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Research Article

The Correlation between Lumbar Bone Density and Kidney Stone Size Based on CT-Scan; a Retrospective Study

Amir Reza Abedi1, Mohammad Ali Ganji Jameshouran[2], Mohammad Ali Tasharrofi[2], Mohammad Mersad Mansouri Tehrani[2]*

[1]*Urology Department of Urology, Shahid Beheshti University of Medical Sciences, Iran*
[2]*Department and Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Iran*

***Corresponding author**

Mohammad Mersad Mansouri Tehrani, Department and Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Student Research Committee, Tehran, Iran, Tel: 98-9128101-398; Fax: 98-212243-9789; Email: mersad.mansouri@sbmu.ac.ir

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Abstract

Background: Previous studies have recognized the association between nephrolithiasis and several systemic conditions, such as low bone mineral density (BMD). With non-contrast CT scans routinely performed as a part of urinary stone evaluation, the aim of this study is to assess the relation between the non-contrast CT based BMD and the stone size of patients with urinary stones.

Methods: In this retrospective study, 391 urinary stone patients who had undergone stone removal surgery between the years of 2013-2018, had a major calcium stone component and CT-imaging were enrolled. Stone size was defined as the maximum collected stone diameter on CT. BMD for each subject was calculated at the L1 vertebral level, with the CT attenuation being measured in Hounsfield Units (HU). As instructed by prior literature, a cut-off of 160 HU was selected to distinguish the normal BMD from the low BMD.

Results: Our analysis showed a significant statistical association between stone size and BMD ($P < 0.005$). Furthermore, when dividing subjects under 3 subgroups of stone size (smaller than 20 mm, between 20 and 30 mm, larger than 30 mm), lower BMD was more prevalent among those with lager stones. Additional analysis demonstrated no meaningful association between stone size and basic patient variables (Age, gender, BMI), thus proving the independence of the relation between stone size and BMD.

Conclusion: Larger stones are associated with lower CT-based BMD in urinary stone patients. Therefore, patients with larger stones are at a higher risk for osteoporosis, and should be properly assessed.

ABBREVIATIONS

BMD: Bone Mineral Density; PCNL: Percutaneous Nephrolithotomy; TUL: Transurethral Lithotripsy; BMI: Body Mass Index; CT: Computed tomography; HU: Hounsfield Units

INTRODUCTION

Nephrolithiasis is a globally common disorder, affecting any general populations regardless of geographical and socioeconomic factors. Overall, 10-15% of people in the developed world experience nephrolithiasis at some point during their lifetime; with the risk being higher as 20-25% in the Middle East [1,2]. Previous studies also suggested a prevalence as high as 1.9% in the general population of Iran, especially in the central and southern provinces [3,4]. Several systematic implications and pre-factors have been established for nephrolithiasis; type 2 diabetes, dyslipidemia, and hypertension have been shown to independently associate with kidney stone formation [5]. Furthermore, bone mineral content is lower in renal stone formers, stemming from several proposed pathogeneses including genetic factors, metabolic disorders such as renal leak hypercalciuria, immunological processes, dietary, environmental and iatrogenic effects [6-8]. The decrease in bone mineral density is shown to happen regardless of urinary calcium excretion and is witnessed in both hypercalciuric and normocalciuric patients [6,9]. The reduction in bone mineral density is of critical importance since nephrolithiasis patients are at a greater risk of bone fracture compared with the normal population [6,10,11].

Non-contrast computerized tomography (CT) has been universally recognized as the gold standard to detect urinary stones; being utilized in up to 71% of emergency department visits, replacing other imaging modalities such as x-rays and ultrasounds [12]. Guidelines provided by the American Urological Association (AUA) for surgical management of stones, strongly recommend non-contrast CT scans as a pre-operative assessment [13]. Obtaining data through CT imaging for urolithiasis minimized the need for additional testing and imposes no extra cost or radiation exposure to the patients [14]. Studies such as those conducted by Pickhardt et al., and Alacreu et al., establish abdominal CT imaging as a reliable method of BMD assessment compared to the gold standard dual-energy x-ray absorptiometry (DEXA) scan, by measuring Hounsfield Units (HU) at several vertebral levels, specifically the L1 [15,16].

Henceforth, using CT-scans to extract additional clinically significant information may be a cost-effective measure for both the patients and the healthcare systems. While BMD values extracted by CT scans are shown to be solely reliable [15,16], analyzing their relation with the available stone data may prove beneficial for the physicians from a diagnostic standpoint. This study aims to identify the association between the patients' BMD and stone size, in those undergoing percutaneous nephrolithotomy (PCNL) and transurethral lithotripsy (TUL) through ureteroscopy (URS).

MATERIALS AND METHODS

Patients and setting

The sample population for this study was selected among the patients admitted to Shohada-e-Tajrish Hospital's urology ward between 2013-2018. The inclusion criteria for this study were as follows: Patients having undergone either the PCNL or the TUL procedure for stone removal, stones with a major calcium component on lab testing, and having a non-contrast abdominal/pelvic preoperative CT scan. 458 PCNL and 984 TUL patients were identified in Shohada-e-Tajrish Hospital's database. Of the 458 consecutive PCNL patients, 203 met our inclusion criteria. 188 TUL patients were also considered eligible for the study, the rest were excluded for not fulfilling the criteria. Each patient's CT imaging and stone composition was extracted from the database. Additional data retrieved from the patient profiles included age, gender, and body mass index (BMI) if available. Urinary and serum chemistry studies were not available in Shohada-e-Tajrish Hospital's patient database and hence are not provided in the study.

CT-based data retrieval

The stone size and BMD of each patient were assessed through their CT scans with *Infinitt pacs* software. Stone size was defined as the maximum collected diameter of the stone on either the axial or coronal planes, measured in mm. As demonstrated in Figure 1, BMD was estimated by selecting an oval region of the trabecular bone of the vertebral body on the axial plane, and an oval region centermost of the vertebral body on the coronal plane, both at L1 level [14]. Mean attenuation was measured in Hounsfield Units (HU). As established by previous studies, a discriminatory threshold of 160 HU was selected to distinguish the normal BMD from low BMD (Mean sensitivity 73.9%, mean specificity 70.6%) [15,16].

Statistical analysis

Independent-samples t-test and chi-square tests were used to compare patients' BMD in low (<160 HU) and normal (>160 HU) subgroups. Statistically, a significant difference was defined as a two-sided *P*-value<0.05. Statistical analyses were performed through IBM's Statistical Package for Social Sciences (SPSS) version 22 software.

RESULTS

A total of 391 subjects were included in the study, 284 males and 107 females, of which 203 had undergone PCNL, and 188 TUL. The mean age (SD) of the subjects was 46.89 (14.4). Of all the subjects, 168 had a normal BMD score (>160 HU) while 223 showed a lower than 160 HU density. BMD across all the subsections is compared between patients with low (<160 HU) and normal (>160 HU) density. Younger patients were shown to have a higher BMD when compared to the older subjects (41.63 vs 54 yrs, $P < 0.001$).

Table 1 displays the association between the subjects' urinary stone size and BMD. The mean (SD) stone size for all the subjects, PCNL, and TUL patients were 23 (13) mm, 28 (11) mm and 9 (2) mm, respectively. For a precise analysis, the stone data for all the patients regardless of their method of intervention was divided into 3 subdomains of ≤20 mm, 20-30 mm and >30 mm. A drastic statistical association was shown between stone size and BMD, both in total and across each subdomain (Chi^2, $P < 0.001$). Table 1 also includes additional patient data. A significant male predominance was seen in subjects with low BMD (77.7% male subjects versus 22.2% females).

Statistical evaluation of the stone subdomains and the relation between calculi size and basic patient variables were evaluated by categorization of the patients' mean age, gender, mean BMI, mean stone size and mean BMD for each of the subdomains. The data is presented in Table 2 and Table 3.

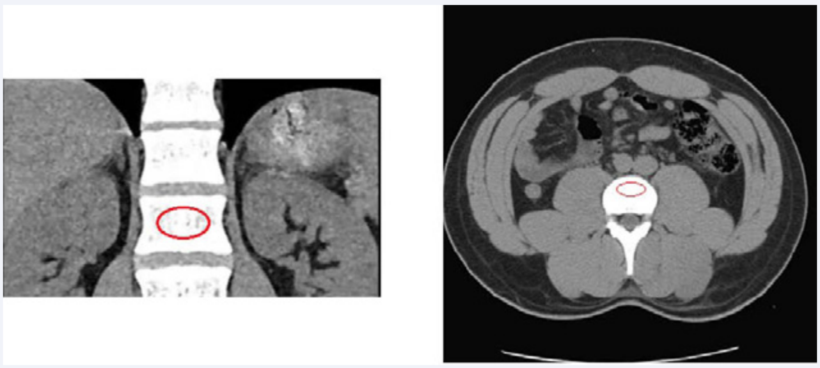

Figure 1 Oval regions selected at the L1 vertebral level of the trabecular bone for BMD estimation on axial and coronal CT-imaging.

Table 1: Comparison of patients with and without low bone mineral density per CT HU measurements (threshold 160 HU).				
	N=391	**Low Bone Mineral Normal Bone Mineral Density, HU >160 (n=168)**	**Density, HU<160 (n=223)**	***P*-value**
Stone size (mm)				<0.005
Under 20 mm	185 (47.3%)	143 (64.7%)	42 (25%)	
20-30 mm	102 (26%)	55 (24.8%)	47 (27.9%)	
More than 30 mm	104 (26.5%)	23 (10.5%)	79 (47%)	
Gender				0.014
Male (%)	284 (72.6%)	112 (66.6%)	172 (77.8%)	
Female (%)	107 (27.3%)	56 (33.4%)	49 (22.2%)	
Age (Years) ± SD	46.89 ± (14.4)	41.63 ± (12.7)	54.0 ± (13.5)	<0.001

Abbreviations: HU: Hounsfield Units
[a]Data are presented as mean ± SD or number (percent).

Table 2: Distribution of PCNL patient data for each of the stone size subdomains.					
	Mean stone size (mm)	**Mean age (Years)**	**Gender (M/F)**	**Mean BMI (Kg/m^2)**	**Mean BMD (HU)**
Group 1 Under 20 mm	16.66 ± (3.10)	45.12 ± (13.47)	(26 / 17)	25.43 ± (4.37)	223.02 ± (42.89)
Group 2 20-30 mm	25.33 ± (2.79)	48.07 ± (14.91)	(57 / 20)	26.44 ± (3.05)	190.18 ± (50.69)
Group 3 >30mm	40.93 ± (9.12)	49.26 ± (13.61)	(57 / 24)	26.17 ± (3.56)	160.93 ± (44.85)

Abbreviations: PCNL: Percutaneous Nephrolithonomy; BMI: Body Mass Index; BMD: Bone Mineral Density
[a]Data are presented as mean ± SD

Table 3: Distribution of patient data for the PCNL and TUL groups.					
	Mean stone size (mm)	**Mean age (Years)**	**Gender (M/F)**	**Mean BMI (Kg/m^2)**	**Mean BMD (HU)**
PCNL patients	28.68 ± (11.59)	47.91 ± (13.1)	(140 / 61)	26.13 ± (3.41)	182 ± (49)
TUL patients	9.34 ± (2.61)	46.27 ± (14.82)	(144 / 44)	26.76 ± (3.76)	194 ± (47)

Abbreviations: PCNL: Percutaneous Nephrolithonomy; TUL: Transurethral Lithotripsy; BMI: Body Mass Index; BMD: Bone Mineral Density
[a]Data are presented as mean ± SD

While TUL is commonly performed on stones with small diameters, PCNL is routinely utilized on stones with any size [13]; as such, compiling the results of the both groups would result in outlier data, since the majority of the TUL subjects would be distributed in the lowest domain (≤20 mm). Therefore, the subdomains of Table-2 were chosen purely of PCNL subjects. A significant statistical difference was shown between the mean BMD scores of each subdomain ($P = 0.016$ for groups 1, 2. $P < 0.001$ for groups 2, 3. $P < 0.001$ for groups 1, 3). Similar differences were observed between mean stone size values of the subdomains (P value across all boards <0.001). Our analysis showed no significant difference between the mean age ($P = 0.262$ groups 1, 2. $P = 0.611$ groups 2, 3. $P = 0.099$ groups 1, 3) and gender ($P = 0.915$) for the subdomains. A similar lack of difference between the mean BMI scores for each of the subdomains ($P = 0.136$ for groups 1, 2. $P = 0.748$ for groups 2, 3. $P = 0.083$ for groups 1, 3) was also demonstrated.

As stated prior, TUL patients' stone size information was classified under a separate subdomain, and as such was compared with the PCNL group as the total sum of the three subdomains in the following analyses. Similar to the internal analysis between the PCNL subdomains, significant difference was demonstrated between the mean BMD scores ($P < 0.001$) and the mean stone size values ($P < 0.001$) of the two groups, while no notable difference was observed when comparing the mean age ($P = 0.376$), gender ($P = 0.915$) and the BMI ($P = 0.109$) data. Defining TUL as a separate domain provided us with less outlier points; Furthermore, it provided another measure of evaluating the association between BMD and stone size; there's a notable difference in stone size between TUL and PCNL patients (9.34 mm vs 28.68 mm, $P < 0.001$), and as such comparing BMD values between the two may be beneficial towards the main goal of the study. This data is presented in Table 3.

DISCUSSION

The main objective of this study was the establishment of a statistical association between urinary stone patients' calculi size and bone mineral density through their abdominal/pelvic CT-imagine. What our analysis highlighted, was the inverse relation between stone size and BMD; both across the entire sample population and between designated subdomains based on size ($P < 0.001$).

Patients with urinary stones are known to have a lower BMD than the general population, so they may suffer from a higher risk for fractures [6,10,11,17]. The cardinal mechanisms of this state are not clear, with several studies suggesting different iatrogenic, metabolic, environmental, immunologic and genetic etiologies [6-8,18,19]. Furthermore, it is stated in a multitude of studies that 75-80% of urinary stones contain a major calcium component, often bound with oxalate or phosphate [11,14,20,21]. With bone being the maximum calcium storage organ in the human body, a negative calcium balance is expected to directly affect BMD [22,23]. As such, the sample population of the study was comprised of patients whom were known calcium stone formers. However, it is worth noting that the direct effects of urinary calcium excretion on BMD in urinary stone patients are subject to controversy [24], and a lower BMD is also seen in normocalciuric subjects [9].

Hence, regardless of serological and urinary status, patient screening for reduced BMD and the subsequent increased fractured risk is of great importance. As established by previous studies, non-contrast CT-scans provide valuable data in this regard, and the HU parameters proposed in the studies above propose an acceptable sensitivity and specificity compared to the gold standard DEXA scan [15,16]. What our study presents, the association between the BMD retrieved from CT-scans and size of the stones further solidifies the reliability of non-contrast abdominal/pelvic CT-scans as a screening tool for fracture risk in urinary stone patients. Our method of L1 trabecular bone density assessment required a minimal amount of time, training and resources, and could be performed by any physicians in training.

Our data analysis demonstrated a powerful association between the stone size and BMD in patients across all boards as demonstrated in Table 1, regardless of the method of intervention ($P < 0.001$). For a precise analysis, urinary calculi were organized into 3 subdomains depending on their size; stones with a maximum diameter lower than or equal to 20mm, between 20mm and 30mm, and equal to or greater than 30mm. This section of our analysis demonstrated a constant regression in mean BMD values concurrent with increased stone sizes, which is supported by prior studies such as those conducted by Patel et al., establishing stone volume as an independent risk factor for low BMD [14].

To evaluate the structural authenticity of the subdomains, the statistical association between each of the subdomains' mean stone size and, BMD score was calculated ($P < 0.001$). It is also important to note that since the mean stone size for TUL patients was less than our lowest domain (9.34 mm), the TUL subjects were distributed in a separate subdomain entirely to avoid any outlier data points and were not included in the first analysis, which was conducted purely on the PCNL subjects' data. A separate analysis was conducted to compare the data of the TUL patients with the PCNL subjects as a whole, and the results were included in Table 3. The significant relation between each subdomain's stone size and each BMD score, as presented in both Table 2 and Table 3, supports the construct validity of the subdomains while also solidifying the findings in Table-1 regarding the inverse association between BMD and urinary calculi size. Moreover, subjects' mean age, gender, and BMI values were also compiled in Table 2 and 3, and similar to stone size and BMD, the association between each of the subdomains' respective data was analyzed. Lack of any meaningful statistical difference across all boards was noted with the results stated above. It can thus be inferred that gender, age and BMI, while confirmed by the current and previous literature as factors affecting BMD in patients [25-29], constitute no noteworthy influence on the relation between BMD and urinary stone size; meaning that the association between BMD and calculi size is henceforth independent of any co-imposing factors in our study.

As previously mentioned, the proposed data in our study suggests a significant male predominance among low BMD patients, which is contradictory to the previously accepted data. BMD regression is more prevalent in women due to the decreased estrogen levels in postmenopausal ages [28]. However, it resulted from our weighted sample population, wherein the male population markedly outnumbers the female population (72.6% versus 27.3%). Urolithiasis is known to be more prevalent among men than women, to which such curbs in sample selection may be contributed [30,31].

The data provided therefore establish stone size as a pertinent risk assessment tool in urinary stone patients. Since up to 35% of the 24-hour urine studies in these patients may be presented normally [32], stone size on the CT-scan can be utilized in clinical decision making regarding further management of urinary stone patients, either through subsequent lab-testing or medical management.

This is the first study to associate urinary stone size and low BMD retrieved from CT-imaging in an Iranian sample population. Thus, a number of limitations must be addressed.

First, Shohada-e-Tajrish Hospital's database did not include the patient's serum and urine biochemical analysis. Therefore, data regarding patients' serum PTH, Calcium, or 24-hours urine analysis are not presented in our study. However as stated before, the circumstances surrounding the hypercalciuric state in urinary stone patients are unclear and controversial. Moreover, our study aimed to link stone size to the decreased BMD on non-contrast CT imaging, thus providing a reliable risk-assessment tool regardless of previous serological or urinary data. Associations between serum and urinary calcium levels and BMD, as discussed in previously published researches [14], are not the main goal of the current study.

Second, despite the previous studies proving low BMD's diagnostic threshold of 160 HU on CT imaging to be valid compared to DEXA [15,16], our study was purely conducted through CT-scan results and did not have access to the gold standard DEXA. Moreover, the 160 HU is the defined cut-off for osteopenia and as such, there may be a sample of patients with normal BMD falsely included in the low BMD subgroup.

CONCLUSION

To sum up, urinary stone size is significantly associated with bone mineral density, retrieved from non-contrast abdominal/pelvic CT-imaging; patients with larger urinary calculi are shown to suffer from a lower BMD. This data can be used as a valuable screening tool to identify those urinary stone patients with higher risks of osteoporosis and fractures and to help physicians deal with such patients properly through laboratory and medical means.

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