Radiology Section

Determination of Attenuation Values of Urinary Calculi by Non-Contrast Computed Tomography and Correlation with Outcome of Extracorporeal Shock Wave Lithotripsy – A Prospective Study

#### DEEPTI NAIK, ADITI JAIN, AMNA ARUNACHALA HEGDE, ASHOK ADEKAL KUMAR

# ABSTRACT

**Introduction:** Urolithiasis is a common disease with an increasing incidence worldwide. Non-Contrast Computed Tomography (NCCT) is the gold standard imaging modality for the patient presenting with acute renal colic. Extracorporeal Shock Wave Lithotripsy (ESWL) has emerged as the treatment of choice for urolithiasis. The attenuation value in Hounsfield units evaluated by NCCT is reported to be a strong predictive factor for the successful outcome of ESWL.

**Aim:** To determine the attenuation value of urinary calculi by NCCT and to correlate it with the outcome of ESWL.

Materials and Methods: This study is a prospective

analytical study. All 75 urolithiasis patients who have undergone NCCT and ESWL at M.S Ramaiah Medical College and Hospitals, Bengaluru, India, between November 2013 to June 2015 were considered for the study.

**Results:** The successful outcome post ESWL in different groups of attenuation value are 100% in group 1(<500HU), 92.6% in Group 2(500-1000HU) and 33.3% in Group 3(>1000HU). The failure rate was 7.3% in Group 2 and 66.7% in Group 3. The calculus density above 1000 HU decreases the rate of successful outcome post ESWL.

**Conclusion:** The attenuation value of the urinary calculi estimated by NCCT predicts the ESWL outcome thus identifying patients suitable to undergo ESWL.

Keywords: Calculus density, Hounsfield unit, Renal colic, Urolithiasis

### INTRODUCTION

Incidence of urolithiasis is increasing across the world. Life style related risk factors like obesity, diminished fluid consumption and animal protein intake are some of the contributory reason for this increase [1]. ESWL was introduced as a non-invasive method for treatment of urinary calculi by Chaussy et al., in 1980. Since then it has become the preferred treatment option for urinary calculi of less than 20 mm diameter [2-5]. Alternative surgical and endo-urological options exist for the management of stone disease. Also, ESWL failure results in it being repeated or in opting other procedures. Hence, there is a need to identify variables that predict successful outcome of ESWL.

The outcome of ESWL depends on the fragility of the calculus. This in turn depends on density and composition of the calculus. Since, NCCT provides very good density discrimination, it is preferred over the conventional radiographs

to evaluate patients with renal colic [2]. Determination of calculus density, attenuation value in Hounsfield Units (HU) by NCCT, increases the efficacy in determining the probability of clearance of calculi by selecting patients suitable to be treated with ESWL. CT-scan is highly sensitive in detecting ureteric calculus which is difficult to detect in ultrasonography due to obscuration of ureter by bowel gas. Plain radiograph is usually unable to detect low density and small size calculus and even radiopaque calculus can be missed due to obscuration by stool or bowel gas. CT-scan is the choice of investigation for identification and characterization of urinary calculi since it can detect even low density calculus and tiny calculi measuring 1 mm. The accuracy in identification and analysis of calculus is greatly increased by interpreting both axial and multi-planar reformatted images [6,7]. The secondary signs of urinary obstruction like hydronephrosis, ureteric dilatation, perinephric and periureteric edema, perinephric fat stranding and renal

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enlargement are well visualized in CT-scan. The efficacy of ESWL depends on the composition of calculus [8]. NCCT can reliably identify the composition of calculus by measuring its attenuation value. The Hounsfield Unit of various urinary calculi at 120 kV are usually as follows:

Uric Acid - 200-450 HU; Struvite - 600-900 HU; Cysteine - 600-1100 HU; Calcium Phosphate - 1200 -1600 HU; Calcium Oxalate Monohydrate and; Brushite - 1700-2800 HU [9-13].

ESWL has been the most opted method of treatment for calculi less than 20 mm. For calculi larger than 20 mm Percutaneous Nephrolithotomy (PCNL) is preferred.

# MATERIALS AND METHODS

This study is a prospective analytical study conducted at M.S Ramaiah Medical College and Hospitals, Bengaluru, India between November 2013 to June 2015. All patients who underwent NCCT for urolithiasis and later underwent ESWL were considered for the study. Ethical clearance was obtained from the institution before embarking on this study. A total of 75 subjects, of which 52 were males and 23 were females, were included in the study. Most of the patients (85%) were in the age group of 20-60 years. The mean age of the study population was 43.68 years.

#### **Inclusion Criteria**

Patients with urinary calculi who were advised ESWL.

#### **Exclusion Criteria**

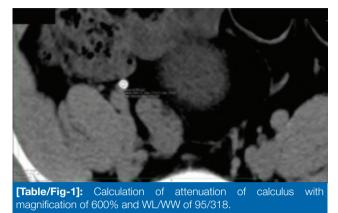
1. Patients with urinary calculi who were not treated by ESWL for various reasons including size, uncontrolled sepsis, uncontrolled hypertension and bleeding disorders.

2. Patients with known cases of obstruction for passage of stone.

3. Patients who cannot undergo CT-scan. For e.g., due to pregnancy.

NCCT was performed in Siemens Somatom Perspective 128 slice CT-scanner (Siemens Health Global, Germany) in all suspected acute urinary colic patients when their urinary bladder was moderately distended. CT-scan was done from the region of upper pole of kidney to pubic symphysis with slice thickness of 5 mm followed by 1 mm thin reconstruction and coronal and sagittal reformations using 3 mm thick sections. No oral or intra-venous contrast was utilized. The tube potential was 100 – 130 KV and tube current was 150-300 mA.

Calculation of attenuation value is the most important criteria for the study, therefore the parameters were standardized. Region of Interest (ROI) was drawn by tracing the contour of the calculus on the slice with maximum diameter axially with the following parameters: Window level of 95 and window width of 318 and magnification of 600%. ROI was drawn within 1 mm of margin of the calculus to avoid partial volume averaging [Table/Fig-1]. The preset software calculates the area, maximum, minimum and mean attenuation value of the calculus and these readings were recorded.



ESWL was performed using Dornier Compact Delta Lithotripter machine aided with both fluoroscopy and ultrasound for focusing the cup at the region of calculus and for assessing the fragmentation of the calculus. Patients were explained about the study, ESWL procedure and informed consent was obtained. The entire procedure in each session lasted for 30 to 45 minutes with maximum of three sessions. The number of shock waves in each session ranged from 1000 to 2000.

The follow-up was done using fluoroscopy, ultrasonography or radiography after 4 to 12 weeks of last ESWL session allowing enough time for spontaneous passage of fragments. The treatment outcome of urinary calculi depends on how effectively the patient's complaints and obstruction of the kidney are resolved. ESWL treatment outcome is measured in terms of fragmentation and clearance of the stone fragments. After ESWL treatment the clinical outcome can be labeled as successful if there is complete clearance of the urinary calculi.

# STATISTICAL ANALYSIS

Descriptive and inferential statistical analysis has been carried out in the study. Results on continuous measurements are presented as mean±SD (min-max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

Student's 't'-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (inter group analysis) on metric parameters.

Chi-square/Fisher's exact and one-way-ANOVA test has been used to find the significance of study parameters on categorical scale between two or more groups. Data was analyzed using SPSS version 17.

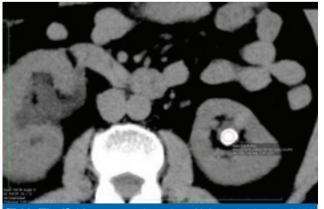
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# RESULTS

The study included 75 patients, 52 men and 23 women who underwent NCCT for detection of urinary calculi, ESWL treatment and were available for follow-up. The age range of the patients was 19 to 75 years. The mean±SD of age is 43.68±14.08. In 46 patients (61.3%) the calculus was located in the ureter (excludes pelvi-ureteric junction but includes vesico-ureteric junction) and in 29 patients (38.8%) the calculus was located in the kidney. The stone size varied from 5 to 20 mm. The mean stone size was 9.5 mm. There were 45(60%) patients with stone size less than the mean stone size. A linear correlation was seen between the mean attenuation value of the calculus and number of sessions required for fragmentation of calculus by ESWL. One-way-ANOVA showed significant correlation between the two.

Out of 75 patients, 31(41.3%) patients had mean attenuation value of less than 500HU; 41(54.6%) patients had mean attenuation value between 500-1000 HU and only 3 (4.0%) patients had mean attenuation value of more than 1000 HU. The success rate was 92.6% [Table/Fig-2] for the calculi with mean attenuation between 500-1000 HU and failure rate was 7.31% [Table/Fig-3a,b]. The success and failure rates are 33.3% [Table/Fig-4]. and 66.6% for calculi with attenuation value more than 1000 HU [Table/Fig-5]. Chi-square test correlation co-efficient is <0.001 which is statistically significant. Residual fragments were seen only in cases of median attenuation value more than 552 HU. The Fisher's exact test value is 0.002 which is statistically significant.

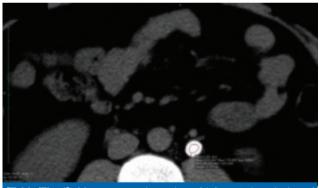
On comparing largest dimension of the calculi with median attenuation value, out of 38 patients with HU < 552, 84.2% patients had largest dimension ranging from 5 to 10 mm and in 5.2% the largest dimension was between 16 to 20 mm. In patients with HU more than 552, in 45.9% and 16.2% patients the size was between 5-10 mm and 16-20 mm respectively. The mean attenuation value was 590 HU. Forty three patients



[Table/Fig-2]: Mean attenuation value of left renal calculus of 878 HU with successful outcome.



[Table/Fig-3a-b]: (a) Mean attenuation value of right renal calculus of 957 HU with treatment (ESWL) failure; (b) Mean attenuation value of right ureteric calculus of 964 HU with treatment (ESWL) failure.



[Table/Fig-4]: Mean attenuation value of left ureteric calculus of 1070 HU with successful outcome,

Outcome	Mean A	Total				
	<500	500-1000	>1000			
Success	31 (100%)	38 (92.7%)	1 (33.3%)	70 (93.3%)		
Failure	0	3 (7.3%)	2 (66.7%)	5 (6.7%)		
Total	31 (41.3%)	41 (54.6%)	3 (4%)	75 (100%)		
[Table/Fig-5]: Comparison of mean attenuation value with treatment outcome.						

had attenuation value less than the mean and 32 patients had attenuation value more than the mean value [Table/Fig-6]. Out of 75 patients ESWL failure was noted in only 5 patients.

The largest residual fragment of the failure cases is calculus measuring 9 mm noted in a patient with mean attenuation value of 966 HU. Clinically insignificant residual fragments are seen in 3 patients with HU ranging from 631 to 962 HU.

Out of 49 patients with calculus measuring <11 mm, complete clearance was achieved in 46 patients. Out of 24 patients with calculus measuring 11–18 mm, complete clearance was achieved in 22 patients. In 2 patients with calculus size > 18 mm, complete clearance was obtained in both the patients [Table/Fig-7]. This suggests that the outcome of ESWL treatment does not depend on calculus size.

Largest	Median Atter	Total	
Dimension (mm)	<552 HU	> 552	
5 – 10	32 (65.3%)	17 (34.7%)	49
11 – 15	4 (22.2%)	14 (77.8%)	18
16 – 20	2 (25.0%)	6 (75.0%)	8
Total	38 (50.6%)	37 (49.4%)	75
Table/Fig.61	Lorgoot dimons	tion of coloulus	with modion

[Table/Fig-6]: Largest dimension of calculus with mediar attenuation value.

Largest	Outo	Total			
Dimension (mm)	Success	Failure			
< 11	46 (65.7%)	3 (60.0%)	49 (65.3%)		
11 – 18	22 (31.4%)	2 (40.0%)	24 (32.0%)		
> 18	2 (2.9%)	0	2 (2.7%)		
TOTAL	70 (100%)	5 (100%)	75 (100%)		
[Table/Fig-7]: Comparison of largest dimension of calculus with					

# DISCUSSION

Urolithiasis is a common disease worldwide. It affects all kinds of patient population in different age group and gender. Appropriate management of urolithiasis has important clinical implications as they are associated with complications like infection and chronic kidney disease. There is also a higher risk of recurrence of calculus. NCCT-scan is regarded as the gold standard for initial diagnosis [14], treatment planning and follow-up of the patients with urolithiasis. Its advantages include high sensitivity (95-98%), high specificity (96–100%), easy availability, higher detection rate (especially for stones in the distal ureter) and speedy diagnosis. Furthermore, there is no need for intravenous contrast media administration and can be easily used in renal failure patients.

NCCT is accurate in determining the location, size, density and composition of the stones which can affect treatment planning and management [8]. NCCT detects almost all types of calculi, including uric acid, cysteine and xanthine stones which are otherwise radiolucent on conventional radiographs. CT-scan measures the attenuation of calculus in Hounsfield units enabling the assessment of its density and fragility by ESWL.

In our study the mean age of presentation was 43.6 years. The agerange was 19 to 75 years. 46 (61.3%) patients belonged to the age group between 20 to 50 years.

In the study by Gupta NP et al., the mean age of the patients undergoing ESWL for urinary calculi was 33.6 and 39.4 years with the range 19–54 and 20-63 years respectively [2].

Tanaka M et al., the study included patients with overall mean age of 56.3±11.8 and 52 years respectively [3].

In our study 69% and 31% were men and women respectively. In the study by Tanaka M et al., the percentage of men and women were 61.3% and 38.7% respectively [3]. The percentage of men and women were 60.3% and 39.7% respectively in the study by Massoud AM et al.,[15].

In our study, out of 75 patients 46 (61.3%) who had undergone ESWL for ureteric stones and 29 (38.7%) patients for renal calculi. In the ureteric calculi the distribution in the proximal, mid and distal ureter are 15 (20%), 11 (14.6%) and 15 (20%) patients. 4 (5.3%) and 1 (1.3%) in the left and right vesico-ureteric junction respectively. Upper, mid and lower calyces are 2 (2.6%), 13 (17.3%) and 8 (10.6%) patients. Two (2.6%) and 1 (1.3%) patient had calculi in the right and left pelviureteric junction respectively. Two (2.6%) patients had calculus in the renal pelvis. Out of the 5 failure cases, in 1 case the calculus was in mid calyx, 2 in proximal ureter, 1 in mid ureter and 1 in distal ureter.

In the study Tanaka M et al., showed that among 75 patients 46 were ureteric calculi and 29 renal calculi but he had not given the break up in the renal and ureteric calculi [3]. Ouzaid I et al., had studied the location of nephrolithiasis, out of 50 patients, lower calyceal 9 (18%), Upper/mid calyceal 12 (24%) and renal pelvic/PUJ 29 (58%) [1]. In the study done by Pareek G et al., out of 50 patients, a total of 30 stones (60%) were located in the ureter and 20 stones (40%) were located in the kidney. Of the intrarenal calculi 10 (50%), 5 (25%), 4 (20%) and 1 (5%) were in the in the renal pelvis, upper pole, mid pole and lower pole, respectively [16].

Though, there is no statistical significance in assessing the location of the calculus, ureter is the most often location as patients are symptomatic secondary to ureteric obstruction. In the study 45 (60%) patients had stone size less than the mean stone size of 9.5 mm. The stone size varied from 5 to 20 mm. The mean stone size and SD for the successful outcome group is  $9.3\pm3.4$  and the failure group is  $12\pm5$ . The p-value, difference between means is not statistically significant.

In the study by Ouzaid I et al., the mean stone size is 10.8 mm in the success group and 9.1 mm in the failure group which is

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# not statistically significant [1].

In our study of 75 patients, the number of patients in Group 1 (<500HU) were 31 (41.3%); Group 2 (500-1000 HU) were 41 (54.6%) and Group 3 (>1000 HU) were 3 (4%). The success rate is 100% for Group 1 and 92.6% for Group 2 with a failure rate of 7.31%. The success and failure rates are 33.3% and 66.6% for Group 3. Chi- square test correlation co-efficient value is <0.001 which is statistically significant. The median attenuation value is 552 HU. Out of 67 patients with complete clearance 38 patients had HU < 552 and 29 had HU>552. All 8 patients with residual fragments had median attenuation value more than 552.

In a study of 30 patients by Joseph P et al., who compared the density of calculi with the outcome of ESWL in vivo found that patients with calculi of < 500 HU had complete clearance, while 500–1000 HU had a clearance rate of 86% and patients with calculi of  $\geq$  1000 HU had a clearance rate of 55% [17].

Pareek G et al., correlated calculus density with clearance in a study of 50 patients treated with ESWL concluded that 36% of patients with residual calculi had a mean calculus density of  $\geq$  900 HU, compared with mean of 500 HU in 74% of patients who had clearance. In the study no correlation of calculus density with fragmentation was done [16].

Gupta NP et al., studied relationship between renal calculus density (mean HU), size, number of ESWL sessions and outcome showed a linear relationship between the calculus density and number of ESWL sessions. Calculi with HU <750 and diameter < 11 mm had best outcome with a clearance rate of 90% and stones with HU > 750 and diameter of > 11 mm had worst outcome with clearance rate of 60% and more number of ESWL sessions. The study analysis showed that the attenuation value had a greater impact on outcome than the calculus size [2].

A study by Tanaka M et al., showed stone attenuation value was the only independent predictor of ESWL success and stone cross-sectional area as a continuous variable is associated with ESWL success. Attenuation value of 780 HU or less and a stone cross-sectional area of 0.4 cm<sup>2</sup> or less were 11.6 times more likely to have successful result [3].

In the study Ouzaid I et al., showed that a stone density of 970 HU represented the most sensitive (100%) and specific (81%) point on the receiver-operating characteristic curve using the Youden Index. Calculi with < 970 HU had a clearance rate of 96% as compared to 38% for stones of  $\geq$  970 HU [1]. Tarawneh E et al., has said that the success rate of ESWL is high (94%) for low density stone of HU < 500. CT densities of 750 HU or less was almost always successfully treated by ESWL and above 950 HU was associated with failure [4].

Study by Pathak S et al., had results of 100%, 69% and

32% successful ESWL outcomes for patients with a mean stone density <500, 500 - 799 and  $\geq$ 800 HU respectively. It concluded that the mean stone density  $\geq$ 800 HU is a predictor of ESWL failure [18].

Massoud AM et al., had made three groups of mean attenuation value similar to this study of <500, 500-1000 and >1000 HU for 305 patients. The stone clearance rate was 100 %( 81) in Group 1, 95.7% (135/141) in Group 2 and 44.6% (37/83) in Group 3. The results were similar to the present study. The present study concurrence with above mentioned studies has shown that ESWL outcome is dependent on the density of the calculu and increase in density of the calculus results in poor outcome [15].

In the present study number of ESWL sessions for the mean attenuation value of the calculi is studied which showed a linear relationship between the two. Out of 75 patients 52 patients underwent single session. The mean (SD) of the attenuation value of calculi which required one session is 487.1(183.4). 13 and 10 patients needed 2 and 3 sessions respectively for fragmentation of the calculi. The mean attenuation value is 712 and 969 for 2 and 3 sessions.

In a study by Massoud AM et al., it is seen that out of 95.7% successful cases in Group 2 (500-1000HU), on an average about 2 sessions are required only few cases needed three ESWL sessions. In Group 3 (>1000 HU), 16 (43%) of the 37 (44.6%) successful cases required three sessions but none of them in a single session [15].

### LIMITATIONS

1. Chemical composition of the calculus in vitro was not determined hence density and chemical composition could not be confirmed and correlated.

2. Other factors that can influence the ESWL outcome like BMI of the patient and number of shock waves in each session are not included in the present study.

## CONCLUSION

This study concludes that non-contrast CT-scan is accurate in determining the attenuation value of urinary calculi which is an independent and most important factor in determining the fragility of calculi and thus the outcome of ESWL treatment.

#### REFERENCES

- [1] Ouzaid I, Al-qahtani S, Dominique S, Hupertan V, Fernandez P, Hermieu JF, et al. A 970 Hounsfield units (HU) threshold of kidney stone density on non-contrast computed tomography (NCCT) improves patient selection for extracorporeal shock wave lithotripsy (ESWL): evidence from prospective study. BJU Int. 2012;110(11 Pt B):E438-42.
- [2] Gupta NP, Ansari MS, Kesarvani P, Kapoor A, Mukhopadhyay S. Role of computed Tomography with no contrast medium enhancement in predicting the outcome of ESWL for urinary calculi. BJU Int. 2005;95:1285-88.

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- [3] Tanaka M, Yokota E, Toynaga Y, Shimizu F, Ishii Y, Fujime M, et al. Stone attenuation value and cross sectional area on CT predict the success of shock wave lithotripsy. Korean J Urol. 2013; 54(7):454-59.
- [4] Tarawneh E, Awad Z, Hani A, Haroun AA, Hadidy A, Mahafza W, et al. Factors affecting urinary calculi treatment by extracorporeal shock wave lithotripsy. Saudi J Kidney Dis Transpl. 2010; 21(4):660-65.
- [5] McAdam S and Shukla AR. Pediatric extracorporeal shock wave lithotripsy: Predicting successful outcomes. Indian J Urol. 2010; 26(4):544–48.
- [6] Lin WC, Uppot RN, Li CS, Hahn PF, Sahani DV. Value of automated coronal reformations from 64-section multidetector row computerized tomography in the diagnosis of urinary stone disease. J Urol. 2007;178:907–11.
- [7] Metser U, Ghai S, Ong YY, Lockwood G, Radomski SB. Assessment of urinary tract calculi with 64- MDCT: the axial versus coronal plane. Am J Roentgenol. 2009;192(6):1509–13.
- [8] Wang LJ, , Wong YC, Chuang CK, Chu SH, Chen CS, See LC, et al. Predictions of outcomes of renal stones after extracorporeal shock wave lithotripsy from stone characteristics determined by unenhanced helical computed tomography: a multivariate analysis. Eur Radiol. 2005;15 (11):2238–43.
- [9] Motley G, Dalrymple N, Keesling C, Fischer J, Harmon W. Hounsfield unit density in the determination of urinary stone composition. Urology. 2001; 58(2):170–73.
- [10] Matlaga BR, Kawamoto S, Fishman E. Dual source computed tomography: a novel technique to determine stone composition. Urology. 2008; 72 (5):1164–68.
- [11] Bellin MF, Renard-Penna R, Conort P, Bissery A, Meric JB, Daudon M, et al. Helical CT evaluation of the chemical composition of

urinary tract calculi with a discriminant analysis of CT-attenuation values and density. Eur Radiol. 2004;14(11):2134–40 .

- [12] Williams JC Jr, Paterson RF, Kopecky KK, Lingeman JE, McAteer JA. High resolution detection of internal structure of renal calculi by helical computerized tomography. J Urol. 2002;167(1): 322– 26.
- [13] Mostafavi MR, Ernst RD, Saltzman B. Accurate determination of chemical composition of urinary calculi by spiral computerized tomography. J Urol. 1998;159(3):673–75.
- [14] Dahiphale D, Apte A, Dahiphale AP. Non-contrast spiral computed tomography diagnosis of urolithiasis and associated features: hospital based study. Int J Res Med Sci. 2016;4(10): 4286-89.
- [15] Massoud AM, Abdelbary AM, Al-Dessoukey AA, Moussa AS, Zayed AS, Mahmmoud O. The success of extracorporeal shockwave lithotripsy based on the stone attenuation value from noncontrast computed tomography. Arab J Urol. 2014;12(2):155
- [16] Pareek G, Armenakas NA, Fracchia JA. Hounsfield units on computerized tomography predict stone free rates after extracorporeal shock wave lithotripsy. The Journal of Urology. 2003;169:1679–81.
- [17] Joseph P, Mandal AK, Singh SK, Mandal P, Sankhwar SN, Sharma SK. Computerized tomography attenuation value of renal calculus: can it predict successful fragmentation of the calculus by extracorporeal shock wave lithotripsy? A preliminary study. J Urol. 2002;167(5):1968-71.
- [18] Pathak S, Lavin V, Vijay R, Hall J. Radiological determination of stone density and skin-to-stone distance – Can it predict the success of extracorporeal shock wave lithotripsy? BJMSU. 2009;2(5):180-84.

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