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Clinical Course of Recurrent Urolithiasis: A Pilot Study

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ABSTRACT

BACKGROUND: Urolithiasis is one of the most common urological disorders, characterized by a chronic recurrent course. Various predictive models have been proposed to assess the risk of stone recurrence. However, their effectiveness remains limited, which necessitates further investigation into the clinical features of the disease, including its recurrent nature.

AIM: To evaluate the features of the clinical course of recurrent urolithiasis.

METHODS: This study included 471 patients admitted to a urology department between 2019 and 2021 with a diagnosis of urolithiasis (ICD-10 codes N20, N23). Statistical analysis of data was performed using RStudio (version 4.3.3).

RESULTS: Compared to patients with first-onset urolithiasis, those with recurrent disease had a higher body mass index (28.0 and 27.4 kg/m^2, respectively; $p = 0.043$), a higher prevalence of overweight (76.6% and 67.5%, respectively; $p = 0.002$), and a greater number of stones in each kidney and overall in both kidneys. The total stone volume was also significantly higher in recurrent urolithiasis: median 855 mm^3 and 433 mm^3, respectively ($p < 0.001$). A history of spontaneous stone passage was reported in 42% of patients, whereas 58% had previously undergone surgical intervention for urolithiasis. Patients with a history of surgical interventions for urolithiasis had a higher body mass index, a more frequent presence of obesity compared to patients with spontaneous stone passage (39.2% and 23.8%, respectively; $p = 0.011$), as well as a greater number of urinary stones in both kidneys.

CONCLUSION: Recurrent urolithiasis is more common among patients with excess body weight and is associated with more intensive stone formation than in patients with first-onset of urolithiasis. In recurrent urolithiasis, obesity is linked to an increased need for surgical intervention and a lower probability of spontaneous stone passage. In this context, body weight normalization appears to be the most appropriate strategy for reducing the risk of urolithiasis recurrence.

Keywords: urolithiasis; obesity; overweight; recurrent urolithiasis.

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Особенности течения рецидивирующего уролитиаза: пилотное исследование

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АННОТАЦИЯ

Обоснование. Мочекаменная болезнь — одно из самых распространенных урологических заболеваний, для которого характерно хроническое рецидивирующее течение. Для оценки рецидива камнеобразования предлагаются различные прогностические модели. Тем не менее эффективность предлагаемых моделей все еще остается недостаточной, что требует дополнительного изучения особенностей течения заболевания, в том числе с учетом его рецидивирующего характера.

Цель — оценить особенности течения рецидивирующего уролитиаза.

Материалы и методы. Исследование включало 471 пациента, госпитализированных в урологическое отделение в период с 2019 по 2021 г. с диагнозом «мочекаменная болезнь» (коды по МКБ-10 N20, N23). Статистическая обработка данных была выполнена при помощи программного обеспечения RStudio (версия 4.3.3.).

Результаты. Для пациентов с рецидивирующей формой уролитиаза по сравнению с пациентами с первичной манифестацией мочекаменной болезни характерен более высокий индекс массы тела (28,0 и 27,4 кг/м^2 соответственно, p=0,043), более высокая распространенность избыточной массы тела (76,6 и 67,5% соответственно, p=0,002), большее количество камней как в каждой почке по отдельности, так и суммарно в обеих почках. Суммарный объем камней при рецидивирующем уролитиазе был также выше: медиана 855 и 433 мм^3 соответственно (p <0,001). У 42% пациентов ранее отмечалось самостоятельное отхождение конкрементов, в то время как у 58% ранее требовалось оперативное вмешательство по поводу мочекаменной болезни. У пациентов с перенесенными оперативными вмешательствами по поводу мочекаменной болезни был более высокий индекс массы тела, чаще присутствовало ожирение по сравнению с пациентами после самостоятельного отхождения камней (39,2 и 23,8% соответственно, p=0,011), а также было большее количество мочевых камней в обеих почках.

Заключение. Рецидивирующий уролитиаз чаще встречается у пациентов с наличием избыточной массы тела и характеризуется более интенсивным камнеобразованием, чем у пациентов с первичной манифестацией мочекаменной болезни. Ожирение при рецидивирующем уролитиазе ассоциировано с более частой необходимостью оперативных вмешательств при снижении вероятности самостоятельного отхождения конкрементов. В данном аспекте концепция нормализации веса представляется наиболее оптимальной стратегией для снижения риска рецидивирования уролитиаза.

Ключевые слова: мочекаменная болезнь; ожирение; избыточная масса тела; рецидивирующее течение мочекаменной болезни.

Как цитировать

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BACKGROUND

Urolithiasis is one of the most common urological diseases worldwide. In Russia, there has been a continuous increase in the incidence of urolithiasis since 2005, which is associated with a widespread increase in risk factors and improved diagnosis. Although slightly more than 650,000 new cases were registered in 2005, almost 800,000 cases were reported in 2020. From 2005 to 2019, the incidence of urolithiasis increased by 35.45%, confirming the relevance of this disease in Russia [1].

Urolithiasis is characterized by chronic recurrent course. Research has demonstrated that 30%–50% of patients experience a recurrence of urolithiasis within five years following the initial manifestations. This underscores the need for preventive measures to identify and mitigate potential risk factors for this condition [2]. Notably, urolithiasis is a polyetiological disease characterized by many risk factors. The proven causes of urolithiasis occurrence and recurrence are metabolic factors, a family history of urolithiasis, episodes of stone formation, comorbidities such as hypertension, diabetes mellitus, and obesity, as well as dietary and water-drinking habits [3, 4].

Several prognostic models have been developed to estimate the likelihood of urolithiasis recurrence. For example, Xia et al. [5] found that patients with multiple calculi and bilateral renal injury were at a higher risk of stone recurrence, based on an analysis of nearly 660 patients' data. Furthermore, the authors found that the risk of urolithiasis recurrence increases with urine acidity in the range of 5 to 7, as well as with higher serum creatinine and apolipoprotein B concentrations, which result in cholesterol accumulation in vessel walls [5].

In 2014, a nomogram for predicting urolithiasis recurrence was proposed; it was called ROKS (Recurrence of Kidney Stone). The development of this nomogram entailed a comprehensive analysis of over 2200 case histories of patients diagnosed with urolithiasis between 1984 and 2003. During the study, 707 individuals experienced symptomatic recurrence. The factors evaluated when calculating the probability of recurrence included age, sex, race, family history of urolithiasis, macrohematuria, uric acid stones, location of the calculus in the intravesical region of the ureter, symptomatic stones in the pelvis or lower calyx group, and additional multiple asymptomatic calculi [6]. A prospective study by Costa et al. [7] assessed symptomatic and radiological recurrences of urolithiasis using the proposed ROKS normogram. Although the ROKS score had limited capacity to predict symptomatic recurrence (concordance C-index = 0.63), it reliably predicted any symptomatic or radiologic recurrence (concordance C-index = 0.79). In another study, the authors evaluated the efficacy of the ROKS nomogram in identifying patients who would require medical care for recurrent urolithiasis following primary surgical treatment of the condition. Although the ROKS nomogram demonstrated moderate discriminatory ability, calibration of prognosis based on ROKS was ineffective, and its clinical utility was minimal [8].

In view of the 2020 results, the ROKS nomogram was refined because it was clear that it could not predict recurrence in cases involving two or more episodes of symptomatic stone formation. Some demographic parameters, constitutional features, and diagnostic tests were introduced into the model [9]. Kavoussi et al. [10] evaluated the performance of the new model, but its ability to discriminate between recurrences two and five years after manifestation was still moderate (ROC-AUC0.67 vs 0.63, respectively).

Thus, due to the absence of widely accepted and effective models for predicting urolithiasis recurrence, more research is needed on the disease characteristics, particularly in patients with recurrences.

The *study aimed* to evaluate the features of the clinical course of recurrent urolithiasis.

METHODS

The study included 471 patients who were hospitalized in the Urology Department of the University Clinic of the Medical Research and Education Institute at Lomonosov Moscow State University between 2019 and 2021 and were diagnosed with urolithiasis (ICD-10 codes N20, N23). Basic clinical, laboratory, and instrumental data were collected for all patients, including age, features of somatic status, parameters of blood chemistry analysis and urinalysis, as well as the results of abdominal computed tomography (CT) with assessment of the presence, number, and size of urinary calculi in each of the kidneys. Furthermore, the data on urolithiasis recurrences and prior surgical interventions for the condition, or a history of spontaneous stone passage were collected. A comparative analysis of the primary clinical and laboratory tests of patients was conducted, with consideration given to recurrent urolithiasis and the history of prior surgeries.

Statistical Data Processing

Statistical analysis was performed using the R programming language in RStudio software (version 4.3.3). The normality of the distribution of quantitative variables was assessed using the Shapiro–Wilk test. The data were presented as mean and standard deviation ($M \pm SD$) if the distribution was normal and as median and quartiles (Me [Q_1; Q_3]) if the distribution was not normal. Categorical variables are presented as absolute values (n) and percentages (%). Normally distributed quantitative variables were compared using a Student's t-test;

variables with a non-normal distribution were compared using a Mann–Whitney test. Categorical variables were compared using the chi-square test, the Yates-corrected chi-square test, and Fisher's exact test. The differences were considered statistically significant at $p < 0.05$.

RESULTS

The mean age of the study participants ($n = 471$) was 52.9 years (SD = 14.9 years). The median age was 55 years (41.0; 64.0). The maximum and minimum ages were 19 and 89 years, respectively. Recurrent urolithiasis was observed in 53.3% ($n = 251$) of patients. A comparative analysis of clinical, laboratory, and instrumental parameters revealed that patients with recurrent urolithiasis had a higher body mass index (BMI) (28.0 kg/m^2 vs 27.4 kg/m^2; $p = 0.043$) than those with primary urolithiasis (Table 1). The prevalence of obesity was comparable in both groups, but overweight patients were much more prevalent in the recurrent urolithiasis group (76.6% vs 67.5%, respectively; $p = 0.002$). Furthermore, patients with recurrent urolithiasis were more likely to have hypertension (53.2% vs 38.8%, respectively; $p = 0.002$).

No statistically significant differences in blood chemistry parameters, including lipid metabolism, were found between the studied groups. This may be due to a similar frequency of statin use in each group. Despite the absence of statistically significant differences in the comparative analysis of urine parameters, a tendency toward increased bacteriuria diagnosis in cases of recurrent urolithiasis was observed. The indicator demonstrated borderline significance (28.6% vs 20.7%, respectively; $p = 0.083$).

A comprehensive evaluation of the parameters that characterize urinary calculi revealed specific differences. Recurrent urolithiasis was characterized by a greater number of stones in each kidney and in both kidneys combined. The mean median stone count was 2.0 [1.0; 3.0] at primary manifestations, whereas it was 3.0 [1.0; 5.0] in recurrent urolithiasis ($p < 0.001$). Furthermore, a higher total stone volume was observed in recurrent urolithiasis cases ($Me = 855$ vs 433 mm^3, respectively; $p < 0.001$), though mean CT density of these stones was slightly lower ($Me = 895$ vs 968 HU, respectively, $p = 0.002$). The detailed results are presented in Table 1.

Fig. 1 shows a graphical representation of major statistically significant differences in data between patients with recurrent and primary urolithiasis.

Patients with recurrent urolithiasis had between 1 and 11 previous recurrences, with an average of 1.9 ± 1.32 (1.0; 3.0).

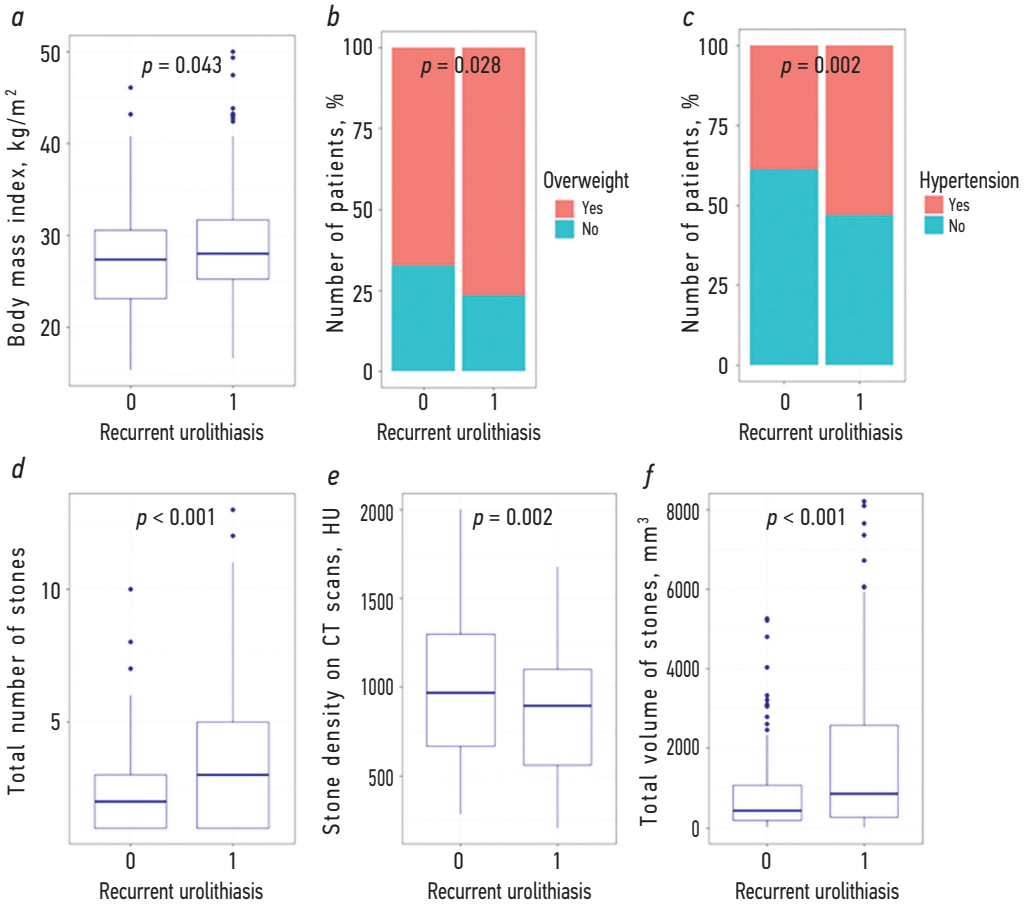

Fig. 1. Comparative characteristics of patients with recurrent and primary urolithiasis: body mass index (*a*), excess body weight (*b*), hypertension (*c*), total number of stones (*d*), stone density according to computed tomography (*e*), total stone volume (*f*).

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Table 1. Comparative analysis of clinical, laboratory, and instrumental parameters of patients depending on the recurrent nature of urolithiasis

Parameters	Primary manifestations (*n* = 220)	Recurrent urolithiasis (*n* = 251)	*p*
Clinical parameters			
Age, years (*Me* [Q_1; Q_3])	56.0 [39.0; 65.0]	55.0 [43.0; 63.0]	0.781
Sex:			0.823
• Men, % (*n*)	59.6% (131)	60.6% (152)	
• Women, % (*n*)	40.4% (89)	39.4% (99)	
Body mass index, kg/m^2 (*Me* [Q_1; Q_3])	27.4 [23.1; 30.6]	28.0 [25.3; 31.7]	0.043
Obesity, % (*n*)	29.7% (63)	32.7% (81)	0.497
Overweight, % (*n*)	67.5% (143)	76.6% (190)	0.028
Hypertension, % (*n*)	38.8% (85)	53.2% (133)	0.002
Diabetes mellitus, % (*n*)	12.3% (27)	14.0% (35)	0.594
Chronic heart failure, % (*n*)	6.9% (15)	8.4% (21)	0.529
Statin use, % (*n*)	12.2% (26)	13.2% (32)	0.744
Laboratory parameters			
Uric acid, μmol/L (*M* ± SD)	330.1±82.2	342.8 ± 93.4	0.392
Cholesterol, mmol/L (*Me* [Q_1; Q_3])	5.2 [4.4; 6.2]	5.4 [4.6; 5.9]	0.880
Triglycerides, mmol/L (*Me* [Q_1; Q_3])	1.1 [0.9; 1.6]	1.3 [1.0; 1.9]	0.283
Low-density lipoproteins, mmol/L (*M* ± SD)	3.4±1.2	3.2±0.8	0.663
High-density lipoproteins, mmol/L (*M* ± SD)	1.2±0.3	1.3±0.5	0.518
Very low-density lipoproteins, mmol/L (*Me* [Q_1; Q_3])	0.5 [0.4; 0.5]	1.0 [1.0; 1.3]	0.171
Urine protein, % (*n*)	65.4% (123)	58.8% (137)	0.164
Bacteriuria, % (*n*)	20.7% (34)	28.6% (57)	0.083
Instrumental parameters			
Bilateral urolithiasis, % (*n*)	35.0% (77)	43.6% (108)	0.059
Number of stones on the right (*Me* [Q_1; Q_3])	1.0 [0.0; 1.5]	1.0 [0.0; 3.0]	<0.001
Number of stones on the left (*Me* [Q_1; Q_3])	1.0 [1.0; 2.0]	1.0 [0.0; 3.0]	0.003
Total number of stones (*Me* [Q_1; Q_3])	2.0 [1.0; 3.0]	3.0 [1.0; 5.0]	<0.001
Volume of stones on the right, mm^3 (*Me* [Q_1; Q_3])	300.0 [105.0; 704.0]	264.0 [91.1; 1001.0]	0.619
Volume of stones on the left, mm^3 (*Me* [Q_1; Q_3])	228.0 [68.0; 745.0]	510.0 [81.0; 1947.0]	0.023
Total volume of stones, mm^3 (*Me* [Q_1; Q_3])	433.0 [193.0; 1064.0	855.0 [263.1; 2570.5]	<0.001
Density of stones on the right, HU (*Me* [Q_1; Q_3])	1035.0 [669.0; 1280.0]	900.0 [541.0; 1150.0]	0.067
Density of stones on the left, HU (*Me* [Q_1; Q_3])	1000.0 [695.0; 1319.0]	888.0 [630.0; 1100.0]	0.008
Mean density of all stones, HU (*Me* [Q_1; Q_3])	968.0 [669.0; 1300.0]	895.0 [563.0; 1100.0]	0.002

Among the previous episodes of urolithiasis, 106 (42.2%) patients experienced spontaneous stone passage and did not require surgical interventions. Among the remaining 145 (57.8%) patients, a previous surgery for urolithiasis was required. Fig. 2 shows the distribution of patients with recurrent urolithiasis depending on the number of stones and previous surgical interventions.

Fig. 2 shows that only 28% of patients with recurrent urolithiasis had a single stone, whereas 72% had two or more stones. Of these patients, 42% had spontaneous stone passage that did not require surgery, whereas 58% required surgery.

Subsequently, a comparative analysis of the main clinical, laboratory, and instrumental parameters of patients with recurrent urolithiasis was performed depending on the previous surgeries (see Table 2). Patients with a history of urolithiasis surgeries exhibited higher BMI, with obesity and overweight being more prevalent. Thus, obesity was present in 39.2% of patients who underwent surgery and in only 23.8% of those who experienced spontaneous stone passage ($p = 0.011$). Furthermore, hypertension was more prevalent among patients with a history of surgical interventions (62.1% vs 41.0%, respectively; $p < 0.001$).

No statistically significant differences in blood chemistry parameters, including lipid metabolism, were found between the studied groups. This may be due to a similar frequency of statin use in each group.

No statistically significant differences were found when assessing instrumental parameters that characterize urinary stones. However, a characteristic pattern emerged: patients who had undergone previous surgery for urolithiasis had more urinary stones in both kidneys (median of 3.0 vs 2.0, respectively), though with a borderline significance ($p = 0.052$). The detailed results are presented in Table 2.

Fig. 3 shows a graphical representation of the major statistically significant differences in data between patients with recurrent urolithiasis depending on previous surgeries.

DISCUSSION

This study examined the characteristics of recurrent urolithiasis in patients who presented at the urology department of the University Clinic of the Medical Research and Education Institute at Lomonosov Moscow State University between 2019 and 2021. We found that patients with recurrent urolithiasis had a higher BMI than those with primary urolithiasis (28.0 vs 27.4 kg/m^2, respectively; $p = 0.043$). Furthermore, patients with recurrent urolithiasis have a greater number of stones in each kidney and overall in both kidneys, as well as a greater total volume of calculi. Additionally, patients who had previously undergone surgery for urolithiasis were shown to have a higher BMI and be more likely to be obese or overweight. In this regard, weight normalization appears to be the optimal strategy for reducing recurrence risk and increasing the likelihood of spontaneous stone passage in case of recurrence.

Previous studies have reported similar results regarding the relationship between patients' constitutional characteristics and recurrent urolithiasis. For example, the NHANES study, which included almost 10,000 patients, found that the prevalence and recurrence of urolithiasis increased alongside an increase in visceral obesity. Thus, the probability of recurrent urolithiasis increases by 1.52-fold (or 52%) in patients with a visceral obesity index in the upper quartile [11]. A study by Lee et al. [12] showed that obesity increases the risks of stone recurrence after primary manifestations by 2.6-fold (odds ratio [OR] = 2.572; 95% confidence interval [CI]: 1.376–4.807; $p = 0.003$). However, a similar analysis of patients with recurrent urolithiasis did not reveal this correlation, which underscores the importance of weight loss in preventing stone recurrence after primary manifestations [12].

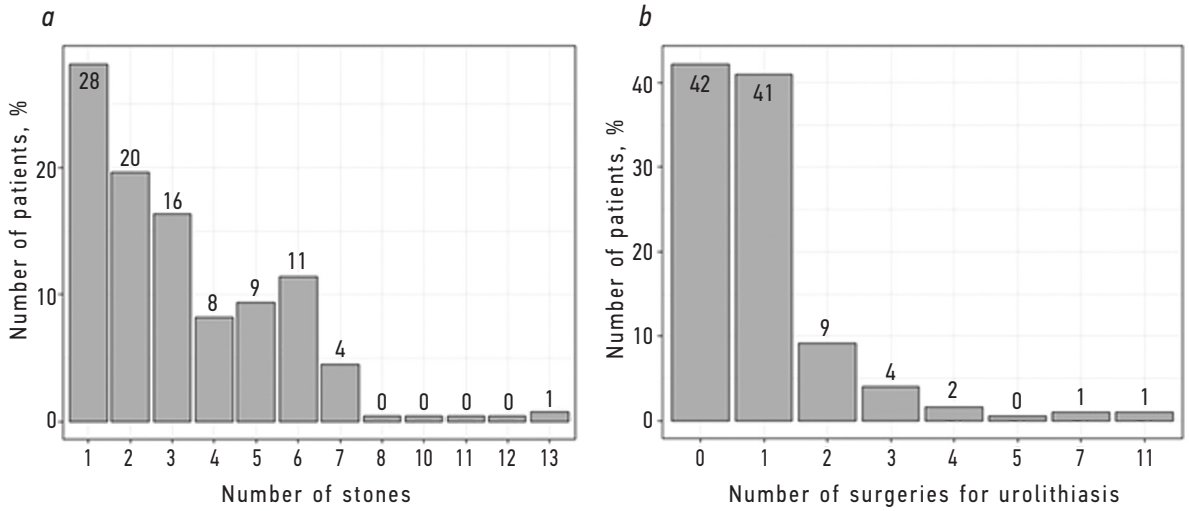

Fig. 2. Distribution of patients with recurrent urolithiasis depending on the number of stones (*a*) and previous surgeries for urolithiasis (*b*).

Table 2. Comparative analysis of clinical, laboratory, and instrumental parameters in patients with recurrent urolithiasis depending on previous surgeries

Parameters	Spontaneous stone passage without surgery (*n* = 106)	Previous surgeries for urolithiasis (*n* = 145)	*p*
Clinical parameters			
Age, years (*Me* [Q_1; Q_3])	53.0 [42.0; 62.0]	55.0 [44.0; 64.0]	0.312
Sex:			0.636
• Men, % (*n*)	62.3% (66)	59.3% (86)	
• Women, % (*n*)	37.7% (40)	40.7% (59)	
Body mass index, kg/m^2 (*Me* [Q_1; Q_3])	26.8 [24.7–29.8]	29.0 [25.8–32.6]	0.002
Obesity, % (*n*)	23.8% (25)	39.2% (56)	0.011
Overweight, % (*n*)	70.5% (74)	81.1% (116)	0.050
Hypertension, % (*n*)	41.0% (43)	62.1% (90)	<0.001
Diabetes mellitus, % (*n*)	12.4% (13)	15.2% (22)	0.530
Chronic heart failure, % (*n*)	6.7% (7)	9.7% (14)	0.542
Statin use, % (*n*)	12.5% (13)	13.7% (19)	0.790
Laboratory parameters			
Uric acid, μmol/L (*M* ± SD)	342.2±106.7	343.2±83.2	0.962
Cholesterol, mmol/L (*Me* [Q_1; Q_3])	5.3 [4.7; 5.8]	5.4 [4.6; 5.9]	0.857
Triglycerides, mmol/L (*Me* [Q_1; Q_3])	1.6 [1.0; 2.4]	1.3 [1.0; 1.7]	0.415
Low-density lipoproteins, mmol/L (*M* ± SD)	3.1±0.7	3.3±0.9	0.594
High-density lipoproteins, mmol/L (*M* ± SD)	1.2±0.5	1.3 ± 0.4	0.482
Very low-density lipoproteins, mmol/L (*Me* [Q_1; Q_3])	2.4 [1.8; 2.9]	1.0 [0.7; 1.0]	0.139
Urine protein, % (*n*)	60.6% (57)	57.6% (80)	0.639
Bacteriuria, % (*n*)	23.1% (18)	32.2% (39)	0.163
Instrumental parameters			
Bilateral urolithiasis, % (*n*)	38.7% (41)	47.2% (67)	0.181
Number of stones on the right (*Me* [Q_1; Q_3])	1.0 [0.0; 2.0]	1.0 [1.0; 3.0]	0.053
Number of stones on the left (*Me* [Q_1; Q_3])	1.0 [0.0; 3.0]	2.0 [0.0; 3.0]	0.356
Total number of stones (*Me* [Q_1; Q_3])	2.0 [1.0; 4.8]	3.0 [2.0; 5.0]	0.052
Volume of stones on the right, mm^3 (*Me* [Q_1; Q_3])	336.0 [90.8; 1001.0]	262.1 [109.0; 970.7]	0.848
Volume of stones on the left, mm^3 (*Me* [Q_1; Q_3])	378.0 [80.0; 1169.9]	510.2 [168.5; 2122.7]	0.397
Total volume of stones, mm^3 (*Me* [Q_1; Q_3])	780.0 [210.0; 1800.0]	915.4 [313.8; 3257.0]	0.108
Density of stones on the right, HU (*Me* [Q_1; Q_3])	925.0 [618.0; 1171.3]	850.0 [500.0; 1100.0]	0.256
Density of stones on the left, HU (*Me* [Q_1; Q_3])	858.5 [697.5; 1033.5]	925.0 [575.0; 1100.0]	0.841
Mean density of all stones, HU (*Me* [Q_1; Q_3])	900.0 [637.5; 1100.0]	868.8 [533.3; 1083.0]	0.279

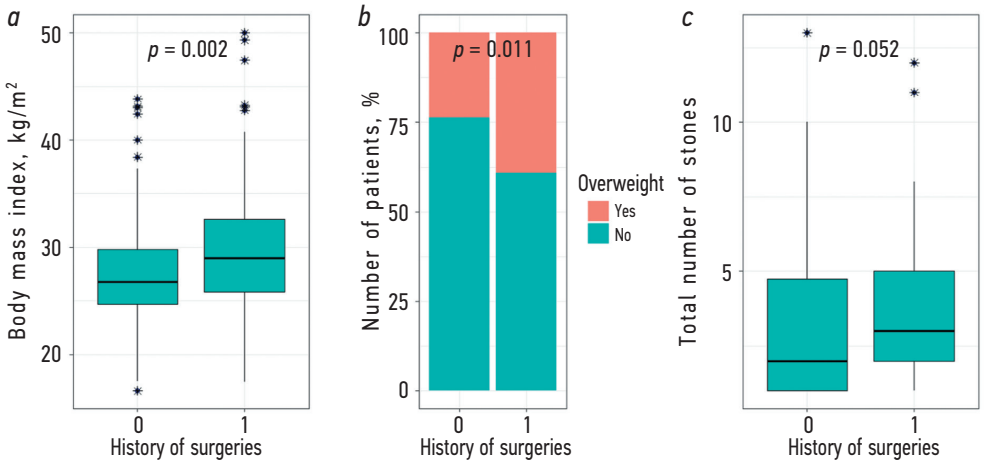

Fig. 3. Comparative characteristics of patients with recurrent urolithiasis depending on previous surgeries: body mass index (*a*), obesity (*b*), total number of stones (*c*).

Huang et al. [13] demonstrated that the risk of urolithiasis recurrence is associated with paranephric tissue thickness, which was more pronounced in patients with elevated BMI and hyperlipidemia. The presence of thick pararenal tissue increased the likelihood of stone recurrence by more than threefold [13]. Similar results were obtained by Yamashita et al. [14], finding that patients with recurrent urolithiasis had significantly higher visceral fat volumes than those with primary manifestations.

Interesting data were obtained in a large Spanish study published in January 2025. Rodríguez-Monsalve et al. [15] assessed the impact of obesity on the hospitalization rate of patients with urolithiasis between 1997 and 2021. Notably, obesity increased the likelihood of hospitalization for urolithiasis by 15.6-fold and was associated with higher treatment costs. Researchers concluded that preventive strategies aimed at combating obesity should be implemented to reduce the overall burden on the healthcare system [15]. Similar results were obtained in the present study. We have shown that obesity was much less common among patients with recurrent urolithiasis and spontaneous stone passage than among those with recurrent urolithiasis who had undergone previous surgeries (23.8% vs 39.2%, respectively; $p = 0.011$). A similar pattern was observed for BMI, which was 26.8 and 29.0 kg/m^2 in the two groups, respectively ($p = 0.002$). Spontaneous stone passage usually does not require hospitalization. Therefore, patients with recurrent urolithiasis who are not obese require inpatient treatment much less frequently than obese and overweight patients. Therefore, patients with urolithiasis and obesity placed a greater burden on the healthcare system.

The relationship between obesity and urolithiasis is mediated by several mechanisms. Obesity may result in decreased urine acidity and increased excretion of oxalates, sodium, phosphates, and uric acid. Insulin resistance affects the tubular exchange of sodium and hydrogen ions, promoting the formation of ammonium ions and, consequently, the acidification of urine. This further enhances stone formation [16]. Our work indirectly confirmed this relationship as well. We have demonstrated that patients with recurrent urolithiasis are more likely to be obese and have lower stone density on CT scans. This finding may indirectly suggest a correlation between stone density and BMI in this patient group, though this correlation has not been confirmed directly in our work. Additionally, patients who have undergone bariatric surgery are at a significantly increased risk for urolithiasis due to increased oxalate absorption in the intestine [17].

Based on data regarding the relationship between obesity, stone recurrence, and spontaneous stone passage, this relationship may also be applied to patients' lipid status. This is supported by several published studies. For example, Wang et al. [18] showed that an increase in the atherogenic index is associated with an increased likelihood of both the onset and recurrence of urolithiasis. Hong et al. [19] found that the ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol is associated with stone recurrence. Thus, a one-unit increase in this ratio leads to a 9% increase in the risk of urolithiasis recurrence [19]. Kang et al. [20] demonstrated that hypertriglyceridemia increases the risk of urolithiasis recurrence by 1.86-fold. However, the study found no difference in lipid status depending on the recurrent course of urolithiasis. In patients with recurrent or primary urolithiasis, cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, and very low-density lipoprotein levels were comparable. This may be due to the similar frequency of statin use in the study groups (13.2% vs 12.2%, respectively; $p = 0.744$).

Additionally, this study revealed that recurrent urolithiasis was characterized by a greater number of stones in each kidney and in both kidneys cumulatively.

Accordingly, the total volume of stones in patients with recurrent urolithiasis was greater than in those with primary urolithiasis (855.0 vs 433 mm^3 respectively; $p < 0.001$). Our findings are indirectly supported by a retrospective study by Kang et al. [21], which included nearly 1000 patients. The Cox regression analysis revealed that multiple stones in primary urolithiasis was associated with an almost 2.5-fold increase in recurrence risk at a median follow-up period of 35 months (OR = 2.343; 95% CI: 1.302–4.220; $p = 0.005$) [21]. Similar results were obtained by Xia et al. [5]. As part of the study to develop a nomogram for predicting stone recurrence, the authors identified multiple stones and bilateral kidney involvement as risk factors, increasing the likelihood of recurrence by 1.83- and 1.78-fold, respectively [5]. In our study, bilateral stones were more prevalent among patients with recurrent urolithiasis than among those with primary manifestations of the disease (43.6% vs 35.0%, respectively). However, despite this clear trend, the differences were not statistically significant ($p = 0.059$).

Additionally, the present study found that patients with recurrent urolithiasis and those who had undergone prior surgeries for the condition were more likely to have hypertension. It was present in 53.2% of patients with recurrent urolithiasis, compared with 38.8% of patients with primary manifestations ($p = 0.002$). In patients with previous surgical interventions for urolithiasis, hypertension was observed in 62.1% of cases, whereas in patients with spontaneous stone passage, this figure was 41.0% ($p < 0.001$). Our data are confirmed by several other studies. For example, Alshehri et al. [22] demonstrated that hypertension increases the risk of urolithiasis recurrence by 2.34-fold, irrespective of sex, water intake, dietary habits, or hyperparathyroidism. Similar findings were reported in a meta-analysis by Wang et al. [4], which identified hypertension as a risk factor for recurrent urolithiasis. A study published in May 2024 used Mendelian randomization to show that urolithiasis may be a risk factor for hypertension. No such association was found for diabetes mellitus or obesity [23]. The results of this study suggest a potential vicious cycle involving hypertension and urolithiasis. Urolithiasis increases the likelihood of hypertension, which, in turn, increases the probability of urolithiasis recurrence. Consequently, hypertension treatment may prevent stone formation. Similarly, the prophylaxis of stone formation may also prevent hypertension [23].

Another risk factor that is actively discussed for urolithiasis recurrence is urinary tract infections. Several urease-producing microorganisms have been proven to be associated with the development of struvite, an infectious stone. However, the vast majority of calculi are non-infectious. However, it is suggested that microorganisms may be associated with the development of urolithiasis, even in cases of non-infectious stones. Urine contains a diverse microbial community, or microbiome, whose members may alter the chemical composition of urine and influence stone formation [24]. Additionally, the urinary microbiome can interact with the immune system, triggering an inflammatory response in the urinary tract. Chronic, sluggish inflammation may be associated with the onset and recurrence of urolithiasis [25]. However, a study by Liu et al. [26] that included over 350 patients found that the presence of microorganisms in culture tests was not associated with recurrent urolithiasis. The only independent predictor of recurrence was the presence of multiple stones. Similar results were obtained in the present study. We demonstrated that the prevalence of bacteriuria in patients with primary and recurrent urolithiasis was comparable. However, there was a clear tendency for more frequent bacteria detectability in the urine of patients with recurrent urolithiasis, reaching borderline statistical significance (28.6% in recurrent urolithiasis vs 20.7% in primary manifestations; $p = 0.083$).

CONCLUSION

Our study found that patients with recurrent urolithiasis were more likely to be overweight or obese, have hypertension, and have a greater number of stones in each kidney and in both kidneys cumulatively. However, the average density of these stones was lower on CT scans. Spontaneous stone passage was more likely in patients with recurrent urolithiasis who were not obese, had a lower BMI, and did not have hypertension. In the presence of these factors, patients were more likely to undergo surgical treatment. However, no statistically significant differences were found in the results of the blood chemistry tests, including those related to lipid metabolism, between the study groups. This may be because the frequency of statin use was similar in each group. Based on our data, the optimal strategy for preventing kidney stone recurrence and increasing the likelihood of spontaneous stone passage is reducing fat mass and achieving a healthy weight.

ADDITIONAL INFO

Author contributions: A.A. Kamalov: conceptualization, methodology, supervision, writing—review & editing; O.Yu. Nesterova: conceptualization, methodology, data curation, formal analysis, writing—original draft; I.D. Burlakov: data curation, formal analysis, writing—original draft; N.I. Sorokin: data curation, writing—original draft; D.M. Kamalov, A.A. Strigunov: data curation, writing—original draft; D.O. Stepanchenko, D.S. Derevnina: data curation. The authors have approved the version for publication and have also agreed to be responsible for all aspects of the work, ensuring that issues relating to the accuracy and integrity of any part of it are properly considered and addressed.

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Вклад авторов. А.А. Камалов — концепция и дизайн исследования, научное руководство, критический обзор; О.Ю. Нестерова — концепция и дизайн исследования, сбор и обработка материалов, написание текста, анализ полученных данных; И.Д. Бурлаков — сбор и обработка материалов, написание текста, анализ полученных данных; Н.И. Сорокин — сбор и обработка материалов, написание текста; Д.М. Камалов, А.А. Стригунов — сбор и обработка материалов, написание текста; Д.О. Степанченко, Д.С. Деревнина — сбор и обработка материалов. Авторы одобрили версию для публикации, а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой ее части.

Этическая экспертиза. Проведение исследования одобрено локальным этическим комитетом Медицинского научно-образовательного института ФГБОУ ВО «Московский государственный университет им. М.В. Ломоносова» (протокол № 03 от 02.06.2025). Все участники исследования добровольно подписали форму информированного согласия на участие в исследовании / использование результатов обследования и лечения с научной целью. Исследование и его протокол не регистрировали.

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Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, данные).

Доступ к данным. Все данные, полученные в настоящем исследовании, доступны в статье.

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Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали один рецензент (член редакционной коллегии, член редакционного совета или внешний рецензент), рецензирование двойное слепое.

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