Original article

Use of non-contrast computed tomography determined urinary stone fragility in predicting the outcome of extracorporeal shockwave lithotripsy treatment: a single-center study

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ABSTRACT

Background: Renal stones represent a common urological pathology where standard treatment advised is ESWL in current practice. However, NCCT based determination of stone fragility may help to predict the outcome of ESWL treatment, hence optimizing its clinical use. Therefore, this study evaluated the role of NCCT determined urinary stone fragility in predicting the outcome of ESWL treatment in local clinical settings.

Patients and methods: One hundred patients with single renal calculus of 0.6-2 cm in size were included. NCCT based determination of stone fragility in HU units was done for all patients. Patients were then subjected to ESWL, with a maximum of 3000 shock waves given per ESWL session. Plain film and/or ultrasonography was used to monitor ESWL treatment progress with a final NCCT evaluation at 12 weeks to determine the clearance of the calculi for each patient. Association of NCCT based stone fragility and outcome of ESWL was statistically analyzed using Fisher exact test.

Results: The mean age of the patients was 37.7 ± 10.9 years with 54% being male. Decreasing stone fragility on NCCT (high = <500HU, moderate = 500-1000HU, and high = 1000HU) required more number and intensity of ESWL sessions (1-2 visits and 3000-6000 shock waves for high stone fragility group, 3-5 visits and 7000-18000 shock waves for the moderate group, and 6 visits and >18000 shock waves for low fragility group, respectively) necessary for clearance of urinary stones ($p<0.001$). In 98% of patients, the clearance of urinary stones was excellent.

Conclusion: Renal stone patients with NCCT determined high and moderate stone fragility show an optimal response after ESWL treatment, whereas, for low fragility renal stones attenuative treatment like percutaneous nephrolithotomy and/or ureteroscopy should be considered instead of ESWL. This approach can enable patient stratification before ESWL therapy ensuring better clinical management of the renal stone disease.

Keywords:
Urinary stones; Extracorporeal shock-wave lithotripsy; Calculus density; Computed tomography; Prediction

INTRODUCTION

Urinary stones remain a global health problem with a prevalence of 4-20% in different regions across the globe. It represents the third most common disease of the urinary system constituting 50% of the urological workload.[1] Urinary calculi develop more commonly (three times) in men than in women with the highest incidence during the 4^{th}-6^{th} decades of life. Urolithiasis is a lifelong disease and causes high patient morbidity including frequent stone recurrences with an average of ≥ 3 renal stone events during five years translating to high healthcare costs.[2,3] The optimal clinical management of renal stones involves maximal stone clearance with minimal patient morbidity. Significant progress has been made in this regard with the availability of multiple treatment modalities including non-invasive (ESWL) and surgical (percutaneous nephrolithotomy, ureteroscopy, and rarely laparoscopic stone surgery) options.[4] Because of its non-invasive nature, the ESWL has revolutionized the treatment of urolithiasis and represents the treatment of choice for the majority of "simple" renal calculi, achieving stone clearance in about 80-85% cases.[5] Various factors such as stone size, location, the type of shockwave generator used, intensity of shockwaves, complications by urinary tract obstruction and/or infection, and most importantly stone composition and density/fragility have been shown to influence the success of ESWL treatment.[6,7] Owing to its increased sensitivity and density discrimination ability, the NCCT represents a valuable and non-invasive tool to determine composition and fragility based upon differences in their HU densities.[8] NCCT use for determination of fragility of the urinary stone before ESWL represents a simple way to predict the success of ESWL treatment

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and may highlight the need for alternative treatment measures in patients where a sub-optimal outcome from ESWL therapy is predicted.[9] This will not only help in avoiding patient morbidity and discomfort in terms of a number of hospital visits, clinical complications in patients with the obstructed renal system, needless ionizing radiations, and shockwave exposure but also reduce the wastage of healthcare resources and costs.[10]

This study evaluates the role of NCCT-determined renal stone fragility in predicting the ESWL treatment outcome in a single-center study from Pakistan.

PATIENTS AND METHODS

This single-center prospective study was performed at the Department of Urology in collaboration with the Department of Diagnostic Radiology, Lahore General Hospital Lahore from 2016 to 2017. After approval by the Institutional Ethical Committee, the study participants were requested to provide written informed consent before study enrollment. One hundred patients of solitary renal calculus of 0.6-2 cm in size were recruited. A non-probability/consecutive sampling method was employed for patient selection. Renal stone patients aged >16 years, of either gender, were included in this study. Patients having a reported congenital anomaly, requiring reconstructive surgery, compromised renal functions (serum creatinine >3mg/dl), calyceal stone, bleeding disorder, pregnancy, uncontrolled hypertension, and urinary tract infection were excluded from the study.

Patient history including demographic information like name, age, sex and ethnicity was recorded. Clinical examination of patients included evaluation for vitals (blood pressure, pulse rate, temperature, and weight, etc.) and routine clinical laboratory tests including plain X-ray and ultrasonography using kidney, ureters, bladder (KUB) protocol, and urine complete examination. All patients were subjected to NCCT, in the Radiology Department of Lahore General Hospital, Lahore, without any contrast medium before ESWL treatment using a helical CT scanner (Toshiba Aquilion 16™, Toshiba, Japan) at 120 kV and 150 mA. The NCCT protocol involved 5mm contiguous sections through the renal stone with 300 and 40 HU soft tissue settings for window width and level, respectively. Reconstruction interval, collimation thickness, and the total number of images in which the stone was envisioned enabled calculation of the longitudinal stone dimension. Drawing a region of interest over the stone rendered determination of the mean stone density or attenuation value (measured in HU) and the maximum diameter of the stone. Based on NCCT obtained mean stone density in HU, the renal stone fragility was classified as high (<500HU), moderate (500-1000HU), and low (>1000HU).

Under analgesia (intramuscular Diclofenac sodium 75mg injection given stat), all patients in a day case setting underwent ESWL treatment (Modulith SLX-F2™, Storz Medical, Switzerland), initially at 0.5 kV with stepwise gradual increase after every 200 shockwaves to a maximum of 6 kV in each case. The maximum number of shock waves given to a single patient during each ESWL session was 3000. The stone fragmentation during the ESWL therapy was monitored using ultrasonography or fluoroscopy. A plain film or ultrasound using KUB protocol was performed before each ESWL session to document stone fragmentation, and also to evaluate the position and clearance of the stone fragments. A maximum of six ESWL sessions was administered per patient when required. All patients were followed for the outcome of ESWL treatment where renal stone clearance was documented by a final CT scan done 3 months after the final ESWL session and was defined as excellent (complete disappearance of the renal stone), or good (detection of stone fragments <5mm in size considered as a clinically insignificant residual fragment), or poor (incomplete fragmentation of the renal calculus, size ≥5mm) or failure (failure of renal stone fragmentation). In cases, if ESWL was unsuccessful for 12 weeks, renal stones were retrieved by percutaneous nephrolithotomy, ureteroscopic extraction, or surgical removal. SPSS version 20 was used to enter and analyze all the patient data. Quantitative variables like age and stone size were described as mean and standard deviation. The qualitative variables like sex, stone location, the severity of pain, stone density, visits of ESWL, and clearance of stone were presented as frequency and percentages. NCCT determined stone fragility in terms of HU values was analyzed with the result of ESWL, the number of shockwaves, and the number of sessions required for complete fragmentation/clearance of the renal stone by means of Fisher exact test. A p-value of less than 0.05 was considered significant for any comparisons made.

RESULTS

The mean age of patients was 37.7 ± 10.9 years. Of the 100 patients, 54% were male with a male to female ratio of 1.17. Regarding the site of renal stone, 44% had right renal calculus, 51% had left renal calculus and 5%

had bilateral renal calculi. The CT determined stone size ranged between 5-10mm in 14%, 11-15mm in 42%, and 16-20mm in 44% of patients. About 3% of patients had mild pain, the majority (91%) had moderate pain and 6% of patients had severe pain. It was observed during the study that out of 100 patients 8 (8%) had pain during ESWL while the majority 92 (92%) had no pain. Regarding urine complete examination, 64% had microscopic hematuria, 22% had pus cell in the urine and 14% of patients, no abnormality was detected. The demographic, clinical, and laboratory features of patients are presented in Table 1. The demographic and clinical parameters for renal stone patients in the present study were comparable to previous such studies. For example, in the study by Massoud and co-workers, the mean age of renal stone patients was 39.9 years with 65% of patients being male and a mean stone size of 1.91cm [10]. Likewise, in a similar study by Gupta and others, 112 renal stone patients had a mean age of 33.6 years but a slightly higher percentage of men (71%) and presented with stone sizes of 0.5-2cm [9].

A significant association between the CT determined stone fragility and the number and intensity of ESWL sessions required for clearance of urinary stones was observed as presented in Table 2. For a successful outcome (excellent clearance of renal stone), 11% of patients with high stone fragility (stone density of <500 HU) needed 2 ESWL visits and 3000-6000 shock waves. Whereas 60% of patients with moderate stone fragility (stone density of 500-1000 HU) required 3-5 ESWL visits and 7000-18000 shock waves. 27% of patients had low stone fragility (>1000 HU) and required 6 ESWL visits and >18000 shock waves for complete removal of stone. In 98% of patients, clearance of urinary stones was excellent, however, in 2% of patients (both with stone fragility value of >1000 HU) stone clearance was recorded as poor.

Table 1. Demographic, clinical and laboratory characteristics of patients

Characteristics	Frequency (%)
Demographics	
Mean age (years)	37.7±10.9
Males	54%
Clinical features	
Site of stone	
Right renal calculus	44%
Left renal calculus	51%
Bilateral renal calculus	5%
Stone size	
5-10mm	14%
11-15mm	42%
16-20mm	44%
Severity of pain	
Mild	3%
Moderate	91%
Severe	6%
Pain during ESWL	8%
Laboratory findings	
Microscopic hematuria	64%
Pus cells	22%
No abnormality	14%

DISCUSSION

Urolithiasis is a worldwide problem. The situation of renal stone disease in Pakistan is even worse as this region is situated in the "Asian stone-belt" with a relatively high prevalence of renal stone disease (12-15%), manifesting as a significant healthcare burden on already resource local limited clinical settings.[11] ESWL represents significant progress in the optimal clinical management of renal stone disease with a high success rate of >80%. A successful outcome in ESWL therapy is indicated by the complete clearance of renal stone or detection of clinically insignificant stone fragments of <5mm. Many factors may influence the outcome of ESWL treatment including renal stone characteristics (stone size, composition, number or load, and location) and patient features (such as BMI or a body habitus that may pose a barrier for shockwaves). Such cases can be more appropriately managed by surgical treatment modalities (such as ureteroscopy and percutaneous nephrolithotomy) rather than ESWL.

In earlier studies, the stone burden was regarded as the primary factor in the selection of a suitable treatment modality for renal calculi disease cases. It was reported that increased renal calculi burden, including both stone size and number, was inversely associated with stone-free rates after ESWL therapy mediating an increased need for ESWL re-treatments or use of ancillary procedures.[12-14] More recently, the concept of composition based renal stone fragility/density/attenuation value was introduced which was found to be a substantial predictor of ESWL treatment success in various subsequent studies.[9,10,15] The ability to predict renal stone fragility and hence potential outcome after an ESWL therapy is of utmost importance in appropriate management of renal stone patients as a failed ESWL therapy may come with many undesirable outcomes including the potential development of adverse renal complications (such as renal injury), need of multiple ESWL sessions with increased risk of potential side effects and increased healthcare burden. NCCT serves as a suitable method for the investigation of acute flank pain because of the many advantages offered by NCCT over plain film or ultrasonography including high specificity and sensitivity in the detection of renal and ureteral calculi,

Table 2. Relationship between renal stone fragility and number and intensity of ESWL treatment

Variable	CT determined renal stone fragility (density)			
	<500 HU	500-1000 HU	>1000 HU	p-value*
ESWL visits and shockwave intensity for success				
1-2 visits (3000-6000 shockwaves)	11%	0%	0%	<0.001
3-5 visits (7000-15000 shockwaves)	0%	60%	0%	
6 visits (>15000 shockwaves)	0%	0%	27%	
Failure	0%	0%	2%	

*p-value determined from a 3x3 Fisher exact test (df=4)

more efficient detection of uric acid and cystine stones, speed, cost, safety and detection of non-urological pathology. NCCT is particularly useful in providing better density discrimination than conventional radiography with 10 times more resolution power (0.5% for NCCT *vs.* 5% for the plain film).[16] Exploitation of the same proved useful in NCCT based determination of urinary stone composition and fragility as different renal stone types were found to have differentiating values of stone density (mean stone density in the range of 748-1690 HU, 662-1285 HU, and 391-480 HU for calcium oxalate, struvite and uric acid stones, respectively). This implies that uric acid stones can be distinguished with ease from calcium oxalate and struvite stones, but differentiation in the last two types is less pronounced.[9,17] The NCCT determined renal stone density translates directly to their resistance to fragmentation in ESWL therapy with the impression that cystine stones pose most resistant to ESWL, followed by calculi composed of calcium oxalate, struvite, and uric acid. The potential overlap in stone densities may limit an accurate prediction of stone composition, but still NCCT provided stone fragility measurements can be used to group patients and make informed clinical decisions about the best initial treatment modality to be used for each group. Thus, the first line of treatment modalities towards the management of patients with high-density renal stones can be surgical instead of ESWL. The same approach has been investigated in a number of previous studies. In a study by Joseph et al., it was demonstrated that the renal stone clearance rate significantly decreased for patients harboring stones having a density of >1000 HU as compared to those with stone fragility of <1000 HU.[18] Similarly, Gupta and coauthors showed that stone fragility of >750 HU together with a stone size of >1.1cm predicted a poor outcome after ESWL therapy due to requirement of >3 ESWL sessions and stone clearance rate of only 77%.[9] Two other studies also suggested that renal stones with density values of >900 HU significantly predict failure of ESWL therapy and are better managed initially by endoscopic intervention rather than ESWL.[19,20] A recent study by Massoud and coworkers is also concordant with previous literature demonstrating the failure of ESWL treatment in almost 50% of patients with a renal stone attenuation value of >1000 HU.[10] Only a single study on this subject is available from Pakistan previously reporting a significantly lower mean HU stone density for stone-free group *vs.* stone-residual group after ESWL treatment.[21]

The present study confirms the results of previous studies regarding the correlation of NCCT determined renal stone fragility with ESWL outcome. In the present study, the best outcome with a clearance rate of 92% was observed in patients with a stone diameter of <1.5mm (56%) and a density of <1000 HU, 46% of which required 3 or less ESWL treatment episodes. Conversely, the worst outcome was observed in patients having a renal stone diameter of >1.5cm (49%) and fragility value of >1000 HU (29%), 41% of which needed five to six ESWL sessions and a lower clearance rate of 80%. In developing regions of the world, the concept of using stone density is gaining acceptance and more studies from other centers need to be done from such regions to look for the different factors affecting stone clearance after ESWL.

CONCLUSIONS

NCCT based determination of renal stone fragility can serve as a useful indicator of ESWL treatment outcome. For highly fragile calculi (<500 HU), irrespective of size (<2cm), ESWL should be the preferred treatment method. However, moderate to low fragility calculi (generally >500 HU but particularly >1000HU) are associated with a poor outcome when treated with ESWL and other treatment options like percutaneous nephrolithotomy and/or ureteroscopy should be considered in these cases, depending on the location of the stone. Further trials in other centers are warranted to determine a multivariate prediction of factors influencing the outcome of ESWL treatment.

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