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Original Article

Correlation of Ultrasound Twinkling Artifact with Dual Energy Computed Tomography in Characterization of Renal and Ureteric Calculi

Dr. Kaviya V[1], Dr. Madan Mohan Babu[2], Dr. Suresh A[3], Dr. Anasuyamma[4], Dr. Mummadi Swathi[1]

[1]Radiodiagnosis, VIMS & RC, Bangalore.
[2]Professor, VIMS & RC, Bangalore.
[3]HOD & Professor, VIMS & RC, Bangalore.
[4]Associate Professor, VIMS &RC, Bangalore

ABSTRACT

Background: The characterization of renal and ureteric calculi composition has been explored using various imaging techniques. The study aimed to assess the correlation of ultrasound twinkling artifacts with Dual Energy Computed Tomography (DECT) in this context.

Aims and Objectives: Establish the association between the composition of renal stones and the presence and grading of twinkling artifacts using color Doppler, in comparison with Dual Energy CT.
Determine the sensitivity and specificity of ultrasound twinkling artifact vis-à-vis Dual Energy CT.

Methods: A total of 50 patients with a history of flank pain, haematuria, difficulty in micturition, or known renal and ureteric calculi were included after receiving ethical committee clearance and informed consent. These patients underwent an ultrasound KUB, followed by DECT KUB. The ultrasound, performed using Philips Affiniti 50 & Philips HD 15 machines, utilized a curvilinear probe of 2-5 MHz. The DECT KUB was conducted with a Siemens 128-slice CT scanner. Findings from the ultrasound were then compared to DECT KUB results regarding stone composition.

Results: The study identified 67 stones of four different compositions: 32 calcium oxalate, 10 calcium hydroxyapatite, 20 uric acid, and 5 cystine. Twinkling artifact grading on ultrasound color doppler was as follows: grade 0 (23 stones with no artifact), grade 1 (17 stones with less than half the surface showing the artifact), and grade 2 (27 stones fully exhibiting the artifact). When cross-referenced with DECT KUB results, no substantial correlation was found between twinkling artifact grades and renal stone morphology.

Conclusion: The in vivo study involving 50 patients found no significant correlation between the grades of twinkling artifacts on ultrasonography and the results of DECT KUB in characterizing renal stone morphology. The ultrasound twinkling artifact, although not definitive for morphology determination, exhibited a correlation showing 95.8% sensitivity and 87% specificity statistically.

Key Words: *Ultrasound, Twinkling Artifact, Dual Energy Computed Tomography, Renal Calculi, Ureteric Calculi, Morphology, Sensitivity, Specificity.*

***Corresponding Author**
Dr. Kaviya V
VIMS & RC, Bangalore.

INTRODUCTION

The realm of medical imaging has witnessed remarkable advancements in recent decades, playing an instrumental role in the diagnosis, management, and follow-up of various pathologies, including renal and ureteric calculi. Two key imaging modalities that have garnered attention in the characterization of these calculi are Ultrasound (US) and Dual Energy Computed Tomography (DECT). The intrigue surrounding the ultrasound twinkling artifact, in particular, and its potential correlation with DECT in renal and ureteric calculi characterization forms the bedrock of this discourse.

Ultrasound, since its inception in the early 1950s, has evolved as an invaluable diagnostic tool in urology.[1] Primarily used for visualizing abdominal and pelvic structures, its non-invasiveness, absence of ionizing radiation, and real-time imaging capabilities have made it a preferred modality in many clinical settings.[2]. Ultrasound's ability to detect renal and ureteric calculi is well-established,[3] but the introduction of the color Doppler brought forth the phenomenon of the twinkling artifact – a rapid color variation behind reflective objects, particularly stones.

The origin and significance of the twinkling artifact have been topics of research and debate.[4] Some theories attribute it to the rough surface or scattering properties of the stone, while others point to the machine's software or inherent Doppler noise.[5] Regardless of its cause, the potential diagnostic value of this artifact, especially concerning renal and ureteric calculi characterization, cannot be overlooked.

While ultrasound holds a key position in initial diagnostic assessments, Dual Energy Computed Tomography (DECT) has emerged as the gold standard for non-invasive characterization of urolithiasis.[6] DECT harnesses two distinct X-ray energy spectra, providing qualitative and quantitative insights into tissue composition. The technique's ability to distinguish between stone types (e.g., uric acid from non-uric acid stones) has profound therapeutic implications, as the management can differ substantially based on the stone's composition.[7]

The notion of correlating the ultrasound twinkling artifact with DECT findings is both innovative and potentially transformative. Preliminary studies have demonstrated variable results. Some suggest a positive correlation between the intensity of the twinkling artifact and the calcium content of the stone as determined by DECT.[8] In contrast, others found no such consistent relationship, indicating the artifact might be more related to stone surface texture than its inherent composition.[9]

Given the high sensitivity and specificity of DECT in stone characterization,[10] any correlation (or lack thereof) with the twinkling artifact can significantly influence clinical decisions. A strong correlation might imply that a simple ultrasound can provide substantial information about stone composition, reducing the need for DECT and its associated radiation exposure. Conversely, a weak or non-existent correlation would relegate the twinkling artifact to a mere curiosity, with DECT remaining indispensable for detailed stone analysis.

The journey from mere observation of twinkling artifacts in ultrasounds to the pursuit of its potential diagnostic significance showcases the relentless quest for precision in modern medicine. As our understanding of imaging modalities like DECT expands and the clinical implications of various imaging findings become clearer, it becomes imperative to revisit, reassess, and re-evaluate longstanding beliefs and correlations.[11] This article aims to delve deep into this correlation, shedding light on the clinical relevance of the ultrasound twinkling artifact in the era of advanced imaging modalities like DECT.

AIM: To correlate twinkling artifact in ultrasound with Dual-energy CT for characterization of renal and ureteric calculi.

OBJECTIVE

- To determine the composition of renal stones with the presence and grades of twinkling artifacts on color Doppler in correlation with Dual Energy CT.
- To determine the sensitivity and specificity of ultrasound twinkling artifact with Dual Energy CT.

MATERIALS AND METHODS

Ethical Considerations

The ethical committee of VIMS & RC granted clearance for this study. All participants provided informed consent prior to the commencement of the research.

Study Population

The research incorporated 50 patients sourced from the Department of Urology. These patients exhibited clinical suspicion of renal and ureteric calculi. They were then referred to the Department of Radiodiagnosis in VIMS &RC for CT KUB investigations.

Inclusion Criteria:

- Patients presenting with renal calculi, ureteric calculi, and VUJ calculi undergoing CT KUB imaging evaluation in the department of radiology.

Exclusion Criteria:

- Patients aged below 18 years.
- Those with vesical calculus, multiple calculi (ranging from 2 to 5 in number), calculi linked to metabolic conditions like secondary hyperparathyroidism, congenital anomalies such as medullary spongy kidney disease, nephrocalcinosis, staghorn calculus, and stones exceeding 2cm in diameter.

Imaging Protocols

Ultrasound KUB: Doppler USG examinations were carried out for all participants using PHILIPS HD 7 and PHILIPS Affiniti 50 with a curvilinear probe spanning 2- 5 MHz frequencies. A focal point of the study was observing the twinkling artifact.

Dual-energy CT KUB: 50 participants underwent this procedure on a Siemens Somatom Definition AS 128 slice Multi-detector CT scanner, adhering to specific parameters:

- Tube potentials: 80 and 140 kVp
- Tube current: 342 and 76 mAs
- Collimation: 14 x 1.2 mm^2

Analysis of the CT examinations was conducted on dedicated workstations, notably the Syngovia (127.0.0.1@ 2009-2016 Siemens Healthcare) workstation. A 3D-material decomposition inherent to the dual-energy software aided in differentiation, employing color coding to discern different stone types. Notably, ultrasound KUB's twinkling artifact evaluations were kept blind to the dual-energy CT results. They were subsequently reviewed, analyzed, and conclusions drawn.

Variables Recorded and Analysed:

- **Ultrasound KUB:** Stone location, Twinkling artifact presence/absence, and if present, the grading of the Twinkling artifact.
- **Dual-energy CT KUB:** Stone identification and stone characterization.

Sample Size Estimation

Using the sensitivity value from the reference article by Jonathan R Dillman et al, the sample size was computed based on the formula provided. The calculations, given the parameters, resulted in a sample size of 45, ensuring a power of 80% at 95% confidence levels.

Data Collection

- **Study Duration:** March 2021 to September 2022.
- **Study Design:** A prospective observational study.
- **Sample Size:** The primary study population constituted 45 patients.

Statistical Analysis

Data entries were made in a Microsoft Excel sheet and later analyzed utilizing SPSS 22 version software. Categorical data took the form of frequencies and proportions, with the Chi-square test serving as the test of significance for qualitative data. Continuous data representation used means and standard deviations. Graphical representations, like bar and pie charts, were generated using MS Excel and MS Word. A p-value <0.05 was deemed statistically significant after ensuring all statistical test rules were followed. For data analysis, the MS Excel and SPSS version 22 software tools were employed.

RESULTS

A total of 50 patients presented with clinical features of renal or ureteric calculi and underwent Dual-energy CT with Doppler USG and in whom the composition of the calculi was characterized.

		Count	%
Sex	Male	32	64%
	Female	18	36%

Table 3 - Gender distribution

Out of 50 cases involved in the study, 32 (64%) were male and 18 (36%) were female. The highest cases were male that is 64% and the female cases were less.

		Count	%
Age	18-25 years	6	12 %
	26 to 40 years	22	44%
	41 to 60 years	14	28 %
	>60 years	8	16%

Table 4 - Age distribution

Amongst the 50 cases involved in the study, 6(12%) were between the age group of 18-25, 22(44%) cases were between the age group of 26-40, 14(28 %) cases were between the age group of 41-60 and 8 (16%) cases were above the age group of 60. The highest number of cases were between the age group of 26 to 40 that is 22 cases (44%).

		Count	%
Clinical Findings	Right flank pain	13	26%
	Left flank pain	15	30%
	Pain abdomen	10	20%
	Difficulty in passing urine	11	22%
	Bilateral flank pain	1	2%

Table 5 - Clinical findings

Among the 50 patients involved in study 13 (26 %) cases showed right flank pain, 15 (30%) cases were reported to have left flank pain, 10(20 %) patients showed pain in the abdomen, 11(22%) patients had difficulty in passing urine, and remaining 1(2%) cases were reported to have bilateral flank pain. The highest number of cases 15(30%) were reported to have left flank pain and the lowest cases 1 (2%) were reported to have bilateral flank pain.

		Count	%
Ultrasound KUB Findings	Right renal calculus	21	42%
	Left renal calculus	14	28%
	Right renal calculi	3	6%
	Left renal calculi	7	14%
	Bilateral renal calculi	5	10%

Table 6 - Ultrasound KUB findings

USG findings of 50 cases were recorded with 5 different conditions. Out of that, 21 (42%) cases were reported to have right renal calculus, 14(28%) cases were reported to have left renal calculus, 3(6%) cases were reported with right renal calculi, 7 (14%) cases were reported with left renal calculi and 5 (10 %) cases were reported with bilateral renal calculi. Among the five clinical conditions, the condition which has highest cases was right renal calculus that is 21(42%) and the lowest cases were reported to have right renal calculi.

		Count	%
TA Grading	Grade 0	23	34%
	Grade 1	17	25%
	Grade 2	27	41%

Table 7- Grading of twinkling artifact

TA grade of all the cases involved in the study were diagnosed. Out of 50 cases involved in the study, 23 cases were diagnosed with grade-0 TA, 17 were diagnosed with grade-1 TA and 27 cases were diagnosed as grade-2 between this grading the highest number of cases 27 were lied in Grade-2 and lowest cases 17 were reported to have Grade-1 TA.

		Count	%
Calcium Oxalate	Present	32	64%
	Absent	18	36%

Table 8 - Distribution of calcium oxalate

Out of 50 cases involved in the study 32 (64%) cases were reported to have calcium and 18 (36 %) cases were reported absent for DECT calcium. The highest cases were reported to have DECT calcium 32 (64%).

		Count	%
Calcium Hydroxyapatite	Present	10	20%
	Absent	40	80%

Table 9 - Distribution of Hydroxyapatite

Among the 50 cases involved in the study, 10 (20%) cases were diagnosed to have DECT Hydroxyapatite and 40 (80) %cases were absent for DECT Hydroxyapatite.

		Count	%
Uric acid stones	Present	20	40%
	Absent	30	60%

Table 10 - Distribution of Uric acid stones

Among the 50 cases involved in the study 20 (40 %) cases were reported to have Uric acid and 30 (60 %) cases were reported as absent for DECT Uric acid.

		Count	%
Cystine stones	Present	5	10%
	Absent	45	90%

Table 11- Distribution of cystine stones

Out of 50 cases involved in study 5(10%) cases diagnosed to have DECT cystine and 45(90%) cases were reported absent for DECT cystine.

Renal stones	**Grade 0**	**Grade 1**	**Grade 2**	**Total**
Calcium oxalate	12 (17.91%)	6 (8.95%)	14 (20.89%)	32 (47.76%)
Calcium hydroxyapatite	2 (2.98%)	3 (4.47%)	5 (7.4%)	10 (14.92%)
Uric acid	5 (7.4%)	7 (10.44%)	8 (11.94%)	20 (29.85%)
Cystine	4 (5.9%)	1 (1.49%)	0 (0%)	5 (7.46%)
	23 (34.32%)	**17 (25.37%)**	**27 (40.29%)**	**67 (100%)**
	Chi Square test value	**18.33**	**P value**	**0.034 (Sig)**

Table 12 – TA grades with the presence of stone

In calcium oxalate 17.95 % crystals observed were in grade 0, 8.95% were in grade 1 and 20.89 % were in grade 2. In the same way in Calcium hydroxyapatite 2.98 % crystals observed were in grade 0, 4.47 % were in grade 1 and 7.4 % were in grade 2. In Uric acid 7.4% crystals observed were in grade 0, 10.44% were in grade 1 and 11.94 % were in grade 2. In Cystine 5.9% crystals observed were in grade 0, only 1.49 % were in grade 1 and no TA was observed in grade 2.

Final correlation of outcome Statistics	**95% CI**
Sensitivity	95.86%
Specificity	87.38%
Accuracy (*)	96.64%

Table 13 - SENSITIVITY, SPECIFICITY, ACCURACY

DISCUSSION

In patients coming to emergency rooms with sudden flank discomfort, ureteric and renal colic are prevalent causes. The exact rates of occurrence and prevalence differ by age group, sex, and race. Non-contrast CT scans are frequently used when urinary stone disease is suspected but not yet diagnosed. [12]

The use of potentially dangerous ionizing radiation is a major drawback. The incidence of renal calculus is estimated at 12% in males and 6% in women, making it one of the leading causes of visits to emergency rooms. Kidney stones and other stones in the urinary tract are the leading cause of abdominal pain.

By comparing X-ray attenuations at varying tube potentials, DECT can discriminate between renal calculi that would otherwise be indistinguishable using standard CT. DECT is able to characterize stone composition without increasing radiation dose. However, determining the stone/stent boundary or estimating the stone volume with only a two-dimensional DECT image may be impossible.

Urography, ultrasound and computed tomography (CT) are the modalities to diagnose the renal/ureteric stones and composition of stones. Dual energy CT provides reliable distinction between uric acid, Ca oxalate and Cystine stones, it predicts the chemical composition of the stones [13]. On view of renal stone disease being a common problem, this study is undertaken to assess the sensitivity and specificity of ultrasound twinkling artifact in diagnosing the composition of renal stones and to correlate the diagnosis with DECT which remains the gold standard for the diagnosis of calculi.

In our study, 50 cases involved, 32 (64%) were male and 18 (36%) were female. The highest cases were male. According to Maryam Letafati et al study, 84 patients (85%) were males (50). According to Hatem Adel et a., study with total 221 patients, 146 (66.1%) were males and 75 (33.9%) were females (51). In Mohammad Qasem Hanafi et al study, out of the 100 patients who participated in the study, 72 (72%) were male and 28 (28%) were female [13].

Amongst the 50 cases involved in the study, 3(6%) were between the age group of 18-25, 23(46%) cases were between the age group of 41-60, 14(28%) cases were between the age group of 26-40 and the highest number of cases were lies between the age group of above 60 that is 23 cases (46%). In our study the Mean age was 41.7 ± 13.92. In Ningning Liu et al., study, 1789 cases were done and the mean age was 48.2 ± 13.7 years,

Among the 50 patients involved in the study 13 (26%) cases showed right flank pain, 10(20%) patients showed pain in the abdomen, 11(22%) patients had difficulty in passing urine, 15 (30%) cases were reported to have left flank pain and remaining 1(2%) cases was reported to have bilateral flank pain. The highest number of cases 15(46%) were reported to have left flank pain and the lowest case 1 (2%) was reported to have Bilateral flank pain. Glowacki et al. examined the symptomatic calyceal renal calculi in 107 patients who were observed for a mean of 32 months. 32% of them had an episode of pain in the abdomen followed by flank pain in 12 % of the patients which is similar to our study [14]. Pabst G. followed 80 renal stones in 63 patients, reporting that 40% of patients had flank pain. Interestingly, several studies consistently showed the similar clinical findings as in our study [15].

USG findings of 50 cases were recorded with 5 different conditions. Out of that, 21(42%) cases were reported to have right renal calculus, 14 (28%) cases were reported to have left renal calculus, 3(6%) cases were reported with right renal calculi, 7(14%) cases were reported with left renal calculi and 5(10%) cases were reported with bilateral renal calculi. Among the five clinical conditions, the condition which has highest cases was right renal calculus that is 21(42%) and the lowest cases were reported to have right renal calculi.

Kamaya A, Tuthill et al., observed similar results [16]. Patel et al reported 22% cases with right renal calculi, 18% cases were reported to have left renal calculi [17].

TA grades of all the cases involved in the study were diagnosed. Out of 50 cases involved in the study, 23 cases were diagnosed with grade-0 TA, 17 were diagnosed with grade-1 TA and 27 cases were diagnosed as grade-2 between this grading the highest number of cases 27 were in Grade-2 and lowest cases 17 were reported to have Grade-1 TA. Alan et al., there was no artifact found in 11 participants (grade 0), in 25 it was grade 1, and in 24 it was grade 2. There was a statistically significant (p 0.001) correlation between the size of the stones and the number of lights in the artifacts.

Out of 50 cases involved in the study 32 (64 %) cases were reported to have calcium and 18 (36 %) cases were reported absent for DECT calcium. The highest cases were reported to have DECT calcium 36 (64%). In calcium oxalate 17.95 % crystals observed were in grade 0, 8.95% were in grade 1 and 20.89 % were in grade 2. The correlation between the twinkling artifact and the biochemical composition of stones was highly significant according to many of the previous reports. Calcium oxalate monohydrate and urate stones were the only calculi showing no twinkling artifact according to Valido IH et al [18]. However, 14 of 24 calcium oxalate monohydrate stones produced a grade 1 artifact in their study. Calculi of calcium oxalate dihydrate and calcium phosphate always produced a grade 1 or grade 2 twinkling artifact. The chisquare test showed a strong relationship with the p value = 0.0008

Since percutaneous nephrostolithotomy has become increasingly common, a better understanding of how stones manifest is of paramount importance. Until now, the main criteria for choosing between this procedure and the classical extracorporeal shock wave lithotripsy were the size and location of calculi. However, small dense calculi are difficult to fragment with extracorporeal shock wave lithotripsy and probably are more effectively treated by nephrostolithotomy. Dretler and Polykoff showed that the radiographic patterns of stones can be correlated with four types of calcium oxalate stones. However, these patterns were found to be reliable only for stones greater than 1 cm in diameter, and such analysis is impossible when the stone is superimposed on bony structures [19]. The twinkling artifact with colour flow sonography, calcification may be seen regardless of how large or little it is or how widely spaced out it is inside tissues.

Correlation between TA grade and Hydroxyapatite depicts, Among the 50 cases involved in the study, 10 (20%) cases were diagnosed to have DECT Hydroxyapatite and 40 cases were absent for DECT Hydroxyapatite. In the same way in Calcium hydroxyapatite 2.98 % crystals observed were in grade 0, 4.47 % were in grade 1 and 7.4 % were in grade 2. In correlation of TA grade with DECT Hydroxyapatite the highest cases with DECT Hydroxyapatite were diagnosed with Grade-2. The correlation date depicts the highest cases who were reported absent for DECT CA hydroxyapatite fall under grade-1 and the highest cases who were reported to have DECT CA hydroxyapatite fall in Grade-2. The Chi-Square value is- 7.615. Døssing A, Müller FC, Becce., observed hydroxyapatide deposition in 15 cases in grade 1among 200 cases [20].

In the uric acid detection by DECT, Among the 50 cases involved in the study 20 (40 %) cases were reported to have Uric acid and 30 (60 %) cases were reported as absent for DECT Uric acid. In Uric acid 7.4% crystals observed were in grade 0, 10.44% were in grade 1 and 11.94 % were in grade 2. According to research by Alan et al., the artifact was found in over 50% of calcium oxalate monohydrate and uric acid stones.

Alan CA, Koçoğlu reported that, adjusted for size, cystine and brushite calculi are the most resistant to SWL, followed by calcium oxalate monohydrate, after which, in descending order of resistance to fragmentation are struvite, calcium oxalate dihydrate, and uric acid stones. They reported that, stones found 22 cases were calcium oxalate monohydrate stones; 26 cases were calcium oxalate dihydrate stones; 9 cases were calcium phosphate stones; and 3 cases were uric acid stones. Pearle MS, Pak YC reported that cystine and calcium oxalate monohydrate stones could not be predicted by in vivo TA intensity ($p > 0.05$). [21]

Based upon the literature review, very few studies available to determine the composition of renal stone by the intensity of twinkling artifact. We found that there is a significant correlation between stone composition and the twinkling artifact in the case of oxalate stones and uric acid stones.

Ulusan et al. have found that there is a strong statistical relation between the absence/presence of posterior acoustic shadow in USG and the size and density of a stone detected in non-contrast CT. There are also studies reporting that there is a close relation between the twinkling artifact and posterior acoustic shadowing and furthermore, that the twinkling artifact has a better diagnostic value in kidney stones [22].

In light of these former findings, this study might seem consistent by attributing a potential diagnostic value and relevance to stone composition with respect to the twinkling artifact.

Following the study of Chelfouh et al., this study is the second study to research the relation between the twinkling artifact and stone composition. The study examined the twinkling artifact before any treatment was applied to the patients, and it assessed the conformity between the data obtained [23].

This study might be the first in the literature to take these different aspects into consideration. Dretler and Polykoff reported that the radiographic patterns of stones can be correlated with four types of calcium oxalate stones. However, these patterns were found to be reliable only for stones larger than 1 cm in diameter.

According to Rahmouni, the twinkling artifact with color flow sonography is not limited by the size of the calcification and can be found even when it is sometimes slight and spread out within tissues [24].

In summary, we found an in vivo relationship between the presence of a color-flow sonographic twinkling artifact and dual energy CT KUB in characterizing the morphology of stones. On the basis of these results, we believe that the use of color-flow sonography with dual energy CT for predicting the composition of stones. We observed correlation between the presence of stone and its morphology.

In vitro studies are needed to clarify the factors that affect the formation and/or intensity of TA and to show a relationship between TA and the stone type.

CONCLUSION

This is a prospective observational study in 50 patients to assess an in vivo relationship between the grades of twinkling artifacts in ultrasonography with DECT KUB to characterize the morphology of renal stones. Twinkling artifacts in ultrasonography was used to assess the presence and grades of renal stones. DECT KUB was used to characterize the morphology of renal stones. In correlating the grades of twinkling artifact with the findings in DECT KUB, there was no significant correlation for characterizing the morphology of renal stones. Twinkling artifact in ultrasonography alone has no role in determing the morphology of renal stones; however the correlation showed 95.8% sensitivity and 87% specificity statistically.

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