluate their chemical composition. Several studies tried to predict stone composition using CT density measurements (Hounsfield units) but could only differentiate uric acid from non–uric acid stones.[16,17]

Nephrolithiasis in our study were more common in females (55 %) than males (45 %) (Table 1). These results were agreed with Manglaviti et al.[18] who found that renal stones were more common in females (70 %), and were in contrast to series which was done by Sellaturay and Fry[19] who they reported that the number of renal stones in males (70 %) exceeded that in females (30 %). In our study, most of the patients with renal stones were found in middle age group (30 years to 50 years) i.e., 67.5 %. Mean age of occurrence of renal stone was found to be 44.8 years (table1).

In our study, in vivo analysis using DECT showed most common type of stone was calcium oxalate seen in 20 cases 88 compromising 50 % of total cases. Next common type was uric acid stone (22.5 %) followed by cysteine (17.5 %) and calcium hydroxyapatite (10 %) respectively (table 2). When the same stones were subjected to ex-vivo chemical analysis one of the calcium oxalate stone came to be calcium phosphate and one of the cysteine stone came out to be mixed stone (Table 3). Thus, out of 40 stones, 38 stones were found to have the same result in ex-vivo chemical analysis as that of in-vivo analysis by dual energy CT. Thus, accuracy of dual energy CT in diagnosis of renal stones was found to be 100 % with CI 91.19 % to 100 %. Sensitivity was 100 % with CI 69.15 % to 100 %. Specificity was 100 % with CI 88.43 % to 100 %. Positive predictive value and negative value being 100 %, (Table 4), the statistical values derived from Table 2 and 3. Thus, in our study to describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean and S.D were used for continuous variables. To find out the significance in categorical data, Kappa statistic test was used. In the above statistical tool, the probability value 0.05 % is considered as significant level. Using kappa statistic test, significance value was calculated. It was found to be p - 0.0001 and z-value 7.9200. Thus, dual energy CT in diagnosis of renal stones was found to be significant (Table 3). The distribution of uric acid and non-uric acid stones in-vivo and ex-vivo is shown in table 5.

Daniel boll et al.[7] gave the dual energy behaviour of different renal calculi. Uric acid calculi (453 to 629 HU for low energy CT, 443 to 615 HU for high energy CT). For cystine calculi (725 to 832 HU for low energy CT, 513 to 747 89 HU for high energy CT). For struvite, (1337 to 1530 HU for low energy CT, 1007 to 1100 HU for high energy CT). High energy clusters showed attenuation value overlap. Polycrystalline calcium oxalate and calcium phosphate calculi were found throughout the entire spectrum and dense brushite had attenuation values of more than 1500 HU for low energy CT and more than 1100 HU for high energy CT. An article proposed by American Journal of Roentgenology showed that dual energy CT was very effective in in-vivo diagnosis of renal stones when compared to ex vivo chemical composition of renal calculi. In this study, dual energy CT was first used for evaluation of renal stones in a known or suspected nephrolithiasis patient (tube voltage, 140 and 80 KVp). Then these patients were treated with extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy or therapeutic ureterorenoscopy. Then the stones which were retrieved were subjected to ex vivo crystallography and the coincidence with results of dual energy CT was calculated using Cohen kappa coefficient. In this study, dual energy CT didn’t identify four stones with mixed composition, resulting in substantial agreement between dual energy CT and crystallography. Thus, this study concluded that dual energy CT had excellent accuracy in identifying renal stone calculi composition. Graser et al. (2008) study was done to determine the accuracy of dual energy CT in characterization of renal stone and ureteral stones. Results showed that DECT was able to differentiate uric acid calculi from other calculi. In dual energy, CT calculi were displayed in specific colours. Uric acid in red colour and calcified stones in blue colour. Hence with DECT uric acid, cystine, struvite and mixed renal calculi can be differentiated from other types of renal stones in-vitro and in vivo. Thus, dual energy CT was very useful in identifying uric acid calculi in vivo which can be treated pharmacologically, hence avoiding unnecessary surgery. Primak[11] et al. (2009) study also showed dual energy CT had 100 % accuracy in diagnosis of uric acid calculi from other calculi. Daniel T boll[7] et al. (2009) pilot study was done to prospectively evaluate the capability of non-invasive, simultaneous dual energy multi-detector CT to improve characterization of human renal calculi in an anthropomorphic DE renal phantom by introducing advanced post processing techniques, with ex vivo renal stone spectroscopy as reference standard. This study showed that DE multi-detector CT with advanced post processing techniques improves characterization of renal stone composition beyond that achieved with single energy multi detector CT acquisitions with basic attenuation assessment. Giorgio ascent et al. (2010) was a study done on 39 patients with suspected renal colic in which ureteral stones were shown at low dose unenhanced CT were enrolled. Stone composition could be established in 24 patients and these patients represented the study population regarding the CT characterization of stones. Correct chemical composition was obtained by dual energy analysis in all 24 ureteral calculi. Thus, it was concluded that the use of DECT attenuation values made it possible to characterize all ureteral, discriminating uric acid stones from calcium salt stones. Paul stolzman[20] et al. (2010) in their study calculated the sensitivity, specificity, positive and negative predictive value (NPV) for detection of uric acid containing urinary stones using DECT. This study concluded that DECT detected 110/180 patients (61 %) with renal stone disease. Sensitivity, specificity, PPV, and NPV for uric acid stone were 89 %, 98 %, 95 % and 98 %.

This study concluded that DECT permits accurate differentiation of uric acid stones from non-uric acid stones. Ruth Eliahou[21] et al. (2010) In this study, patients were scanned with single source, dual layer detector DECT scanner, and low/high energy density ratios were calculated for each stone scanned in vivo. Ratios were compared with values from an in vitro stone library obtained with a phantom model: 1.1 for uric acid, 1.1 to 1.25 for cysteine and 1.24 for calcified stones. In this series, they showed that DECT can differentiate between uric acid, cysteine and calcium stones. However, struvite and subtypes of calcium oxalate stones could not be distinguished.

CONCLUSIONS

With dual energy CT, it is possible to determine the composition of renal calculi in vivo non-invasively (with specificity of 95 % in our present study). Therefore, this helps in deciding the modality of treatment pre-operatively whether the stone is amenable to medical management (e.g., uric acid stones) or requires ESWL or surgical intervention can be determined pre-operatively. This helps to reduce the unnecessary financial burden and is found to be time saving. It is also found to be useful in advising appropriate measures to prevent recurrence of the stones in future.

Limitations of the Study

The main limitation of DECT is its relatively high radiation exposure and failure to identify some mixed stone composition accurately. Dual energy CT is expected to replace conventional single energy CT (SECT) as an important imaging modality in evaluating patients with suspected urinary calculi, as it provides images and same anatomical information as well as stone composition.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
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