

Assessment of the Fractures Risk in Patients with Nephrolithiasis

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Abstract. Kidney stone disease is a common polyetiological urological disease that is also often combined with bone mineral density (BMD) disorders. Currently, no common recommendations exist for managing patients with comorbid conditions such as osteoporosis and kidney stone disease. Therefore, the aim of the study was to evaluate bone mineral density, the trabecular bone score index, fracture risk assessment tool and trabecular bone score-adjusted fracture risk assessment tool risk in patients with nephrolithiasis. Materials and methods. The study was conducted based on the Urology Department of the O.O. Bogomolets National Medical University, Kyiv (Oleksandrivska Clinical Hospital, Kyiv), Department of Urology, Kyiv Regional Clinical Hospital, Kyiv, Ukraine. 80 patients took part in the study, among them 15 men and 65 women. All patients were divided into 2 groups. The 1st group with somatic diseases in remission without kidney stone disease and those

without exclusion criteria (32 patients, women 31 (96.9%), men – 1 (3.1%), age 64 [58-72] y.o. The II group was introduced patients with kidney stone disease (48 patients, women – 34 (70.8%), men – 14 (29.2%), age 55.5[51.5-62.5] y.o. Results. Comparative analysis of X-ray densitometry did not establish a difference between bone mineral density in the comparison groups. However, the trabecular bone score was lower in patients with kidney stone disease ($p=0.02$). When evaluating anamnestic data in patients with the presence of nephrolithiasis, no differences were found in the frequency of fractures in the past ($p<0.05$). According to the 10-year assessment of the probability of fractures, the value of fracture risk assessment tool all trabecular bone score in the II group is probably higher, both in comparison with the I group and the fracture risk assessment tool all indicator. Conclusions. The need to recalculate the 10-year fracture prognosis taking into account the fracture risk assessment tool all

trabecular bone score index is very relevant in patients with nephrolithiasis, as it can help to start therapy as early as possible to prevent fractures.

Keywords: nephrolithiasis, osteoporosis, trabecular bone score, fracture risk assessment tool.

Introduction. The aging global population leads to an increase in age-related diseases, such as cardiovascular, oncological, and musculoskeletal disorders. Among these, the decrease in bone mineral density – osteoporosis and other metabolic bone diseases – holds significant importance. Increasing attention is being paid to the pathogenetic mechanisms of secondary osteoporosis caused by somatic diseases, as young people can also be affected. One of the negative impacts on bone metabolism is kidney disease, which affects vitamin D metabolism and leads to secondary hyperparathyroidism, a risk factor for nephrolithiasis. When addressing disorders of bone mineral density, another concern is the safety of calcium supplementation in relation to the risk of urolithiasis (kidney stone disease). Kidney stone disease is a polyetiological disease associated with a metabolic disorder accompanied by stone formation in the urinary tract [1]. Currently, no common recommendations exist for managing patients with comorbid conditions such as osteoporosis and kidney stone disease. The relevance of this problem is underscored by the fact that a decrease in bone mineral density increases the risk of bone fractures, as assessed using the fracture risk assessment tool calculator. However, there is insufficient data to assess the fracture risk in patients with nephrolithiasis.

The purpose of the study was to evaluate bone mineral density, the trabecular bone score index, fracture risk assessment tool and trabecular bone score-adjusted fracture risk assessment tool risk in patients with nephrolithiasis.

Materials and methods. The study was conducted based on the Urology Department of the Bogomolets National Medical University, Kyiv (Oleksandrivska Clinical Hospital, Kyiv), Department of Urology, Kyiv Regional Clinical Hospital, Kyiv, Ukraine, according to the scientific work of the Urology Department “Development of personalized approaches to stenting of the upper urinary tract during endoscopic treatment of ureterolithiasis”. All participants signed the appropriate form of informed consent.

Population

80 patients took part in the study, among them 15 men and 65 women. The average age of the patients was 58 [Interquartile Range 49–64] years; the median duration of menopause in women was 12 [Interquartile Range 5–20] years. 21 participants (26.3%) were diagnosed with kidney stone disease before inclusion in the study, 10 men (12.5%) and 11 women (13.75%). After an additional examination, the diagnosis of kidney stone disease was additionally made in 27 patients (33.75%), 2 men (2.5%) and 25 women (31.25%).

All patients were divided into 2 groups. The 1st group with somatic diseases in remission without kidney stone disease and those without exclusion criteria (32 patients, women 31 (96.9%), men – 1 (3.1%), median age 64 (interquartile range 58-72) years. The median duration of menopause was 17 (Interquartile Range 8–20) years. The II group was introduced patients with kidney stone disease (48 patients, women – 34 (70.8%), men – 14 (29.2%), median age 55.5 (interquartile range 51.5-62.5). The median duration of menopause in women was 12 (interquartile range 5-18) years.

Materials and methods. The diagnosis of kidney stone disease was established based on the criteria according to the recommendations of the European Association of Urology [2] using a questionnaire, about awareness of the presence of urolithiasis in their past medical history, conducting an ultrasound examination of the kidneys, and computed tomography with contrast (if necessary).

The study was carried out in accordance with the research plan and is a part of the scientific research project “Optimization of Management of Patients with Urolithiasis and Concomitant Osteoporosis” (State Registration Number 0125U000958). Resolution of the Cabinet of Ministers of Ukraine dated March 13, 2024 No. 296 “On approval of the Procedure for conducting rehabilitation

(post-isolation, reintegration) measures, adaptation, support (support) measures for persons in respect of whom the fact of deprivation of personal liberty as a result of armed aggression against Ukraine has been established, after their release” The study protocol was approved by the Bioethics Committee Bogomolets National Medical University, Kyiv (Protocol No. 193, March 24, 2025). The study did not include patients with a chronic disease with a glomerular filtration rate calculated using the chronic kidney disease epidemiology collaboration formula approved by the kidney disease: improving global outcomes 2013 recommendations (glomerular filtration rate < 60 ml/min/1.73 m²) [3].

Assessment of the bone mineral density and trabecular bone score was carried out based on the Ukrainian Osteoporosis Center and Department of Clinical Physiology and Pathology of Locomotion Apparatus of the State Institution “Institute of Gerontology named after D.F. Chebotarev of the National Academy of Medical Sciences of Ukraine”, Kyiv, Ukraine (Chief of the Department Prof. N.V. Grygorieva). Dual X-ray absorptiometry was performed on the Hologic Discovery device.

The following indices were evaluated: bone mineral density (g/cm²) of the lumbar spine, right and left femoral necks, ultradistal radius. The degree of bone mineral density impairment was assessed by the T-score, which is the deviation from the reference value of the peak bone mass of a healthy person.

According to the international osteoporosis foundation recommendations in postmenopausal women the T-criterion from -1 to -2.5 standard deviation is considered as osteopenia, a decreased T-score < -2.5 standard deviation as osteoporosis.

The trabecular bone score iNsight method, developed by medimaps (Bordeaux, France), was used to assess the bone tissue quality (trabecular bone score, units). This is bone microarchitecture visualization software for dual X-ray absorptiometry.

The analysis of this index is based on the variation of gray shades and the amplitude of the pixel density of the X-ray image (<https://www.medimapsgroup.com/tbs-osteo-re-duce-fracture-risk>) [4].

In order to calculate the risk of fractures, we used the calculator fracture risk assessment tool all (10-year risk assessment of all fractures, (%), fracture risk assessment tool hip (10-year risk assessment of femoral neck fractures), fracture risk assessment tool all trabecular bone score and fracture risk assessment Tool hip trabecular bone score (taking into account the trabecular bone score) [5].

Statistical analysis

Data processing was carried out using Microsoft Excel and Statistica easy R version 1.62-2023 statistical programs. The Shapiro-Wilk W test was used to test the distribution for normality.

The frequency of quantitative indices was indicated in absolute (n) and relative (%) frequencies.

The quantitative indices are presented in the form of median (Me) for variables with a distribution that was different from the normal one and the interquartile range of quartile I ÷ quartile III indices.

The Mann-Whitney U test was used to assess differences between groups. The difference between the groups was considered statistically significant at $p < 0.05$.

Results and discussion. It was established that a normal bone mineral density in the 1st group was revealed in 10 patients out of 32 (31.2%), among them 9 women (28.1%) and 1 man (3.1%). Abnormalities of bone mineral density within the limits of osteopenia were found in 13 patients (40.7%), all were women. Osteoporosis was diagnosed in 9 patients (28.1%), all were women.

In the 2nd group with established kidney stone disease, normal bone mineral density was observed in 11 patients out of 48 (22.9%), among them 4 women (8.3%) and 7 men (14.6%). Bone mineral density abnormalities within osteopenia were found in 16 patients (33.3%), among them 12 women (25%) and 4 men (8.3%). Osteoporosis was diagnosed in 21 patients (43.8%), 18 women (37.5%) and 3 men (6.25%).

Comparative analysis of the results of X-ray absorptiometry (Table 1) did not establish a difference between bone mineral density dates. While the trabecular bone score index was significantly lower in patients with nephrolithiasis ($p < 0.05$).

The purpose of assessing the state of bone tissue is to prevent fractures. Therefore, an anamnestic inquiry was conducted regarding fractures in the past. It was established that in the 1st group, the total

number of fractures was 9 cases (28.1%, absolute risk 0.28 (95% confidence interval 0.13-0.46), among them, 6 patients had spinal fractures (18.8%; absolute risk 0.18 (95% confidence interval 0.07-0.36), and 3 limbs (9.3%; absolute risk 0.03 (95% confidence interval 0.001-0.162).

Table 1. Comparison of bone mineral density indices in patients with and without kidney stone disease, Median (quartile I÷ quartile III).

Parameters	Group I	Group II
Bone mineral density L ₁ -L ₄ , g/m ²	1.035 [0.959-1.12]	0.923 [0.815-0.995]
T-score, Standard Deviation	-0.1 [-0.8...-0.9]	-1.4 [-2.1...-0.6]
Z-score, Standard Deviation	0 [-0.75...-0.9]	-0.2 [-1.4...-0.8]
Bone mineral density hip right, g/m ²	0.814 [0.7545-0.953]	0.693 [0.625-0.835]
T-score, Standard Deviation	0.05 [-0.95...-1.4]	-1.6 [-2.1...-0.6]
Z-score, Standard Deviation	0.8 [-0.5...-1.35]	-0.3 [-1...-0.4]
Bone mineral density hip left, g/m ²	0.856 [0.753-0.936]	0.718 [0.612-0.833]
T-score, Standard Deviation	0.1 [-0.85...-0.8]	-1.2 [-2.1...-0.5]
Z-score, Standard Deviation	-0.25 [-0.8...-1]	-0.4 [-0.9...-0.4]
Bone mineral density radius, g/m ²	0.699 [0.680-0.711]	0.646 [0.57-0.729]
T-score, Standard Deviation	0.1 [-0.4...-0.25]	-1.4 [-2.4...-0.6]
Z-score, Standard Deviation	0.1 [-0.25...-0.35]	-0.2 [-1.2...-0.6]
Trabecular Bone Score, units	1.469 [1.4585-1.535]	1.255 [1.207-1.285] *

Notes: * — significant differences between indicators ($p < 0.05$)

In the 2nd group, the total number of fractures was 8 (16.7%; absolute risk 0.16 (95% confidence interval 0.07-0.3), among them 7 spinal fractures (14.7%; interval assessment 0.14 (95% confidence interval 0.06-0.27) and 3 limbs (2%; interval assessment 0.02 (95% confidence interval 0.001-0.111). Moreover, no difference was found in patients with nephrolithiasis ($p < 0.05$).

The fracture risk assessment tool calculator was used to estimate the 10-year probability of fracture risk. In assessment of fracture risk, the fracture risk assessment tool all score was higher in patients with nephrolithiasis ($p = 0.02$, Fig.1), while the fracture risk assessment tool hip score did not differ between the comparison groups ($p > 0.05$) (Tabl.2).

The finding of a lower trabecular bone score in patients with kidney stone disease raised the question of the possibility of differences in the fracture risk assessment tool-adjusted fracture risk scores.

The analysis showed that fracture risk assessment tool all trabecular bone score was significantly higher (Fig. 2.) in patients with kidney stone disease ($p=0.01$), fracture risk assessment tool hip trabecular bone score did not differ in comparison groups ($p>0.05$) (Table 2).

We also performed a comparative evaluation between fracture risk assessment tool scores in groups with and without trabecular bone score correction.

It was found that fracture risk assessment tool all trabecular bone score was significantly higher compared to fracture risk assessment tool all in group II ($p=0.02$), while in group I no difference was found ($p=0.63$) when comparing fracture risk assessment tool all and ($p=0.83$) when comparing fracture risk assessment tool hip indicators.

Thus, no difference in bone mineral density was established in patient groups depending on the presence of nephrolithiasis. At the same time, the trabecular bone score trabecular bone quality index was significantly lower in patients with established kidney stone disease.

No difference was found in the frequency of already diagnosed fractures in patients with nephrolithiasis.

The assessment of 10-year prediction of fractures showed a significantly higher risk of both fracture risk assessment tool all fractures and fracture risk assessment tool all trabecular bone score-adjusted fractures in group II in patients on kidney stone disease.

Moreover, this date was higher in the II group in comparison with the indicators of this group, which were calculated without taking into account trabecular bone score.

Table 2. Comparative evaluation of the 10-year fracture risk indicators of fracture risk assessment tool and fracture risk assessment tool trabecular bone score in patients depending on the presence of kidney stone disease.

Group	Group I (n=32)	Group II (n=48)	The level of significance of the difference between groups, p
Parameters	M±m Median (quartile I÷ quartile III)		
Fracture risk assessment tool all	3.9[2.7-5.6]	4.8[3.7-6.9]	$p=0.02$
Fracture risk assessment tool hip	0.9±1.5	1.55±1.6	$p>0.05$
Fracture risk assessment tool all trabecular bone score	3.8[2.3-5.7]	5.0[3.9-7.0] *	$p=0.01$
Fracture risk assessment tool hip trabecular bone score	1.05±1.9	1.6±1.8	$p>0.05$

Note: *-significant difference between fracture risk assessment tool all and fracture risk assessment tool all trabecular bone score indicators in the II group.

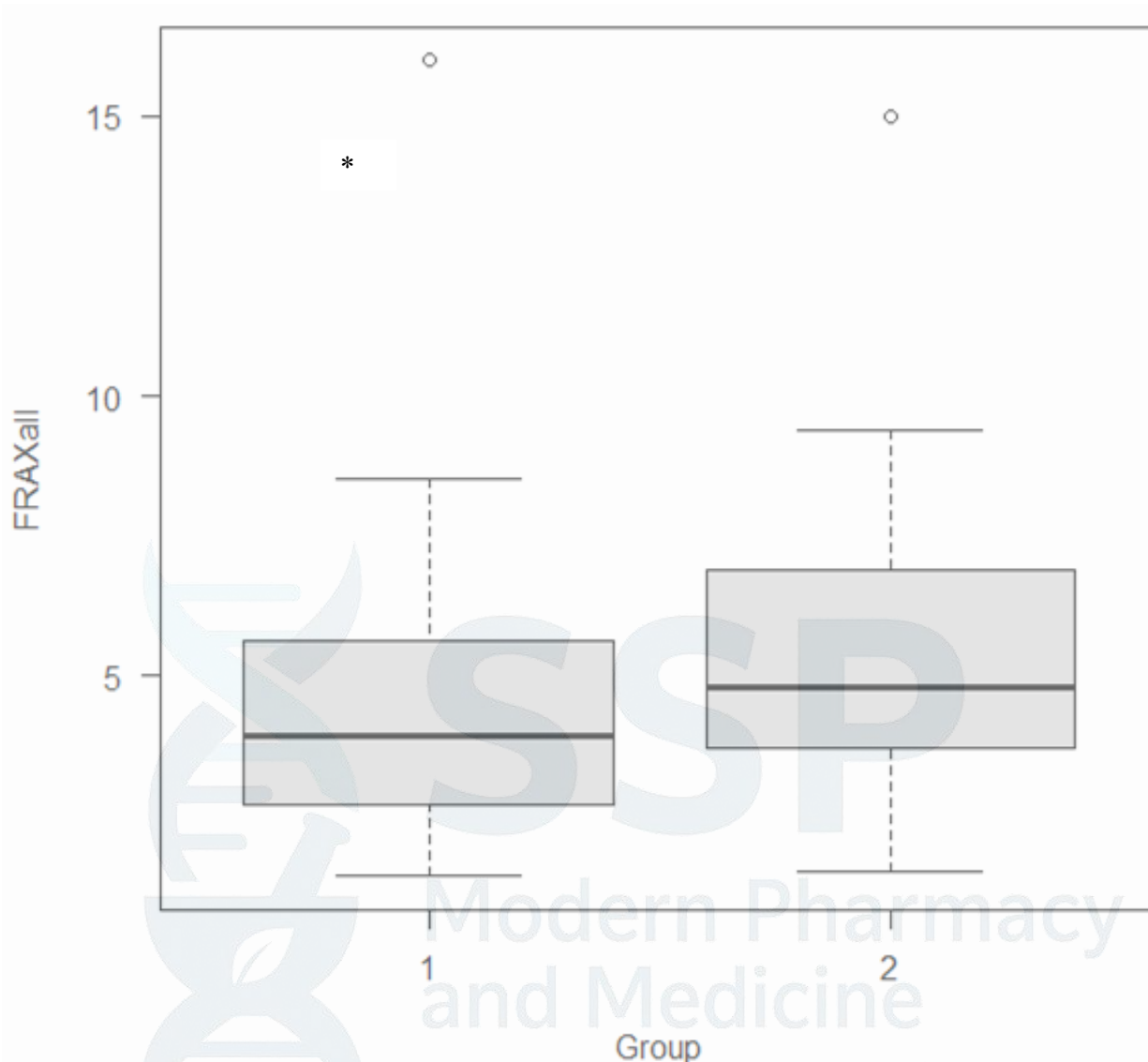


Fig. 1. Comparison of fracture risk assessment tool all in patients with and without kidney stone disease. **Notes:** interval estimation of the average values of trabecular bone score (the average value, the error of the average and the 95% probable interval of the average are indicated); * – significant difference between the indicators, $p < 0.05$

Thus, the study showed that patients with kidney stone disease have lowest indicator of trabecular bone score compare with patients without nephrolithiasis and no difference in bone mineral density.

It is essential for forecasting because a decrease in trabecular bone score even with a normal bone mineral density is also an increased bone fracture risk. That is why studying the features of the pathogenesis of metabolic bone diseases increasing [6].

This explain also the main aim of osteoporosis treatment - the fractures prevention. In our study, the data on the presence of fractures in the past did not have a probable difference between the comparison groups.

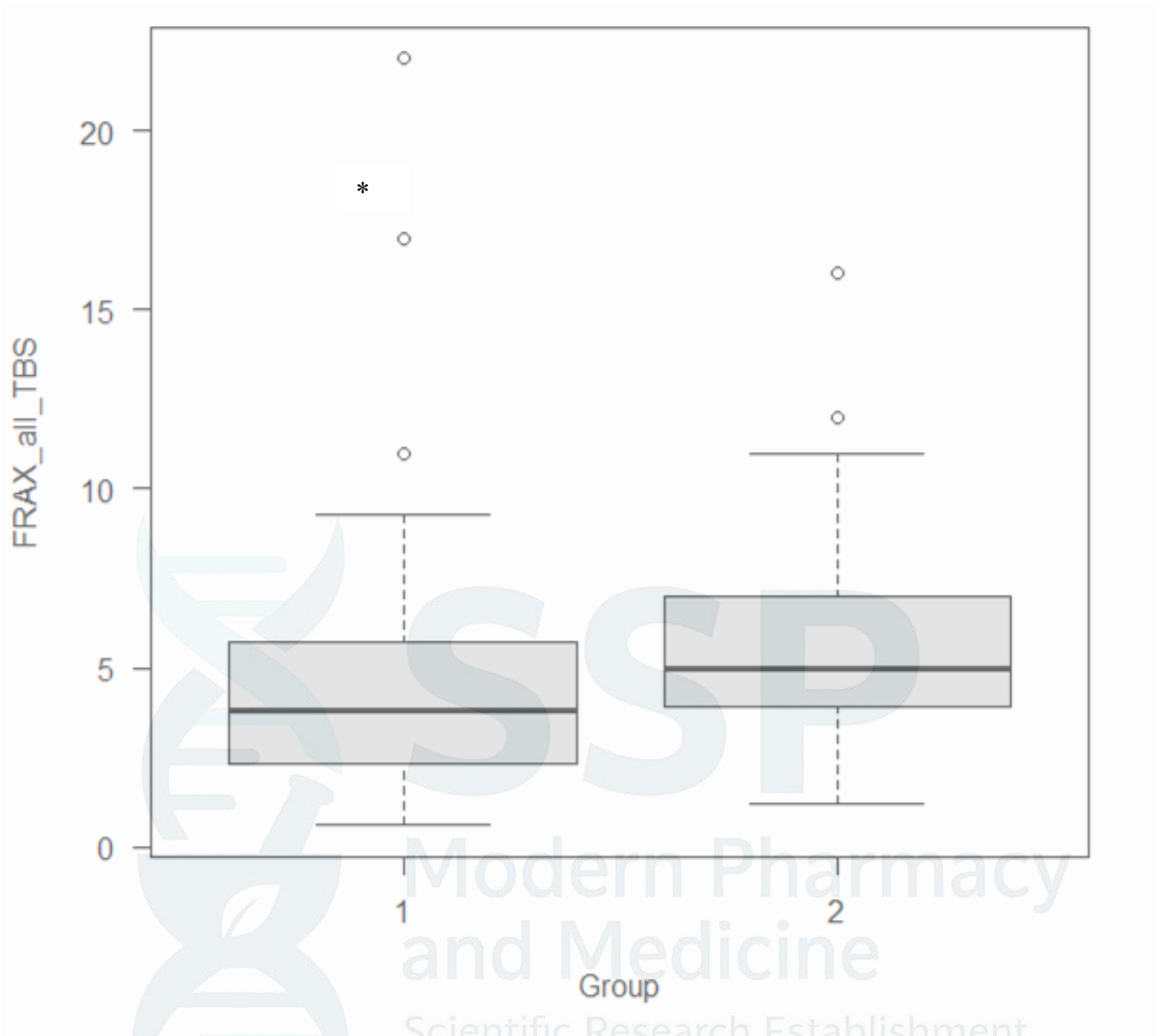


Fig. 2. Comparison of fracture risk assessment tool all trabecular bone score in patients with and without kidney stone disease.

Notes: interval estimation of the average values of trabecular bone score (the average value, the error of the average and the 95% probable interval of the average are indicated); * – significant difference between the indicators, $p < 0.05$

However, regarding the calculation of the 10-year fracture risk using the fracture risk assessment tool model, which is already adapted for the Ukrainian population [7], interesting data have been established.

The result of our study showed a probable increase in fracture risk assessment tool all trabecular bone score in the II group both in comparison with the I group and the fracture risk assessment tool all date.

So, we need to calculate the 10-year fracture prognosis taking into account the trabecular bone score index is very relevant in patients with nephrolithiasis, as it can help to start therapy as early as possible to prevent fractures.

Conclusions.

1. No difference was found in bone mineral density in patients with and without kidney stone

disease.

2. Patients with kidney stone disease have a lower of trabecular bone score, which is also an increased risk factor for bone fractures.

3. The fracture risk assessment tool all trabecular bone score is significantly higher in patients with nephrolithiasis both in comparison with patients without kidney stone disease and with the rate of Fracture Risk Assessment Tool all in their group.

4. In order to assess the risk of fractures, it is advisable to use the determination of the trabecular bone score indicator followed by the calculation of fracture risk assessment tool all trabecular bone score.

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Conflict of interest. The authors declare no conflict of interest regarding this manuscript.

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Ethical approval. Ethical clearance was obtained from the administration of the Bogomolets National Medical University. Permission statement for conducting the experiments was received from the administration of the Bogomolets National Medical University (and/or affiliated medical institutions). Before data collection, the main purpose of the study was clearly explained to each patient (interested personnel).

Data availability statement. The datasets analyzed during the current study are available from the corresponding author on reasonable request

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