



Inconsistency in stone composition among bilateral urolithiasis patients: a multicenter retrospective study

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Abstract

The treatment or prevention strategies vary for different stone compositions. The current guidelines lack specific recommendations for composition analysis in bilateral urolithiasis due to limited data on the analysis of bilateral urinary stone composition. We aimed to calculate the prevalence of discordant stone compositions among bilateral urolithiasis patients, and identify factors associated with the discordance. We retrospectively enrolled 845 bilateral urolithiasis patients across seven centers in China, whose stones on both sides were analyzed separately for stone composition. We calculated the percent prevalence of discordant stone compositions among bilateral urolithiasis patients. Univariate analyses and multivariate logistic regression analyses were used to identify factors associated with this discordance. A total of 24.9% of enrolled patients had discordant stone compositions of bilateral uroliths, which ranged from 17.5 to 32.4% in the seven institutions. Among the 210 patients with discordant stone compositions, the two most common composition combinations were calcium oxalate/carbapatite (51.0%) and calcium oxalate/uric acid (35.7%). Four clinical variables, including sex, age, predominant component of calcium oxalate on one side, and predominant component of uric acid on one side, were associated with a stone composition inconsistency among bilateral urolithiasis in the multivariate logistic analyses. Notably, the pretreatment urinalysis results and preoperative serum biochemical parameters were not related to the stone composition inconsistency. Approximately one-quarter of the patients were identified as discordant stone formers among the bilateral urolithiasis patients in our study, highlighting the importance of separately analyzing the stone composition on both sides in patients with bilateral urolithiasis.

Keywords Urolithiasis · Bilateral upper urinary tract stones · Stone composition · Discordance · Prevalence analysis

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Introduction

Urolithiasis is a common disease of the urinary system and is a global health problem and has caused a tremendous burden on healthcare systems [1]. Over the past few decades, urolithiasis has been reported to be increasing in prevalence and incidence. The lifetime risk of urinary stone formation is estimated at 5–10% [2], and the relapse rate after the formation of an initial stone has been reported to be as high as 50% within 5–10 years and 75% within 20 years [3]. Upper urinary tract stones account for more than 90% of all urinary calculi [4, 5] with 10%–19% of patients suffering bilateral stones [6–8]. Patients with bilateral urolithiasis are at a high risk of recurrence [9].

Knowledge of stone composition is important for determining a treatment strategy, understanding the etiology, and preventing recurrence. The treatment or prevention strategies vary for patients with different types of stone composition. Therefore, the current guidelines recommend that all first-time formers should undergo stone composition analysis [10, 11]. However, they did not specify whether those patients with bilateral urolithiasis need to have the stones on both sides analyzed separately for stone composition. As a result, surgeons have different practices when sending urinary stone for stone composition examination in bilateral urolithiasis patients. Some of them mixed the sample for examination, and some of them only test the stone from one side instead of both sides. To date, limited data have been reported on the analysis of the composition of bilateral upper urinary tract stones [12, 13]. They revealed that discordant stone composition analyses are common in patients with bilateral stone disease. This phenomenon suggested that we should not indiscriminately regard the stone composition result from one side as the composition of the other side. Otherwise, it may lead to deficiencies in disease treatment and prevention. However, these studies are single-center studies and have a small sample size ($n=79$ or 59). The prevalence of discordant stone compositions among bilateral urolithiasis patients should be further evaluated in a larger cohort, providing a basis for the development of stone composition analysis strategies in patients with bilateral urolithiasis.

Thus, the aim of our study was to describe the clinical characteristics of bilateral urolithiasis patients and calculate the prevalence of discordant stone compositions among bilateral urolithiasis based on patients from seven Chinese institutions. We also determined the effects of the clinical factors on the discordance of stone compositions among bilateral urolithiasis patients.

Patients and methods

Study population

This was a multicenter retrospective study, which was approved by the ethics review board of each participating institution. The need for informed consent was waived due to the retrospective nature of our study. In total, 845 eligible patients were enrolled from seven Chinese institutions, including the Sun Yat-Sen Memorial Hospital (SYSMH, $n=216$), the Fifth Affiliated Hospital of Guangzhou Medical University (GMUFH, $n=216$), the Eighth Affiliated Hospital, Sun Yat-sen University (SYSEH, $n=137$), the Fifth Affiliated Hospital, Sun Yat-sen University (SYSFH, $n=110$), the Affiliated Hospital of Guangdong Medical University (AHGMU, $n=110$), the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (WHUH, $n=37$), and the Second Affiliated Hospital of The Chinese University of Hong Kong (CUHKSH, $n=19$). These patients fulfilled the following inclusion criteria: (a) diagnosed with bilateral upper tract urolithiasis; (b) stones on both sides were removed by surgery; and (c) stones on both sides were analyzed separately for stone composition. Patients with incomplete clinical data were excluded from the study.

Stone analysis

All stone composition analyses were performed by Fourier transform infrared spectroscopy, and the results were recorded. Information about the detection instruments is listed in Supplementary Table S1. The component exceeding 50% of the total composition of the stones was considered the predominant component, but stones containing any struvite, cystine, uric acid, brushite, or xanthine were classified as the corresponding named groups [14]. Stones that contain struvite, carbapatite and/or ammonium acid urate were categorized as infection stones, and stones containing more than one component were considered mixed stones.

Outcomes

The primary outcome of our study was the consistency of bilateral stone compositions. The bilateral urolithiasis patients with differences in predominant stone composition between the two sides are termed discordant stone formers. We focused on the prevalence of discordant stone compositions among bilateral urolithiasis patients, as well as the effects of the clinical factors on the discordance of stone compositions among bilateral urolithiasis patients.

Covariates

Baseline clinical data, including age, sex, and surgery date of the bilateral stones, were obtained from the medical records. Body mass index (BMI) was defined as the subject's weight in kilograms divided by the square of height in meters. A personal history of hypertension or diabetes and previous urological surgery history were identified from the medical records or medical examination component. The stone anatomical location was determined by pretreatment computed tomography (CT) or B-mode ultrasound images. Each side of the urinary stone could be located in the kidney and/or ureter. Thus, there were six combinations with regard to the location of bilateral stones, i.e., kidney/kidney, kidney/ureter, ureter/ureter, kidney/kidney & ureter, ureter/kidney & ureter, and kidney & ureter/kidney & ureter (the location of bilateral stones is indicated at the front and back of the slash). Whether the stone disease was recurrent urolithiasis was also obtained from the medical records. A urinalysis was performed before surgery, and the urinalysis results, including urine pH, urine white blood cell count, urine nitrite, and urine culture results, were recorded.

Statistical analysis

Continuous variables are summarized as the median (interquartile range [IQR]) for those without a normal distribution. Categorical variables were reported using numbers and percentages. Mann–Whitney *U* tests or chi-squared tests were used to test associations. The prevalence of discordant stone compositions among patients with bilateral urolithiasis was calculated. The effects of the clinical factors on the discordance of stone compositions among bilateral urolithiasis patients were assessed by logistic regression analyses.

Statistical analyses were performed using R software (R Statistical Computing Base, version 4.2.2, <https://www.r-project.org/>). The Sankey diagram was plotted using the “ggplot2” package. All statistical tests were two-tailed, and a *P* value of <0.05 was considered statistically significant.

Results

The graphical abstract of the results in our study is shown in Fig. S1. The patient recruitment pathway is presented in Fig. 1. As shown in Fig. 1, among the bilateral urolithiasis patients treated in the involved seven institutions, only 42.5% patients' bilateral urinary tract stones were submitted separately for composition analysis. In total, 845 bilateral urolithiasis patients (551 males and 294 females) from seven institutions with a median (interquartile range) age of 54.0 years (46.0, 61.0) were analyzed in our study. Their

median (interquartile range) BMI was 23.6 kg/m² (21.4, 26.0). Table 1 lists the clinical baseline characteristics of the enrolled patients. There were 238 (28.2%) and 113 (13.4%) bilateral urolithiasis patients had hypertension and diabetes, respectively. 56.6% (478/845) of the enrolled patients were suffered from recurrent urolithiasis.

The characteristics of the urinary stones according to the laterality of the stones are presented in Table 2. For stone location, kidney stones are the most common on both the left and right sides, accounting for more than 60%, followed by ureteral stones. A total of 12.0% and 10.8% of patients suffered renal ureteral calculi on the left and right sides, respectively. In terms of the stone composition distribution, the top 3 common components were calcium oxalate, uric acid and carbapatite, accounting for more than 95% of the total. There were no significant differences in the stone location, the distribution of stone composition, or whether the stones were mixed between the left and right sides.

A total of 24.9% of enrolled patients had discordant stone compositions of bilateral uroliths, which ranged from 17.5 to 32.4% in the seven institutions (Table 1), indicating that discordant stone formers are common. A Sankey diagram visually illustrated the composition and consistency of the bilateral urinary tract stones in all enrolled patients (Fig. 2A), and Supplementary Table S2 depicts the urinary stone composition distribution according to laterality. Among the 210 patients with discordant stone compositions, there were a total of 13 composition combinations, and the two most common composition combinations were calcium oxalate/carbapatite (51.0%) and calcium oxalate/uric acid (35.7%). Figure 2B–C depicts the stone composition combination distribution of patients in the discordant group and with a predominant component of calcium oxalate or uric acid on one side. In those discordant stone formers with predominant component of calcium oxalate on one side, the two most common stone composition on the contralateral side were carbapatite (56.0%) and uric acid (39.3%). In those discordant stone formers with predominant component of uric acid on one side, there were three types of composition on the contralateral side, with the vast majority being calcium oxalate (90.4%). The distribution of stone compositions in patients with concordant compositions of bilateral uroliths is presented in Supplementary Table S3. Calcium oxalate/calcium oxalate (82.4%) and uric acid/uric acid (10.4%) were the two most common composition combinations among patients with concordant stone compositions.

As shown in Table 3, four clinical variables, including sex, age, predominant component of calcium oxalate on one side, and predominant component of uric acid on one side, were associated with a stone composition inconsistency among patients with bilateral urolithiasis in the multivariate logistic analyses. Elder bilateral urolithiasis patients were

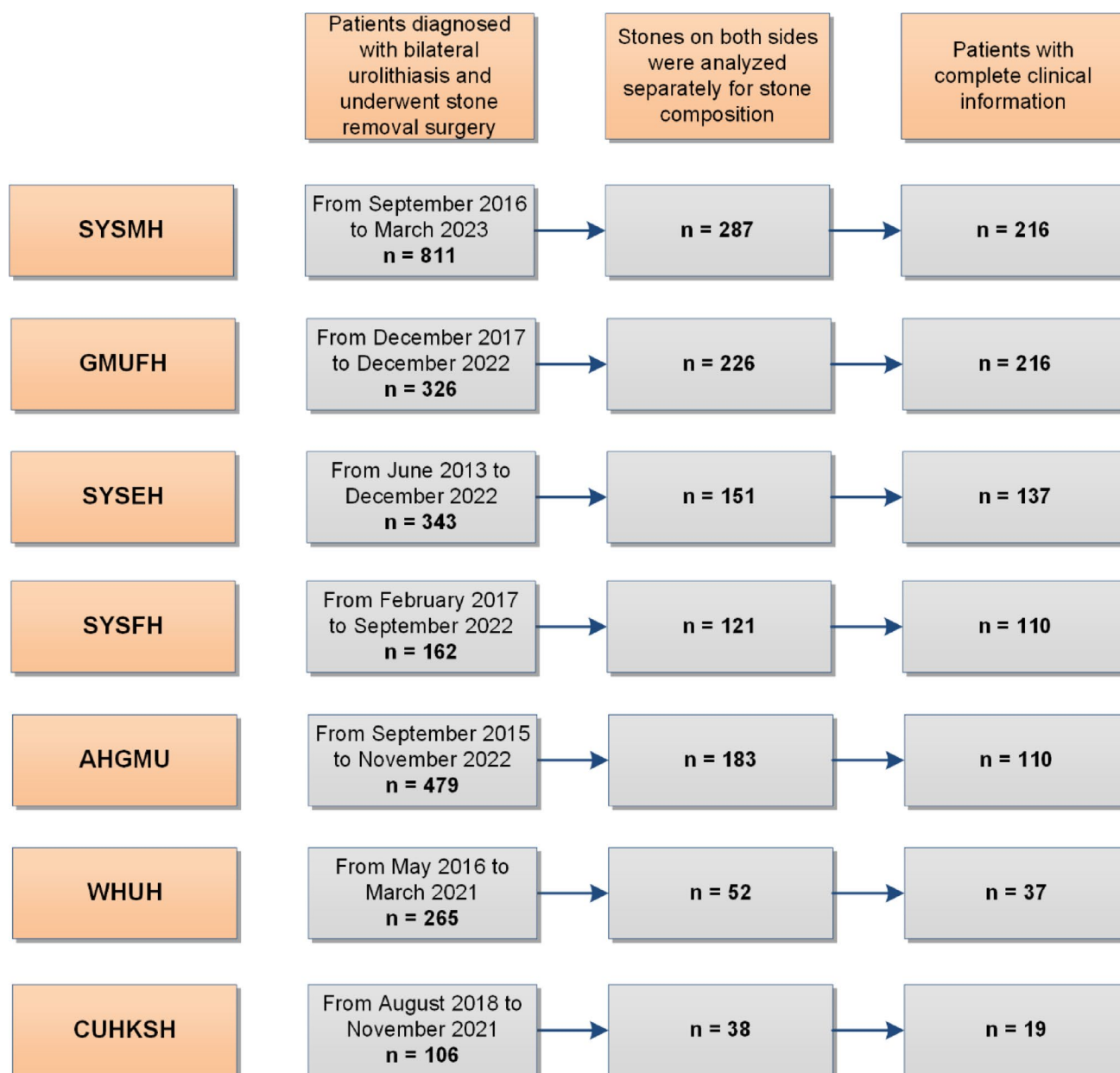


Fig. 1 Recruitment pathways for patients in this study. *SYSMH*=Sun Yat-sen Memorial Hospital, Sun Yat-sen University; *GMUFH*=The Fifth Affiliated Hospital of Guangzhou Medical University; *SYSEH*=The Eighth Affiliated Hospital, Sun Yat-sen University; *SYSFH*=The Fifth Affiliated Hospital, Sun Yat-sen University;

AHGMU=The Affiliated Hospital of Guangdong Medical University; *WHUH*=Union Hospital, Tongji Medical College, Huazhong University of Science and Technology; *CUHKSH*=The Second Affiliated Hospital of The Chinese University of Hong Kong

less likely to have a stone composition inconsistency than younger patients (odds ratio [OR]: 0.976 [95% CI, 0.959–0.993]; $P=0.005$). Female patients had an approximately 2.7 times higher risk of discordant stone composition than male patients. Patients with a predominant component of calcium oxalate or uric acid on one side were more likely to report a composition discordance of bilateral uroliths. Notably, the pretreatment urinalysis results (including urine pH, urine white blood cell count, urine nitrite) and urine culture

results were not related to the stone composition inconsistency. Moreover, the relationships between preoperative serum biochemical parameters (including serum creatinine, uric acid, calcium, and phosphorus) and stone composition inconsistency were also probed in our study. As a result, these parameters were not associated with stone composition inconsistency among patients with bilateral urolithiasis (Supplementary Table S4). The clinical characteristics of the patients with bilateral urolithiasis according to the

Table 1 Baseline characteristics of the enrolled bilateral urolithiasis patients

Characteristic	Overall (N=845)	SYSMH cohort (n=216)	GMUFH cohort (n=216)	SYSEH cohort (n=137)	SYSFH cohort (n=110)	AHGMU cohort (n=110)	WHUH cohort (n=37)	CUHKSH cohort (n=19)
<i>Sex</i>								
Male	551 (65.2)	125 (57.9)	137 (63.4)	100 (73.0)	74 (67.3)	76 (69.1)	25 (67.6)	14 (73.7)
Female	294 (34.8)	91 (42.1)	79 (36.6)	37 (27.0)	36 (32.7)	34 (30.9)	12 (32.4)	5 (26.3)
<i>Age, years</i>								
Median (IQR)	54.0 (46.0, 61.0)	55.0 (48.0, 62.0)	53.0 (45.0, 59.0)	51.0 (43.0, 61.0)	53.5 (45.0, 61.0)	57.0 (50.0, 63.0)	49.0 (44.0, 55.0)	55.0 (47.0, 63.0)
<i>BMI, kg/m²</i>								
Median (IQR)	23.6 (21.4, 26.0)	23.1 (20.3, 25.7)	24.4 (22.3, 26.8)	24.5 (22.4, 26.1)	23.6 (21.5, 25.8)	22.3 (20.8, 25.2)	22.9 (20.2, 25.9)	23.6 (22.9, 24.0)
<i>Hypertension</i>								
Without	607 (71.8)	146 (67.6)	162 (75.0)	93 (67.9)	73 (66.4)	85 (77.3)	32 (86.5)	16 (84.2)
With	238 (28.2)	70 (32.4)	54 (25.0)	44 (32.1)	37 (33.6)	25 (22.7)	5 (13.5)	3 (15.8)
<i>Diabetes</i>								
Without	732 (86.6)	186 (86.1)	191 (88.4)	108 (78.8)	94 (85.5)	100 (90.9)	36 (97.3)	17 (89.5)
With	113 (13.4)	30 (13.9)	25 (11.6)	29 (21.2)	16 (14.5)	10 (9.1)	1 (2.7)	2 (10.5)
<i>Recurrent urolithiasis</i>								
No	367 (43.4)	55 (25.5)	84 (38.9)	72 (52.6)	57 (51.8)	62 (56.4)	26 (70.3)	11 (57.9)
Yes	478 (56.6)	161 (74.5)	132 (61.1)	65 (47.4)	53 (48.2)	48 (43.6)	11 (29.7)	8 (42.1)
<i>History of urological surgery</i>								
No	417 (49.3)	102 (47.2)	90 (41.7)	72 (52.6)	57 (51.8)	66 (60.0)	19 (51.4)	11 (57.9)
Yes	428 (50.7)	114 (52.8)	126 (58.3)	65 (47.4)	53 (48.2)	44 (40.0)	18 (48.6)	8 (42.1)
<i>Bilateral stone component consistency</i>								
Discordant	210 (24.9)	49 (22.7)	60 (27.8)	24 (17.5)	34 (30.9)	27 (24.5)	12 (32.4)	4 (21.1)
Concordant	635 (75.1)	167 (77.3)	156 (72.2)	113 (82.5)	76 (69.1)	83 (75.5)	25 (67.6)	15 (78.9)

Data are presented as No. (%) unless indicated otherwise

SYSMH=Sun Yat-sen Memorial Hospital, Sun Yat-sen University; *GMUFH*=The Fifth Affiliated Hospital of Guangzhou Medical University; *SYSEH*=The Eighth Affiliated Hospital, Sun Yat-sen University; *SYSFH*=The Fifth Affiliated Hospital, Sun Yat-sen University; *AHGMU*=The Affiliated Hospital of Guangdong Medical University; *WHUH*=Union Hospital, Tongji Medical College, Huazhong University of Science and Technology; *CUHKSH*=The Second Affiliated Hospital of The Chinese University of Hong Kong; *IQR*=interquartile range; *BMI*=body mass index

consistency of the stone composition are shown in Supplementary Table S5. In those patients with predominant component of calcium oxalate on one side, 26.8% had discordant stone compositions of bilateral uroliths. And among those patients with predominant component of uric acid on one side, up to 55.7% were discordant stone formers.

Discussion

Among bilateral urolithiasis patients, the most common stone anatomical location is the kidney regardless of whether it is the left or right side, and the distribution of stone components is similar to previous stone composition statistics reports [5, 15]. Therefore, the presence of stones on both sides of the urinary system does not affect the essential characteristics of urinary stone disease.

There is widespread recognition of the importance of stone composition information. The current guidelines

recommend that all first-time formers should undergo stone composition analysis [10, 11]. Patients with bilateral urolithiasis are not uncommon [6–8]. The etiology of stone formation is complex and may represent a combination of multiple factors, including genetics, metabolic derangements, and environmental influences [16]. Therefore, it is reasonable to speculate that the composition of bilateral stones may not necessarily be the same within the same patient. However, the current guidelines do not provide specific recommendations for the composition analysis process in patients with bilateral urolithiasis, since there are limited data reported on the analysis of the composition of bilateral urinary stones [12, 13].

In our multicenter retrospective study, approximately one-quarter of the patients were identified as discordant stone formers among bilateral urolithiasis patients, suggesting that discordant stone formers are common. These results highlight the importance of separately analyzing the stone composition on both sides in patients with bilateral

Table 2 Characteristics of the urinary stones according to their laterality

Characteristic	Left side (n=845)	Right side (n=845)	P
<i>Stone location</i>			0.739
Kidney	541 (64.0)	546 (64.6)	
Ureter	203 (24.0)	208 (24.6)	
Kidney & Ureter	101 (12.0)	91 (10.8)	
<i>Predominant stone component</i>			0.738
Calcium oxalate	615 (72.8)	622 (73.6)	
Uric acid	117 (13.9)	98 (11.6)	
Carbapatite	91 (10.8)	96 (11.4)	
Struvite	13 (1.5)	19 (2.3)	
Ammonium acid urate	2 (0.2)	3 (0.4)	
Cystine	4 (0.5)	2 (0.2)	
Xanthine	0 (0.0)	1 (0.1)	
Hydroxyapatite	1 (0.1)	2 (0.2)	
Brushite	2 (0.2)	2 (0.2)	
<i>Mixed stones</i>			0.660
No	464 (54.9)	474 (56.1)	
Yes	381 (45.1)	371 (43.9)	

Data are presented as No. (%). *P* values were derived from the univariate analyses between each characteristic and the laterality of the stones

urolithiasis. If one side's stone composition result is blindly applied to the contralateral side, it may lead to deficiencies in disease treatment and prevention since the treatment or prevention strategies vary for patients with different types of stone composition. For example, for patients with calcium oxalate stones, it is imperative to adhere to a normal calcium, low protein, low oxalate, and low sodium diet. Medication treatment involves the use of potassium citrate to alkalinize the urine and hydrochlorothiazide to reduce urine calcium excretion [17]. Regarding patients with uric acid stones, allopurinol or febuxostat is utilized to inhibit uric acid formation, and a diet low in animal protein is needed [18]. Stone dissolution can be achieved through medication and prevention. Potassium citrate is employed to regulate urine pH at a level between 6.5 and 6.8, facilitating the dissolution of uric acid crystals in the urine [19]. The management of infection stones, such as carbapatite, struvite, and ammonium acid urate, is particularly challenging. Using antibiotics is essential for infection control during the perioperative period. Complete removal of stones without residual disease is critical to preventing recurrences [20]. Moreover, urinary acidification using methionine or

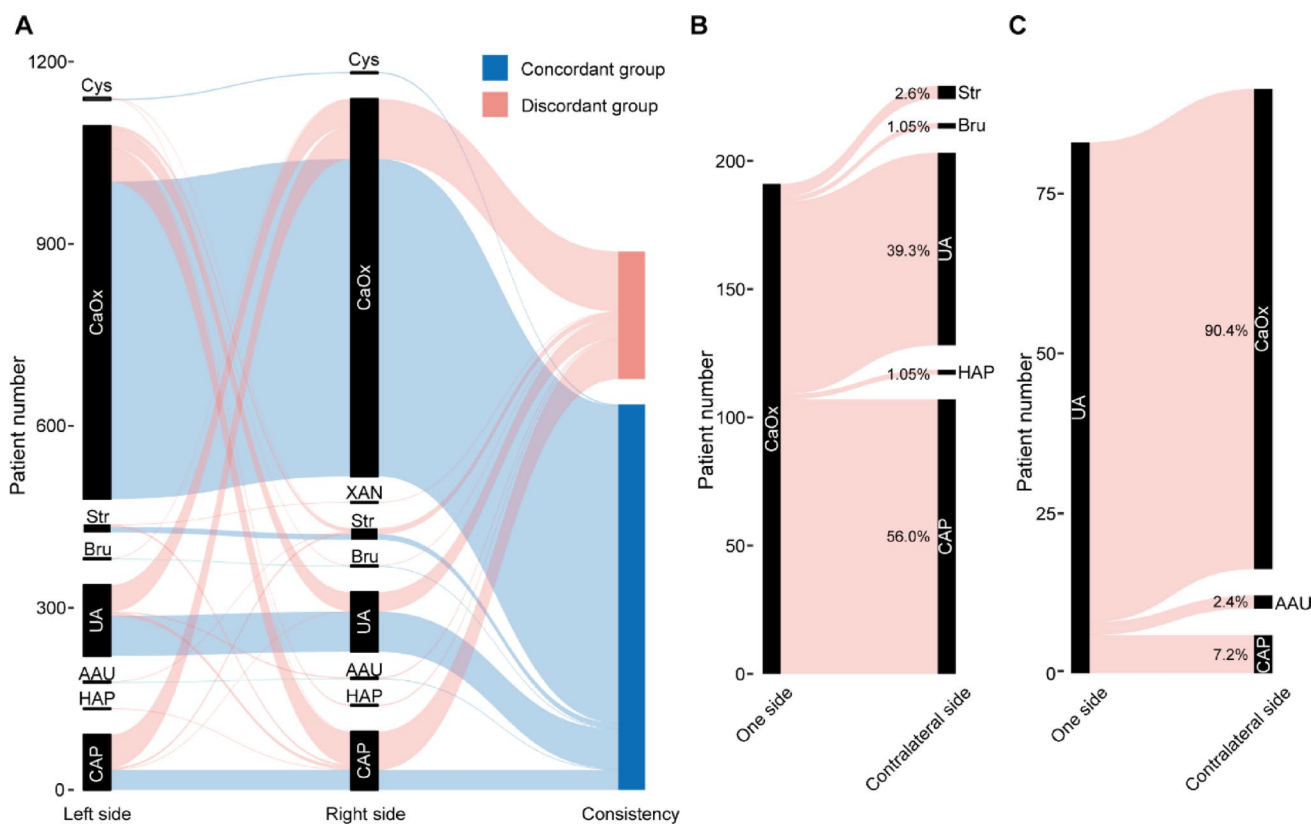


Fig. 2 Sankey diagram of urinary stone composition distribution and the consistency of bilateral stone compositions. **(A)** The Sankey diagram visually illustrates the composition and consistency of bilateral urinary tract stones in patients. Patients in the concordant group are marked in blue, while those in the discordant group are marked in red. **(B)** The stone composition combination distribution of patients in the

discordant group and with a predominant component of calcium oxalate on one side. **(C)** The stone composition combination distribution of patients in the discordant group and with a predominant component of uric acid on one side. *CaOx* = Calcium oxalate; *CAP* = Carbapatite; *Str* = Struvite; *AAU* = Ammonium acid urate; *UA* = Uric acid; *Cys* = Cystine; *XAN* = Xanthine; *HAP* = hydroxyapatite; *Bru* = Brushite

Table 3 Multivariate logistic analysis of the association between the clinical features and the stones

Characteristic	OR (95% CI)	P
Sex (male vs. female)	2.714 (1.864, 3.970)	<0.001*
Age, years (continuous)	0.976 (0.959, 0.993)	0.005*
BMI, kg/m ² (continuous)	0.995 (0.946, 1.045)	0.857
Hypertension (without vs. with)	0.960 (0.613, 1.486)	0.857
Diabetes (without vs. with)	0.762 (0.418, 1.341)	0.358
Recurrent urolithiasis (No vs. Yes)	0.995 (0.568, 1.735)	0.986
History of urological surgery (No vs. Yes)	1.426 (0.826, 2.488)	0.207
<i>Location of bilateral stones</i>		
Kidney & Ureter/Kidney & Ureter	Reference	
Kidney/Kidney & Ureter	1.153 (0.441, 3.197)	0.776
Kidney/Kidney	1.090 (0.479, 2.724)	0.844
Kidney/Ureter	0.964 (0.408, 0.481)	0.937
Ureter/Kidney & Ureter	0.947 (0.213, 3.795)	0.940
Ureter/Ureter	0.590 (0.216, 1.684)	0.311
Predominant component of calcium oxalate on one side (no vs. yes)	25.498 (11.555, 61.514)	<0.001*
Predominant component of uric acid on one side (no vs. yes)	36.972 (19.045, 78.594)	<0.001*
Urine pH (continuous)	1.019 (0.770, 1.343)	0.894
Urine white blood cell count (<100/μl vs. ≥100/μl)	0.818 (0.552, 1.205)	0.312
Urine nitrite (negative vs. positive)	1.324 (0.686, 2.495)	0.392
Urine culture (negative vs. positive)	1.301 (0.784, 2.125)	0.299

*P<0.05

OR=odds ratio; CI=confidence interval; BMI=body mass index

ammonium chloride is also a part of the treatment since the infection stones are stable in an alkaline environment [21]. Our study indicated that the two most common composition combinations were calcium oxalate/carbapatite (51.0%) and calcium oxalate/uric acid (35.7%) among 210 patients with discordant stone compositions. As mentioned above, there are conflicting medical management or prevention strategies for these two composition combinations. Notably, in the composition combination of calcium oxalate/carbapatite, carbapatite belongs to infection stone. If infection stones are misdiagnosed, the risk of postoperative infectious complications will significantly increase, and life-threatening conditions, such as severe sepsis and septic shock may even occur. Therefore, it is highly necessary to submit bilateral urinary tract stones separately for composition analysis to avoid providing patients with inappropriate treatment or prevention strategies.

The mechanism of discordant stone compositions of bilateral uroliths remains to be clarified. Urinary stone formation is a complex and multistep process that includes urinary supersaturation, crystal nucleation, growth and

agglomeration. Several possible modes of stone formation have been proposed [16]. Previous studies have identified many risk factors for stone formation, including systemic and local factors. Conditions such as hypertension, type 2 diabetes mellitus, obesity and metabolic syndrome are systemic risk factors that have effects on bilateral kidneys [22]. Local factors include urinary tract anatomical and functional abnormalities, urothelial cell injury, urinary infection, and urological surgery [23, 24]. Based on this, it could be hypothesized that when bilateral urolithiasis patients have only systemic risk factors, the stone compositions should be consistent between the bilateral stones. However, not all the uroliths in bilateral urolithiasis patients are caused by a single factor or only systemic factors since stone formation is a complex process. In addition, previous studies have shown that vesical and renal pelvic urine from the same person can have different pH and electrolyte levels, indicating that the bilateral kidneys can have different microenvironments [25, 26]. Therefore, the differences in stone composition among patients with bilateral urolithiasis could be explained by the complexity of the stone formation mechanisms and the inconsistent effect on the bilateral kidneys.

Notably, stone composition analysis can only be performed in vitro after obtaining the stone specimen. For patients with bilateral urolithiasis, if one side undergoes stone removal surgery while the other side can be managed conservatively, it may not be possible to confirm the consistency of stone composition of both sides. A misjudgment may result in inappropriate management of urolithiasis. Thus, it is of great clinical significance to seek new methods to achieve in vivo detection of stone composition. Emerging technology, such as dual-energy CT, radiomics and artificial intelligence, has been reported to be useful in predicting stone composition [27–30]. In the future, these methods may further assist clinicians in developing treatment and prevention strategies for patients with bilateral urolithiasis.

This is the first multicenter study to investigate the prevalence of discordant stone compositions among bilateral urolithiasis patients. Our study corroborated the phenomenon of discordant stone compositions of bilateral stones in a significant proportion of patients with bilateral urolithiasis. These findings are of clinical significance and provide valuable insights for the bilateral stone composition analysis strategy in patients with bilateral urolithiasis. Furthermore, the study identified several factors associated with this phenomenon, which provides useful information for the prediction of stone composition in the next step of the research.

Despite these advantages, there are several limitations to our study. First, due to the retrospective nature of this study, we failed to collect complete information about the preoperative 24-hour urine analysis results. Therefore, we were unable to explore the relationship between this metabolic

evaluation and the discordance of stone compositions among bilateral urolithiasis patients. Second, selection bias may exist because of the retrospective study design of our study. Third, all the subjects enrolled in our study were from the Chinese population, and further validation is warranted in other populations. Perhaps the prevalence of discordant stone compositions in patients with bilateral urolithiasis varies among patients from different ethnicities and geographical backgrounds.

In conclusions, patients with discordant stone compositions of bilateral uroliths are common. This phenomenon should be of concern to clinicians and clinical guideline developers. It is important to submit bilateral urinary tract stones separately for composition analysis to avoid providing patients with inappropriate treatment or prevention strategies. These findings have important implications for patients with bilateral urolithiasis.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00240-025-01829-7>.

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Author contributions Junjiong Zheng, Yuhui Yao and Minbo Yan contributed equally to this work. Study concept and design: J Zheng, Z He, G Xu, T Lin. Acquisition of data: Y Yao, H Liu, Y Xu, W Wu, J Qiu, W Dong, Z Zhou, R Zhu, J Pan, R Zhu. Analysis and interpretation of data: J Zheng, Y Yao, M Yan, H Liu, Y Xu. Drafting of the manuscript: J Zheng, Y Yao, M Yan, H Liu. Critical revision of the manuscript for important intellectual content: J Zheng, Z He, G Xu, T Lin. Statistical analysis: J Zheng, Y Yao, M Yan, H Liu. Obtaining funding: J Zheng, T Lin. Administrative, technical, or material support: J Zheng, M Yan, H Liu, Y Dai, X Zhang, X Li, X Chen, Z He, G Xu. Supervision: Z He, G Xu, T Lin.

Data availability Data availability will be through contacting the corresponding author Tianxin Lin.

Declarations

Competing interests The authors declare no competing interests.

Ethical approval This was a multicenter retrospective study, which was approved by the ethics review board of each participating institution.

Informed consent Patient consent was waived due to the retrospective nature of the study. Patient consent was waived due to the retrospective nature of the study.

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References

1. Thongprayoon C, Krambeck AE, Rule AD (2020) Determining the true burden of kidney stone disease. *Nat Rev Nephrol* 16(12):736–746. <https://doi.org/10.1038/s41581-020-0320-7>
2. Spornat D, Kourambas J (2011) Urolithiasis—medical therapies. *BJU Int* 108(Suppl 2):9–13. <https://doi.org/10.1111/j.1464-410X.2011.10688.x>
3. Eisner BH, Goldfarb DS (2014) A nomogram for the prediction of kidney stone recurrence. *J Am Soc Nephrol* 25(12):2685–2687. <https://doi.org/10.1681/asn.2014060631>
4. Moe OW (2006) Kidney stones: pathophysiology and medical management. *Lancet* 367(9507):333–344. [https://doi.org/10.1016/S0140-6736\(06\)68071-9](https://doi.org/10.1016/S0140-6736(06)68071-9)
5. Zhang D, Li S, Zhang Z, Li N, Yuan X, Jia Z et al (2021) Urinary stone composition analysis and clinical characterization of 1520 patients in central China. *Sci Rep* 11(1):6467. <https://doi.org/10.1038/s41598-021-85723-3>
6. Giusti G, Proietti S, Rodriguez-Socarras ME, Eisner BH, Saitta G, Mantica G et al (2018) Simultaneous bilateral endoscopic surgery (SBES) for patients with bilateral upper tract urolithiasis: technique and outcomes. *Eur Urol* 74(6):810–815. <https://doi.org/10.1016/j.eururo.2018.06.034>
7. Boyce CJ, Pickhardt PJ, Lawrence EM, Kim DH, Bruce RJ (2010) Prevalence of urolithiasis in asymptomatic adults: objective determination using low dose noncontrast computerized tomography. *J Urol* 183(3):1017–1021. <https://doi.org/10.1016/j.juro.2009.11.047>
8. Issler N, Dufek S, Kleit R, Bockenhauer D, Smeulders N, Van't Hoff W (2017) Epidemiology of paediatric renal stone disease: a 22-year single centre experience in the UK. *BMC Nephrol* 18(1):136. <https://doi.org/10.1186/s12882-017-0505-x>
9. Iremashvili V, Li S, Best SL, Hedican SP, Nakada SY (2019) Clinical and demographic predictors of repeat stone surgery. *BJU Int* 124(5):836–841. <https://doi.org/10.1111/bju.14844>
10. Turk C, Petrik A, Sarica K, Seitz C, Skolarikos A, Straub M et al (2016) EAU guidelines on diagnosis and Conservative management of urolithiasis. *Eur Urol* 69(3):468–474. <https://doi.org/10.1016/j.eururo.2015.07.040>
11. Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR et al (2014) Medical management of kidney stones: AUA guideline. *J Urol* 192(2):316–324. <https://doi.org/10.1016/j.juro.2014.05.006>
12. Rivera ME, Nottingham CU, Borofsky MS, Kissel SM, Maniar V, Dauw CA et al (2020) Variability in stone composition and metabolic correlation between kidneys in patients with bilateral nephrolithiasis. *Int Urol Nephrol* 52(5):829–834. <https://doi.org/10.1007/s11255-019-02360-6>
13. Kadlec AO, Fridirici ZC, Acosta-Miranda AM, Will TH, Sakamoto K, Turk TM (2014) Bilateral urinary calculi with discordant

- stone composition. *World J Urol* 32(1):281–285. <https://doi.org/10.1007/s00345-013-1113-4>
14. Lieske JC, Rule AD, Krambeck AE, Williams JC, Bergstralh EJ, Mehta RA et al (2014) Stone composition as a function of age and sex. *Clin J Am Soc Nephrol* 9(12):2141–2146. <https://doi.org/10.2215/CJN.05660614>
 15. Ye Z, Zeng G, Yang H, Li J, Tang K, Wang G et al (2020) The status and characteristics of urinary stone composition in China. *BJU Int* 125(6):801–809. <https://doi.org/10.1111/bju.14765>
 16. Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Doizi S et al (2016) Kidney stones. *Nat Rev Dis Primers* 2:16008. <https://doi.org/10.1038/nrdp.2016.8>
 17. Frassetto L, Kohlstadt I (2011) Treatment and prevention of kidney stones: an update. *Am Fam Physician* 84(11):1234–1242
 18. Spradling K, Ganesan C, Conti S (2022) Medical treatment and prevention of urinary stone disease. *Urol Clin North Am* 49(2):335–344. <https://doi.org/10.1016/j.ucl.2021.12.007>
 19. Mousavi A, Takele R, Limbrick B, Thaker KN, Scotland KB (2024) Oral dissolution therapy of uric acid stones: a systematic review. *SIU J* 5(4):284–299. <https://doi.org/10.3390/siuj5040047>
 20. Flannigan R, Choy WH, Chew B, Lange D (2014) Renal struvite stones—pathogenesis, microbiology, and management strategies. *Nat Rev Urol* 11(6):333–341. <https://doi.org/10.1038/nrurol.2014.99>
 21. Morgan MSC, Pearle MS (2016) Medical management of renal stones. *BMJ* 352:i52. <https://doi.org/10.1136/bmj.i52>
 22. Sakhaee K, Maalouf NM, Sinnott B (2012) Clinical review. Kidney stones 2012: pathogenesis, diagnosis, and management. *J Clin Endocrinol Metab* 97(6):1847–1860. <https://doi.org/10.1210/jc.2011-3492>
 23. Hickling DR, Sun TT, Wu XR (2015) Anatomy and physiology of the urinary tract: relation to host defense and microbial infection. *Microbiol Spectr* 3(4). <https://doi.org/10.1128/microbiolspec.UT1-0016-2012>
 24. Sun XY, Ouyang JM, Yu K (2017) Shape-dependent cellular toxicity on renal epithelial cells and stone risk of calcium oxalate dihydrate crystals. *Sci Rep* 7(1):7250. <https://doi.org/10.1038/s41598-017-07598-7>
 25. Shafik A, El Sibai O, Shafik AA, Ahmed I (2004) Do vesical and voided urine have identical compositions? *Scand J Urol Nephrol* 38(3):243–246. <https://doi.org/10.1080/00365590410025344>
 26. Shafik A, Shafik I, El Sibai O, Shafik AA (2005) Changes in the urine composition during its passage through the ureter. A concept of urothelial function. *Urol Res* 33(6):426–428. <https://doi.org/10.1007/s00240-005-0499-x>
 27. Nourian A, Ghiraldi E, Friedlander JI (2020) Dual-energy CT for urinary stone evaluation. *Curr Urol Rep* 22(1):1. <https://doi.org/10.1007/s11934-020-01019-5>
 28. Zheng J, Yu H, Batur J, Shi Z, Tuerxun A, Abulajiang A et al (2021) A multicenter study to develop a non-invasive radiomic model to identify urinary infection stone in vivo using machine-learning. *Kidney Int* 100(4):870–880. <https://doi.org/10.1016/j.kint.2021.05.031>
 29. Zheng J, Zhang J, Cai J, Yao Y, Lu S, Wu Z et al (2023) Development of a radiomics model to discriminate ammonium urate stones from uric acid stones *in vivo*: a remedy for the diagnostic pitfall of dual-energy computed tomography. *Chin Med J*. <https://doi.org/10.1097/CM9.0000000000002866>
 30. Kim US, Kwon HS, Yang W, Lee W, Choi C, Kim JK et al (2022) Prediction of the composition of urinary stones using deep learning. *Investig Clin Urol* 63(4):441–447. <https://doi.org/10.4111/icu.20220062>

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