STONE DENSITY DETECTED BY NON CONTRAST COMPUTED TOMOGRAPHY (LOW DOSE) IS A PREDICTOR OF SUCCESSFUL OUTCOME OF RENAL STONE CLEARANCE BY EXTRA CORPOREAL SHOCK WAVE LITHOTRIPSY

MOHAMMAD AL AMIN¹, MD. SAIFUL ISLAM¹, S.M. YUNUS ALI¹, MD. GOLAM MOWLA CHOU DHURY¹, MOHAMMED MIZANUR RAHMAN²

¹Dept. of Urology, BSMMU, ²Dept. of Urology, NIKDU, Dhaka

Abstract

Objective: To evaluate the usefulness of measuring stone density in Hounsfield Unit by Low-dose Non Contrast Computed Tomography scan in predicting the outcome of extracorporeal shockwave lithotripsy for renal stone clearance.

Materials & Methods - A total of 96 patients with renal stone size d" 20 mm attending at the OPD of BSMMU were included in this study. The outcome measures were complete clearance of stone, number of ESWL sessions and number of shock waves required to become stone free.

Result- The mean size of the stone was 1.8 ± 0.3 cm. The mean stone density was 663.7 ± 69.8 HU. 25% of the patients underwent 2 sessions of ESWL, 52.1% three sessions and 22.9% more than 3 sessions. Of the patients 83.3 % were successfully cleared of their stone. The mean number of shock waves 6689.2±268.4 required for stone fragmentation of d" 750 HU and 9945±375.7 required > 750 HU stone density respectively. 85.5% of the patients with stone density d" 750 HU needed d" 3 sessions to become stone-free; whereas only 55.5% of the patients with stone density > 750 HU became stone-free in d" 3 sessions. 14.5% patients needed > 3 sessions of ESWL with stone density of e" 750 HU. 78.8% of the patients with stone density d" 750 HU exhibited complete clearance of stone as opposed to 37.5% of those with stone density > 750 HU. The chance of having complete stone clearance is 6-fold (95% CI = 1.9-19.4) higher in patients with low density stone (d" 750 HU) than that in patients with high density stone (d" 750 HU) (p = 0.002).

Conclusion- In conclusion a stone density less than 750 HU should be treated with ESWL as first choice of treatment.

Key wards - Stone, Density, ESWL

Introduction: The incidence of nephrolithiasis is reported to be increasing across the world[1,2]. This increase is seen regardless of factors such as age, sex and race. However, obesity, diminished intake of fluid, increased consumption of calcium, sodium, oxalate, animal protein are considered the most important risk factors for renal stone formation[3,4]. Because of its high frequency, urolithiasis is of particular concern of health economics as well as increased of total annual cost. Therefore, scheduling the management of the urolithiasis is of utmost importance in decreasing the subsequent cost after diagnosis.

Since 1980, extracorporeal shock wave lithotripsy is the first-line of treatment for renal stones of < 2 cm in diameter[5]. Analyzing different series, its success rates...
The stone density and ability of a stone to resist ESWL is based in part on the composition as well as microcrystal of the stone. Stone composed of calcium oxalate dihydrate, magnesium ammonium phosphate, uric acid tend to be softer and to fragment more easily with ESWL. Stone composed of calcium oxalate monohydrate, cystine stone are less susceptible to ESWL. The more crystalline dehydrate stones are easiest to break. The monohydrates stones are much harder to break. Therefore, Low density renal stone easily fragments by ESWL and High density renal stone difficult to fragments or not fragmented by ESWL[13].

Repeated ESWL use causes various complications like peri-renal, subcapular or intrarenal hemorrhage, post ESWL hematuria, recurrent urinary tract infection, stone fragments inducing obstructive uropathy and hypertension.

For that reason to reduce the number and complication of the stone diseases, this study proposed to find out the outcome of treatment of renal stone clearance by extra corporeal shockwave lithotripsy after evaluating the stone density detected by non-contrast computed tomography (Low-dose).

Materials and Method:
This prospective observational type of study was carried out in the Department of Urology, BSMMU, Dhaka over a period of 18 months between January 2013 to June 2014 with patients of renal stone attending at the department.

Total 96 adult patients were selected by standard statistical sampling formula and inclusion & exclusion criteria, with solitary renal stone (size>5 mm and d’ 20 mm) except in lower calyx and residual single stone after surgery were included in this study in. All patients were included with informed written consent.

Data were collected using a structured questionnaire (Research Instrument) containing all the variables of interest. The questionnaire were finalized following pre testing. Collected data were checked daily and edited. Data were processed and analysed using computer software SPSS (Statistical Package for Social Sciences). The test statistics used for analysis of data are Chi-square Test (for comparison of categorical data between groups) and Student’s t-Test (for comparison of continuous data between groups). The association between stone density and outcome ESWL were tested by means of univariate analyses. Level of significance was set at 0.05 and p < 0.05 were considered significant.

Detailed procedure:
All patients were evaluated by: Hematological test like CBC and Coagulation profile, Biochemical tests like S. Creatinine, Blood urea, Urine RME and C/S, Plain X ray of KUB region, USG of whole abdomen, Intravenous urography, Non contrast computed tomography (NCCT).

Non Contrast CT scans procedure:
Pre procedural radiological evaluation included plain x-ray of the kidney-ureter-bladder region and non contrast CT of KUB region on a multi-slice CT scanner. All images were obtained with a 4th generation Hitachi CT scanner (appendix-v) without intravenous or oral administration of contrast medium. The section thickness and interval was 3 to 5 mm. Images were obtained with 0.8-second gantry rotation by Low-dose CT protocol that is 120 kVp and 80 mA. (BSMMU CT protocol for abdomen is 140 kVp and 150 mA). Hence HU for each stone were determined on the pretreatment NCCT and only single shot will be taken. Stone size, stone location (pelvis, calyx), stone attenuation values (Hounsfield units) and skin to stone distance were recorded. The lowest, highest and most common attenuation values were recorded and the mean calculus attenuation value was...
calculated. The skin-to-stone distance (SSD) was calculated by measuring three distances from the stone to the skin at 0°, 45° and 90° using radiographic calipers, and the average of these values was calculated to represent SSD for each stone. Whole procedure was done in the department of radiology and imaging of BSMMU and reported by expert radiologist in that department.

ESWL Procedure:
ESWL monotherapy with 3rd generation Siemens Lithoskop lithotripter was used to treat all the enrolled patients with structured procedure followed. The number of shock waves to be delivered to the stone by expert operator during each session. Standard number of shock waves 2000 to 2500 with frequency 90 P/min per session and energy setting of 3.5 KV was applied in each session for lithotripsy. A change in stone size or outline or separation of stone fragments indicated fragmentation which was observed by fluoroscopy. The procedure was terminated if satisfactory fragmentation was noted before 3 session of ESWL or no change in stone size and outline up to 3 session of ESWL. All patients were hospitalized during ESWL procedure and served as day care service. All patients were under antibiotic prophylaxis during the procedure.

Post ESWL evaluation:
Patients were advised to come after 4 weeks with a plain X-ray of KUB region. In the follow up study, history, clinical examination and relevant investigations like urine routine examination, culture and sensitivity were done and data on post ESWL clearance were recorded in data sheet for assessing the outcome. ESWL success is defined as patients being stone free or with remaining stone fragments of <4 mm after three session which is consider as clinically insignificant residual fragments (CIRF) consider as the success of ESWL and complete stone clearance. Remaining fragments of >4 mm or non-fragmented stone were considered as ESWL failure as well as for other treatment option should be choice[14].

Results and observation:
The result shows that mean age of the total 96 patients was 49.4±8.2 years and the youngest and the oldest patients were 35 and 68 years old respectively (Table – I). The majority (77.1%) of the patients were male (74) with male to female (22) ratio is 3:1. Out of 96 patients 36% patients having normal BMI and needed d’ 3 sessions of ESWL where as 64% patients having overweight needed >3 sessions of ESWL. In relation to BMI, complete stone clearance between overweight and normal was 63.8% and 36.2%. But no stone clearance between these was 60.0% and 40.0%. p-value was significant. The association between skin to stone distance and number of ESWL session, shows that the mean skin to stone distance in case of d’3 ESWL session was 84.2±2.9 and >3 ESWL was 87.9±1.8 respectively (Table-II). Statistically significant difference present between these groups (p-value < 0.05). The stone characteristics associated with stone clearance, shows 55.2% of the patients had left kidney and 44.8% had right kidney stone involvement of which 62.5% of the patients had stone in the renal pelvis and 37.5% of the patients had calyceal stone. The mean size of the stone was 1.8 ± 0.3 cm (range: 0.98 – 2 cm). The mean stone density was 663.7 ± 69.8 HU (range: 133 – 1485 HU). The location of stones in calices, this study showed no significant difference was observedin complete stone clearance in relation to site and location of stones (p > 0.05). The mean of stone density in complete stone clearance was 478.3 ± 38.2 (range: 133 – 750 HU) and incomplete stone clearance was 943.6 ± 50.9 (range: 751 – 1485 HU) that was statistically significant (p< 0.001).

The number of ESWL session and stone size in this study shows that 25% of the patients underwent 2 sessions where stone size was 0.98 cm to 1.10 cm. 52.1% of patients needed three sessions where stone size 1.11 cm to 1.94 cm and 22.9% of patients needed more than 3 sessions where stone size were 1.95 cm to 2.0 cm. 83.3% of the patients successfully cleared off stone by ESWL.

The relation between the number of ESWL session and stone density shows that 85.5% of the patients with stone density d” 750 HU needed 3 or less session to have their stone cleared and the rest (14.5%) needed > 3 session with same density. In patients with stone density > 750 HU, 55.5% needed 3 or less session and 44.5% needed >3 sessions. p-value is significant (p<0.001) (Table-III).

The association of the amount of shock wave and stone density shows that 79.7% patients having stone density d”750 needed d” 7500 shock wave of ESWL and 20.3% patients needed >7500 shock wave. 74.1% of patients having stone density >750 needed d”7500 shock wave and 25.9% of patients needed >7500 shock wave of ESWL. The mean shock wave is 6689.2±268.4 in d”750 HU stone and 9945.2±375.7 in >750 HU stone. There was significant difference in amount of shock wave of ESWL and stone density (p<0.05) (Table-IV).
The stone density and complete clearance of stone showed 78.8% of the patients with stone density ≤ 750 HU exhibited complete clearance of stone as opposed to 37.5% of those with stone density > 750 HU. The chance of having complete stone clearance is 6-fold (95% CI = 1.9-19.4) higher in patients with low density stone (≤ 750 HU) than that of patients with high density stone (> 750 HU) (p = 0.002). (Table-V).

**Table I**

_Distribution of patients by their age (n = 96)_

<table>
<thead>
<tr>
<th>Age (Years) *</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>18</td>
<td>18.8</td>
</tr>
<tr>
<td>40-50</td>
<td>38</td>
<td>39.6</td>
</tr>
<tr>
<td>50-60</td>
<td>31</td>
<td>32.3</td>
</tr>
<tr>
<td>≥ 60</td>
<td>9</td>
<td>9.4</td>
</tr>
</tbody>
</table>

*Mean age = (49.4 ± 8.2) years; range = (35 – 68) years*

Table II shows that 25% of the patients underwent 2 sessions where stone size was 0.98 cm to 1.10 cm. 52.1% of patients needed three sessions where stone size 1.11 cm to 1.94 cm and 22.9% of patients needed more than 3 sessions where stone size were 1.95 cm to 2.0 cm. 83.3% of the patients successfully cleared off stone by ESWL.

**Table II**

_Distribution of patients in relation to number of ESWL session and stone size (n=96)_

<table>
<thead>
<tr>
<th>Number of ESWL session</th>
<th>Stone size in cm</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.98 – 1.20</td>
<td>24</td>
<td>25.0</td>
</tr>
<tr>
<td>3</td>
<td>1.21 – 1.96</td>
<td>50</td>
<td>52.1</td>
</tr>
<tr>
<td>&gt;3</td>
<td>1.97 – 2.0</td>
<td>22</td>
<td>22.9</td>
</tr>
</tbody>
</table>

Stone free rate

| Stone free rate | 80 | 83.3 |

Table III shows that 85.5% of the patients with stone density ≤ 750 HU needed 3 or less session to have their stone cleared and the rest (14.5%) needed > 3 session with same density. In patients with stone density > 750 HU, 55.5% needed 3 or less session and 44.5% needed >3 sessions. p-value is significant (p<0.001).

**Table-III**

_Association between number of ESWL session and stone density (n = 96)_

<table>
<thead>
<tr>
<th>Number of ESWL sessions</th>
<th>Stone density (HU)</th>
<th>p-value #</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 750 (n = 69)</td>
<td>&gt; 750 (n = 27)</td>
</tr>
<tr>
<td>≤ 3</td>
<td>59(85.5)</td>
<td>15(55.5)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>10(14.5)</td>
<td>12(44.5)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.7 ± 0.7</td>
<td>3.2 ± 1.1</td>
</tr>
</tbody>
</table>

* Data were analyses using Chi-square (²) Test. Figures in the parentheses denote corresponding percentage. Table III shows that 85.5% of the patients with stone density ≤ 750 HU needed 3 or less session to have their stone cleared and the rest (14.5%) needed > 3 session with same density. In patients with stone density > 750 HU, 55.5% needed 3 or less session and 44.5% needed >3 sessions. p-value is significant (p<0.001).

**Table-IV**

_Association between amount of shock wave and stone density (n=96)_

<table>
<thead>
<tr>
<th>Shock wave ¶</th>
<th>Stone density (HU)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 750 (n = 69)</td>
<td>&gt; 750 (n = 27)</td>
</tr>
<tr>
<td>≤ 7500</td>
<td>55(79.7)</td>
<td>20(74.1)</td>
</tr>
<tr>
<td>&gt; 7500</td>
<td>14(20.3)</td>
<td>7(25.9)</td>
</tr>
<tr>
<td>Average Shock wave #</td>
<td>6689.2 ± 268.4</td>
<td>9945.2 ± 375.7</td>
</tr>
</tbody>
</table>

¶ Data were analyses using Chi-square (²) Test and were presented as n (%.)

# Data were analyses using Unpaired t-Test and were presented as mean ± SD.
Discussion:

Extracorporeal shockwave lithotripsy is one of the preferred treatment modality for calculus in the upper urinary tract since its introduction[5]. It can clear up to 90% of stone in adults[15]. However, shockwave lithotripsy monotherapy is not successful in 9.4% to 26.3% of renal and proximal ureteral stones[16]. The outcome of ESWL depends on many factors, including stone size, location, composition and fragility, number of shockwave generator, and presence of distal obstruction as well as characteristics of the patient. Failure of ESWL leads to increased costs with requirement of auxiliary procedure to clear the stones. It would be useful if we can predict the stones that will be fragmented by ESWL.

In addition to history, physical examination and urinalysis, routine assessment of a patient presenting with renal colic currently includes NCCT in many centers, though it is not a regular practice in our country. This radiographic modality allows rapid and accurate determination of renal stone. Many investigators have studied the usefulness of NCCT for evaluating urinary calculi and observed that it is superior to traditional imaging such as excretory urography[17]. This study provides compelling data suggesting the importance of measuring HU in all patients who undergo NCCT to evaluate urinary calculi. By evaluating patients undergoing ESWL for renal calculi determined whether the success of this procedure could be predicted by pretreatment HU values on NCCT. The ability to assess renal stone characteristics and determine susceptibility to fragmentation is not a new phenomenon. In a study it was compared stone radiodensity with that of spine and concluded that stones are less likely to break if their radiodensity is greater than that of spine[18]. Others studied the opacity of calculi of similar sizes and concluded that fragmentation is less likely with higher opacity[19]. Although these studies provide insight into information needed for therapeutic considerations, they were based on qualitative observations, making them highly subjective and difficult to standardize. CT has long been used clinically to evaluate radiolucent filling defects, using measurements of substance density in HU to distinguish calculi from tumors or blood clots. The ability of CT scan to detect density differences as low as 0.5% has been exploited to determine the composition and fragility of urinary stones[13]. The density of stone affects the fragility, which ultimately governs the clinical outcome of ESWL. Therefore, stone opacity were assessed by using a quantitative measurement to evaluate treatment outcomes. HU calculated on pretreatment NCCT in patients who underwent ESWL provide a simple, easily reproducible and readily available measure of stone opacity. Using this objective study design this study observed that HU determination on NCCT provides crucial information for the treatment (ESWL) outcome was analyzed.

In the present study the mean age of the patients was 49.4 years with a male preponderance (male to female ratio roughly 3:1). There were 55.2% of the patients had left kidney and 44.8% had right kidney involvement. The mean size of the stone was 1.8 ± 0.3 cm. There were 62.5% of the patients had stone in the renal pelvis and 37.5% in calyceal stone except lower calyx. The mean stone density was 663.7 ± 69.8 HU. 25% of the patients underwent 2 ESWL sessions, 52.1% patients underwent 3 sessions and 22.9% more than 3 sessions. Successful stone clearance by ESWL was found to 80%.

BMI is an objective measure of obesity, defined as a person’s weight in kilograms divided by their height in square meters (kg/m$^2$). The American Society of Clinical Nutrition has defined a BMI of less than 25 as normal, 25-29 as overweight and 30 or greater as obese[20]. In present study BMI has no significant effect to stone clearance by ESWL because in our context patients were no so healthy and bulky like American or European people. Therefore, statistically no significance was found

<table>
<thead>
<tr>
<th>Stone density (HU)</th>
<th>Complete clearance</th>
<th>Risk Ratio (95% CI of RR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n = 80)</td>
<td>No (n = 16)</td>
<td></td>
</tr>
<tr>
<td>≤ 750</td>
<td>63 (78.8)</td>
<td>6 (37.5)</td>
<td>6.1 (1.9 – 19.4)</td>
</tr>
<tr>
<td>&gt; 750</td>
<td>17 (21.2)</td>
<td>10 (62.5)</td>
<td></td>
</tr>
</tbody>
</table>

# Data were analyses using Chi-square ($\chi^2$) Test. Figures in the parentheses denote corresponding percentage
in overweight and normal BMI. In a study same result was observed showed a significant negative impact of higher BMI on stone free rate after ESWL[21].

Skin to stone distance (SSD) is an easily measured parameter on NCCT which correlates with ESWL efficacy in the treatment of stones in all locations independent of other factors[22]. This study assessed the SSD in all patients, because the SSD calculated on pretreatment NCCT provides a simple, easily reproducible and readily available quantitative measurement. It is the average of three distances (true posterior, 45° lateral and true lateral) on NCCT. In this current analysis this study included that the mean SSD was 84.2±2.9 where d” 3 ESWL sessions is needed and 87.9±1.8 where > 3 session ESWL session is needed to fragment the stone and SSD ranges from 80-88 mm. So it affects the treatment outcome by ESWL. It was described the SSD to be significantly associated with complete stone clearance[21].

In this study, it also assessed that the mean number of shock waves 6689.2±268.4 required for stone fragmentation of d” 750 HU and 9945±375.7 required > 750 HU stone density respectively. It was concluded that high density renal stone needed greater number of shock waves for complete clearance of stone[23].

The study demonstrated that majority (78.8%) of the patients with stone density d” 750 HU experienced complete clearance of stone compared to 37.5% of those with stone density d” 750 HU (< 0.001). 85.5% of the patients with stone density d” 750 HU needed 3 or less session to become stone-free; whereas only 55.5% of patients with stone density >750 HU not stone-free in 3 or < 3 sessions and the rest required 4 or more sessions. In a study it was demonstrated a linear relationship between the calculus density and number of ESWL sessions required. 41 (80%) of patients with stone density of < or = 750 HU, needed three or fewer ESWL sessions and 45 (88%) had complete clearance (24). Of patients 41 (72%) with stone density of >750 HU, required more than three ESWL sessions, and 37 (65%) had complete clearance. The best outcome was in patients with calculus diameters of < 1.1 cm and mean densities of < or = 750 HU; 34 (83%) needed three or fewer ESWL sessions, and the clearance rate was 90%. The worst outcome was in patients with calculus densities of > 750 HU and diameters of > 1.1 cm; 23 (77%) needed more than 3 ESWL sessions and the clearance rate was only 60%.

Since 1980, NCCT scan has been studied as a possible useful tool to predict stone composition through density measurements (Hounsfield Units). It was stated that NCCT scan could only differentiate the uric acid stones from the rest[25,26]. On the other hand, in a study it was reassures that this instrument can identify uric acid and calcium oxalate stones[27]. Although the development in the technology of endourologic procedures and ESWL increases the management options of renal stones, it also increases the need for more evaluation of their efficacy and indications. Patient, stone and radiographic parameters have been studied as potential predictors of ESWL success. In particular HU attenuation value of NCCT has been shown to be a potentially useful independent predictor of ESWL outcome. Although CT is associated with greater radiation exposure and costs than plain radiography, NCCT stone characteristics predict ESWL success for renal stone. Patient characteristics are not so much predictive. By knowing the composition of a urinary calculus through density measurement is frequently a key factor in determining its most appropriate management. Whether the stone be amenable to extracorporeal shock wave lithotripsy, or should ureteroscopy or percutaneous nephrolithotomy be attempted can anticipated beforehand. Urine pH, urinary crystals, prior stone history, the presence of urea-splitting organisms, and plain radiography are tools currently used to infer the stone composition[28]. Several in vitro studies have suggested that NCCT can extend these tools by demonstrating measured differences in radio density among different urinary stones[13,29].

The density of stone depends upon its composition and affects the fragility of a calculus, which ultimately governs the clinical outcome of ESWL. Therefore, assessing the density of a calculus before ESWL session starts is of immense significance to increase the efficacy of the procedure and reduce the number of hospital visits and treatment cost.

NCCT has emerged as the modality of choice in the evaluation of acute flank pain. It is safe, rapid, and accurate, with one series reporting 96% sensitivity, 99% specificity, and 98% accuracy in the diagnosis of urolithiasis. Once urinary stone disease is identified, NCCT is also useful in providing information necessary for the management of the stone.

**Conclusion:**

Based on this prospective study we concluded that Low density (d” 750HU) renal stone fragmented successfully
by extra corporeal shock wave lithotripsy but stone of high density (e” 750 HU) suggest a poor chance of clearance and could help to plane alternative treatment options, thus reduce the burden of the patients.

References:


