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Research article

Analysis of metabolic syndrome in bilateral upper urinary tract stones: A retrospective study of 3905 cases

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ABSTRACT

Bilateral upper urinary tract stones are significantly related to renal function damage. However, few studies characterized the risk factors of bilateral upper urinary tract stones. We retrospectively enrolled 3905 patients with urinary tract stones from March 2019 to March 2022 at the Second Hospital of Tianjin Medical University. Patients were divided into two groups according to the location of the stones, and the related data were evaluated. In this study, 2485 unilateral and 1420 bilateral stone patients were included. Multivariate logistic regression analysis showed that BMI, gout, hyperparathyroidism, uric acid stone, urine PH, 24-h urinary calcium, blood uric acid, and metabolic syndrome (Mets) were independent risk factors for bilateral stone formation($P < 0.05$). Based on these results, we construct a discrimination model. This model revealed good discrimination with an area under the receiver operating characteristic curves of 0.617, and the sensitivity and specificity were 0.592 and 0.586, respectively. Furthermore, the number of Mets components increased the risk of bilateral upper urinary tract stones. Hypertension, hyperglycemia, and low HDL level were strongly associated with bilateral upper urinary tract stones ($P < 0.05$). Patients with 5 components Mets had 1.89-fold higher risk of bilateral upper urinary tract stones than those with 1 component Mets (OR 3.381; 95 % CI 1.221–9.360; $P = 0.013$). Additionally, male patients with Mets had higher risk of bilateral upper urinary tract stones than female patients. Our analysis revealed that eight clinical factors were associated with the formation of bilateral upper urinary tract stones, namely BMI, gout, hyperparathyroidism, uric acid stone, urine PH, 24-h urinary calcium, blood uric acid, and Mets. This study could help clinicians adjust treatment strategies for high-risk patients with bilateral upper urinary tract stones.

1. Introduction

Upper urinary tract stones are a common urinary system disease that strongly influences people's health and national healthcare expenses [1]. In recent years, the prevalence of urinary stones has been increasing due to global warming and changes in dietary patterns [2]. In the United States, the prevalence of urinary stones was reported to increase from 6 % to 12 % in recent years [3,4]. And the latest studies from China also reported an increased prevalence from 4 % to 6.4 % [5,6]. Against this backdrop, clinicians have

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performed various studies on the formation and recurrence of urinary stones. Clinical epidemiological studies have proven various risk factors associated with the urinary stone formation in the last decades (e.g., low urine output, diabetes mellitus, obesity, dyslipidemia, and urinary infection). Additionally, Iremashvili et al. reported that location and number of stones may indicate the more abnormal metabolic [7]. Although the incidence rate of unilateral upper urinary tract stones is higher than that of bilateral upper urinary tract stones, studies on bilateral upper urinary tract stones formation are still insufficient.

Given an obvious rise in the cost of upper urinary tract stones prevention and treatment, clinical intervention based on the etiology of upper urinary tract stones is an effective method to alleviate the physical and economic burden for both patients and healthcare systems [8]. Mets is a group of disorders characterized by abnormal metabolism, including hypertension, hyperlipidemia, hyperglycemia, low-HDL, and central obesity. Patients were diagnosed as Mets when meeting three or more above criteria. Mets patients are susceptible to calcium oxalate stones, uric acid stones, and infectious stones [9]. Previous studies have reported that metabolic syndrome (Mets) is related to various urinary diseases particularly upper urinary tract stones [10]. Moreover, Kadlec et al. showed that Mets and its factors significantly correlate with urinary stones [11]. Some studies also reported interesting conclusions that increased visceral fat and higher body obesity are often accompanied by insulin resistance [12,13], which further leads to lower urine pH and hyperuricemia, promoting the formation of stones [14]. In addition, hypertension can promote urinary calcium excretion [15], and hyperlipidemia can cause hypoxia and renal tubular injury in the kidney [16], both of which induced the formation of stones. Under these circumstances, a better comprehension of the association between bilateral upper urinary tract stones and Mets will provide a promising measure to reduce the incidence rate of bilateral upper urinary tract stones.

Many reports have explored the risk factors of urinary stones without distinguishing unilateral and bilateral upper urinary tract stones, the latter of which may cause severer damaged renal function. Additionally, treating bilateral upper urinary tract stones is more complicated and costs more. Therefore, we conducted a retrospective analysis to identify the risk factors associated with bilateral upper urinary tract stones, and specifically investigated the effects of Mets on bilateral upper urinary tract stones.

2. Material and methods

2.1. Participates selection

The current study retrospectively enrolled patients diagnosed with urinary tract stones and divided them into two groups: unilateral and bilateral upper urinary tract stones groups. Notably, we compared patients with the same components of bilateral upper urinary tract stones to those with unilateral upper urinary tract stones to reduce the impact of confounding bias. All subjects were diagnosed as upper urinary tract stones and treated at The Second Hospital of Tianjin Medical University between March 2019 and March 2022, and were all older than 18 years. Patients were excluded once met one of the following criteria: missing data on uric acid (UA), body mass index (BMI), glucose, high-density lipoprotein cholesterol (HDL-C), triglycerides, blood pressure (BP), or waist circumference (WC); patients with polycystic kidney disease, deformity, hypoplasia, dysgenesis, renal tumor, kidney transplantation, or post-surgical status, patients with multiple stones on one side, and those with renal failure (defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2).

2.2. Diagnosis methods and stone composition analysis

In the study, all patients were hospitalized and underwent preoperative urinary system ultrasound examination, computerized tomography (CT) with a slice thickness of 2 mm (GE, Boston, USA), and intraoperative ureteroscopy, all confirming the presence of upper urinary tract stones. Stone composition analysis was conducted postoperatively. Stone composition was determined using infrared spectroscopy analysis: After cleaning and drying the stone specimens, they were ground into a powder. Approximately 1–2 mg of the powder was mixed with KBr, and the grinding continued until the particle size was less than 2 μm. Subsequently, the mixture was pressed into a pellet with a thickness of 3–5 mm using a pellet press. Stone composition analysis was performed using an infrared spectrophotometer (Lambda, Tianjin, China) LIIR-2. The stone type was defined based on the main stone components (>50 %).

2.3. Exposure measures and definition of Mets

This study considered demographic characteristics (age, gender, BMI, WC), laboratory parameters (FBG, TG, HDL-C, urinary infection, urine PH, urinary calcium, urinary phosphorus, urinary magnesium, urinary urate, blood uric acid), medical history of other diseases (e.g., gout, hyperparathyroidism, stroke, hyperthyroidism, and other system diseases), and diagnosis of upper urinary tract stones (e.g., calcium oxalate stone, calcium phosphate stone, uric acid stone, infection stone, and other stone). The Mets observation index included BMI, FBG, HDL-C, TG, and WC. Based on the harmonized International Diabetes Federation criteria (2009) for defining Mets, patient was diagnosed as Mets when meeting at least three of the following criteria: (1) Hypertension, which was diagnosed by blood pressure (systolic blood pressure higher than 130 mmHg and/or diastolic blood pressure higher 85 mmHg), reported hypertension history, or history of antihypertensive drugs use; (2) Hyperglycemia diagnosed via blood glucose measurement (fasting blood glucose $\geq$5.6 mmol/L and/or any history of glucose-lowering drugs use; (3)Decreased HDL-C level, defined as HDL-C < 1.0 mmol/L in males and 1.3 mmol/L in females and/or any history of relevant drug use; (4) Hyperlipidemia, defined as TG ≥ 1.7 mmol/L and/or any history of relevant drug use; (5) increased WC, defined as WC ≥ 90 cm in males and 80 cm in females. Meanwhile, subjects when BMI $\geq$25 kg/m2 were regarded as obesity.

2.4. Statistical analysis

All statistical analysis were conducted by IBM SPSS Statistics, version 21 (IBM Corp. Armonk, NY, USA). Demographic characteristics were evaluated by percentages and mean ± standard deviation for categorical and continuous variables. Categorical variables were compared by Pearson's χ^2 test, and continuous variables were compared by independent sample Student's t-test. Logistic regression was conducted to analyze univariate and multivariate results, including BMI, gout, uric acid stone, urine PH, 24-h urinary calcium, blood uric acid, and Mets. Risk model to identify the high-risk population was generated based on the multivariate logistic regression results. Association between MetS or individual components of MetS and stones as well as subtype analysis of MetS and stones were analyzed using Pearson's χ^2 test. Then receiver operating characteristic curve (ROC) was applied to assess the discrimination performance of the model. The value of area under the curve (AUC) $\leq$0.5 indicates no discrimination, while a value of 1.0 represents the perfect discrimination. 5 % significant level was chosen and all statical tests were two-tailed.

3. Ethics statement

Protocol of this study was approved by the institution review board of The Second Hospital of Tianjin Medical University and participants' consent was not necessary. All protocols received approval from the Ethics Committee of the Second Hospital of Tianjin Medical University (KY2023K156) and were conducted in accordance with its regulations and guidelines.

4. Results

4.1. Demographic characteristics of the study participants

The current study retrospectively enrolled 3,905 patients with upper urinary tract stones, of whom 2485 (63.6 %) had unilateral upper urinary tract stones and 1,420 (36.4 %) had bilateral upper urinary tract stones. The mean age of subjects with unilateral and bilateral upper urinary tract stones were 48.1 ± 12.9 and 48.4 ± 13.0 years, respectively (P = 0.464). Of the patients, 3,109 (79.6 %) were male and 796 (20.4 %) were female. Furthermore, patients with bilateral upper urinary tract stones had significantly higher BMI, gout ratio, uric acid stone ratio, urine PH, 24h urinary calcium, blood uric acid, hyperparathyroidism ratio, and MetS patients ratio (P < 0.05). This study also found a difference in urinary calculus components in 231 (13.9 %) bilateral upper urinary tract stones patients. Table 1 summarizes the demographic data of patients in these groups.

Table 1
Demographic characteristics and data of the stone side (unilateral/bilateral).

Characteristics	unilateral	bilateral	χ^2/t	P-Value
N	2485	1420		
Age (year)	48.1 ± 12.9	48.4 ± 13.0	0.733	0.464
Gender (male%)	1975(79.5)	1134(79.8)	0.081	0.775
BMI (kg/m^2)	25.88 ± 3.69	26.27 ± 3.79	3.155	**0.002***
Urinary infection (yes)	510(20.5)	318(21.4)	1.894	0.169
CVD (yes)	117(4.7)	61(4.3)	0.353	0.552
Stroke (yes)	51(2.1)	28(2.0)	0.030	0.864
Liver and gallbladder disease (yes)	244(9.8)	126(8.8)	0.942	0.332
Gastrointestinal disease (yes)	105(4.2)	58(4.0)	0.045	0.832
Respiratory disease (yes)	220(8.9)	109(7.6)	1.623	0.203
Chronic kidney disease (yes)	64(2.6)	41(2.8)	0.336	0.562
Orthopedic disease (yes)	279(11.2)	161(11.3)	0.011	0.916
Tumor disease (yes)	58(2.3)	30(2.1)	0.201	0.654
Gout (yes)	23(0.9)	31(2.1)	10.479	**0.001***
Hyperthyroidism (yes)	11(0.4)	8(0.6)	0.272	0.602
Hyperparathyroidism (yes)	231(9.3)	160(11.3)	3.899	**0.048***
Other diseases (yes)	17(0.6)	9(0.6)	0.035	0.852
Calcium oxalate stone (yes)	1890(76.1)	1047(73.7)	2.618	0.106
Calcium phosphate stone (yes)	214(8.6)	105(7.4)	1.785	0.182
Infection stone (yes)	166(6.7)	101(7.1)	0.265	0.606
Uric acid stone (yes)	145(5.8)	132(9.3)	16.422	**<0.001***
Other stone (yes)	70(2.8)	35(2.5)	0.428	0.513
Urine PH (Acidity%)	849(34.2)	573(39.6)	14.940	**<0.001***
urinary calcium (mmol/24h)	4.41 ± 2.46	5.17 ± 2.52	9.212	**<0.001***
urinary phosphorus (mmol/24h)	14.48 ± 6.77	14.34 ± 6.45	0.661	0.509
urinary magnesium (mmol/24h)	2.89 ± 1.60	2.83 ± 1.58	1.300	0.194
urinary urate (mmol/24h)	3.87 ± 0.44	3.86 ± 0.34	0.8221	**0.412**
Blood uric acid (μmol/L)	329.89 ± 59.55	342.13 ± 68.81	5.836	**<0.001***
MetS status, n(%)				
Non-MetS	2134(85.8)	1158(81.6)	12.027	**0.001***
MetS	354(14.2)	262(18.4)		

Note: *BMI* body mass index, *CVD* cerebrovascular disease, *MetS* metabolic syndrome.

4.2. Risk factors for the incidence of bilateral upper urinary tract stones

Multivariate logistic regression analysis was conducted to investigate risk factors associated with bilateral upper urinary tract stones in contrast to unilateral upper urinary tract stones. The results revealed that higher BMI, gout, hyperparathyroidism, uric acid stone, urine PH, 24-h urinary calcium, blood uric acid, and Mets all significantly increased the risk of bilateral upper urinary tract stones ($P < 0.05$) (Table 2).

4.3. Association between individual components of Mets and bilateral upper urinary tract stones

We conducted chi-square tests to estimate the correlation between each component of Mets and bilateral upper urinary tract stones. The results showed that the ratio of hypertension, diabetes, and low high-density lipoprotein levels was significantly higher among patients with bilateral upper urinary tract stones than those with unilateral upper urinary tract stones ($P < 0.05$) (Table 3). However, no significant difference was observed between MetS and high waist circumference or high triglyceride. Additionally, we performed a separate analysis by splitting 5 components of MetS. Regression analysis showed that hypertension, diabetes, and low high-density lipoprotein levels significantly increased the risk of bilateral upper urinary tract stones ($P < 0.05$) (Supplementary Table 1).

4.4. Association of Mets with an increased risk of bilateral upper urinary tract stones

In addition, our findings indicate that the risk of bilateral upper urinary tract stones increased as the number of components in Mets increased ($P < 0.05$) (Table 4). Specifically, 62.5 % with all five MetS components had bilateral upper urinary tract stones. Regression analysis showed that patients with 5 components Mets had 1.89-fold higher risk of bilateral upper urinary tract stones than those with 1 components Mets (OR 3.381; 95 % CI 1.221–9.360; $P = 0.013$).

4.5. Subgroup analysis of MetS and the bilateral upper urinary tract stones

Subgroup analysis indicate that the risk of bilateral upper urinary tract stones is significantly associated with Mets in age and uric acid stones subgroups ($P < 0.05$) (Table 5). Furthermore, the risk of bilateral upper urinary tract stones was higher in male patients with Mets. Overall, these subgroup analyses support the findings of the overall analysis.

4.6. ROC analysis of the discrimination performance of bilateral upper urinary tract stones

To further evaluate the discrimination performance of the multivariate logistic regression model, we created a regression equation based on the regression coefficients. The equation is as follows: Logit(P) = 0.028 × BMI + 0.764 × Gout + 0.257 × Hyperparathyroidism + 0.336 × Uric acid stone + 0.219 × Urine PH + 0.125 × Urinary calcium + 0.003 × Blood uric acid + 0.242 × Mets - 3.548. For categorical variables including “acidic urine”, “Gout”, “Hyperparathyroidism”, “Uric acid stone” and “Mets”. The area under the ROC curve was 0.617 (95%CI: 0.598–0.635). Therefore, the risk mode displayed a good discrimination value, with sensitivity of 0.592 and specificity of 0.586 (Fig. 1).

5. Discussion

Urolithiasis in the upper urinary tract can be categorized as kidney or ureteral stones based on location, and categorized as unilateral or bilateral upper urinary tract stones based on the side of occurrence. Bilateral upper urinary tract stones raised a challenge for urologists due to greater difficulty to manage clinically. Prolonged presence of urinary stones can lead to mucosal edema and congestion in the urinary tract, and even chronic renal failure. Patients with bilateral upper urinary tract stones are at a higher risk of developing renal failure due to severe urinary obstruction resulting in hydronephrosis. Additionally, urinary obstruction along with severe infection can lead to pyonephrosis and pyelonephritis, resulting in increased rates of emergency visits by patients. However, most studies focused on the risk factors of general upper urinary tract stones no matter it was unilateral and bilateral upper urinary

Table 2
The logistic regression results of univariate and multivariate analysis.

Variables		Univariate analysis			Multivariate analysis		
		OR	95%CI	P-Value	OR	95%CI	P-Value
BMI(kg/m^2)	(continuous)	1.028	(1.011,1.046)	0.002	1.028	(1.010,1.047)	0.002
Gout	(presence vs absence)	2.389	(1.387,4.113)	0.002	2.146	(1.230,3.747)	0.007
Hyperparathyroidism	(presence vs absence)	1.239	(1.001,1.533)	0.049	1.293	(1.013,1.652)	0.039
Uric acid stone	(presence vs absence)	1.654	(1.294,2.114)	<0.001	1.399	(1.068,1.833)	0.015
Urine PH	(Acidity vs Neutral or alkaline)	1.304	(1.139,1.491)	<0.001	1.245	(1.061,1.461)	0.007
urinary calcium(mmol/24h)	(continuous)	1.131	(1.100,1.160)	<0.001	1.133	(1.102,1.165)	<0.001
Blood uric acid(μmol/L)	(continuous)	1.003	(1.002,1.004)	<0.001	1.003	(1.002,1.004)	<0.001
MetS status, n(%)	(continuous)	1.362	(1.143,1.623)	0.001	1.273	(1.062,1.527)	0.009

Note: *BMI* body mass index, *CVD* cerebrovascular disease, *MetS* metabolic syndrome.

Table 3
Association between individual components of MetS and bilateral upper urinary tract stones.

Variable	unilateral	bilateral	F/χ^2	P-Value
BP(mmHg)[a]			11.378	**0.001***
Normal	1826	976		
High	649	444		
FBG(mmol/l)[b]			9.660	**0.002***
Normal	2116	1155		
High	369	265		
HDL-C(mmol/l)[c]			14.383	**0.001***
Normal	1497	767		
Low	988	653		
TG(mmol/l)[d]			0.328	0.567
Normal	1575	913		
High	910	507		
WC(cm)[e]			0.619	0.432
Normal	1830	1062		
High	655	358		

Notes: *MetS* metabolic syndrome, *BP* blood pressure, *FBG* fasting blood glucose, *HDL-C* high-density lipoprotein cholesterol, *TG* triglycerides, *WC* waist circumference.

[a] Systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg, and/or a history of hypertension treated with antihypertensive drugs were defined as high. Systolic blood pressure <130 mmHg and diastolic blood pressure <85 mmHg were defined as normal.

[b] FBG ≥100 mg/dL (5.6 mmol/L) and/or using glucose-lowering medication for increased glucose were defined as high. FBG<100 mg/dL (5.6 mmol/L) was defined as normal.

[c] HDL-C < 40 mg/dL (1.0 mmol/L) in males and HDL-C < 50 mg/dL (1.3 mmol/L) in females and/or drug treatment for decreased HDL-C were defined as low. HDL-C ≥ 40 mg/dL (1.0 mmol/L) in males and HDL-C ≥ 50 mg/dL (1.3 mmol/L) in females and/or drug treatment for decreased HDL-C were defined as normal.

[d] TG ≥ 150 mg/dL (1.7 mmol/L) and/or drug treatment for increased TG were defined as high. TG < 150 mg/dL (1.7 mmol/L) was defined as normal.

[e] WC ≥ 90 cm in males and WC ≥ 80 cm in females were defined as high. WC < 90 cm in males and WC < 80 cm in females were defined as normal.

Table 4
Association between MetS and bilateral upper urinary tract stones.

Groups	unilateral	bilateral	F/χ^2	P-Value
MetS status			12.027	**0.001***
Non-MetS	2134(85.8)	1158(81.6)		
MetS	354(14.2)	262(18.4)		
No. of Mets components			6.970	**0.008***
0	452(18.2)	241(17.0)		
1	923(37.1)	455(32.0)		
2	756(30.4)	462(32.5)		
3–5	354(14.3)	262(18.5)		

Note: *MetS* metabolic syndrome, *No.* number.

Table 5
Subgroup analysis of the association between Mets and bilateral upper urinary tract stones.

Variable	unilateral	bilateral	χ^2	P-Value
Age				
≤60	2022 (295)	1134 (205)	6.630	**0.010***
>60	463 (59)	286 (57)	6.977	**0.008***
Gender				
Female	510 (83)	286 (48)	0.034	0.853
Male	1975 (271)	1134 (214)	14.510	**< 0.001***
Uric acid stone(yes)				
Yes	145 (17)	132 (42)	16.644	**< 0.001***
No	2340 (337)	1288 (220)	4.588	**0.032***

Notes: *MetS* metabolic syndrome.
Compared with the group of Non-MetS respectively.

tract stones. The risk factors of bilateral upper urinary tract stones were rarely studied. Moreover, few studies had investigated the association between other metabolic diseases and the onset of bilateral upper urinary tract stones. Given the potential harm of bilateral upper urinary tract stones to renal function, this study focused on establish risk model for screening high-risk patients and guiding early intervention to decrease the prevalence of bilateral upper urinary tract stones.

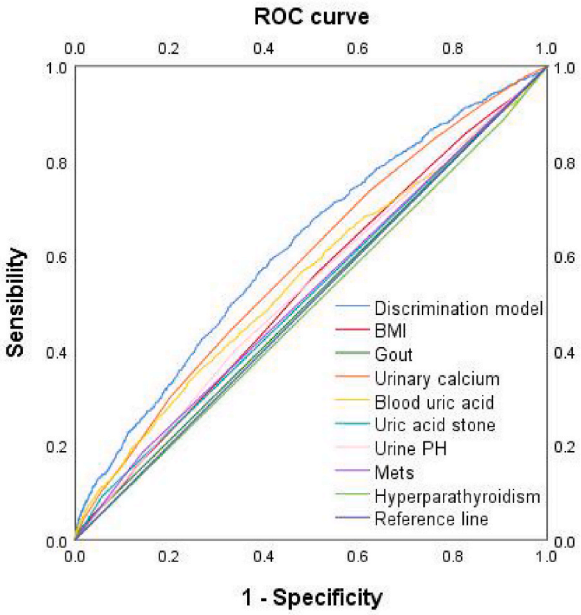

Fig. 1. Discrimination curve analysis for the model and various Characteristics. *ROC* receiver operating curve, *BMI* body mass index, *MetS* metabolic syndrome.

The first factor identified in this study as a risk factor for bilateral upper urinary tract stones is obesity. Several studies reported that obesity usually resulted from unhealthy diet, which significantly increased the urinary stones risk. For example, Crivelli et al. found that obese patients were more likely to suffer from kidney stones compared to patients with normal BMI, which may be due to abnormal urinary stone risk parameters in obese patients [17]. Daudon et al. also reported that uric acid stones had higher prevalence among obese patients, which increased with BMI [18]. Additionally, Kim et al. demonstrated that obesity significantly increased the risk of kidney stones after adjusting for confounding factors such as metabolic factors [19]. Consistent with these findings, our study also found that obesity was a significant risk factor of bilateral upper urinary tract stones. Therefore, reasonable weight loss may be an effective intervention to improve patient's quality of life and reduce medical expenditure.

Hyperparathyroidism and calcium-containing stones are the main components of urinary stones. Minisola et al. reported that hyperparathyroidism leads to excessive secretion of parathyroid hormone (PTH), which may result in hypercalciuria, ultimately contributing to the formation of urinary tract stones [20]. Sarica et al. reported that decrease excretion of citric acid and increase excretion of 24-h urine calcium could accelerate the formation of renal stones [21]. Kuo's research reported that subjects with hypercalciuria had higher risk of COD (also named weddellite) stones formation [22]. Unlike previous studies, our study focused on the association between calcium-containing stones and bilateral urinary tract stones. Our results showed that patients with bilateral upper urinary tract stones had a significantly higher 24-h urine calcium excretion($P < 0.05$). Therefore, patients with a history of calcium-containing stones should be aware of the higher risk for bilateral upper urinary tract stones and receive regular screening. We suggest that patients with hypercalciuria should pay more attention to their daily calcium intake and consider thiazide diuretics to decrease the risk for calcium-containing stone formation only.

Uric acid stones, gout, and hyperuricemia are indicators of abnormal uric acid status. Additionally, low urinary PH indicated acidic urine status of patients, which is reported as the leading risk factor for uric acid stones formation. Frochot et al. demonstrated that uric acid crystals existing in the form of dihydrate in acid urine were usually the important component of uric acid stones [23]. Besides, Wang et al. reported that patients with current or previous uric acid stones are more likely to sufer from kidney stone recurrence [24]. In this study, we broadened the scope and content of known studies, and found that stone recurrence was particularly common in patients with bilateral upper urinary tract stones. In addition, we found a significant association between hyperuricemia and higher incidence of bilateral upper urinary tract stones, which was similar to previous studies. Therefore, monitoring and controlling blood uric acid levels, adjusting high uric acid diets, using medications to lower blood uric acid levels when necessary, and scheduling regular physical examinations are essential for preventing bilateral upper urinary tract stones formation.

With the improvement of quality life, advances in medical testing technology, and variability of testing indices, the incidence of Mets has been risen in recent years. Wang et al. found that patients with kidney stone recurrence were more likely to have complications with Mets compared to those without [24]. Additionally, with regard to the dose-response effect between clinical characteristics of Mets and the risk of bilateral upper urinary tract stones, Kohjimoto et al. showed that the risk of recurrent or multiple urinary tract stones was 1.8 times higher among patients with 4 clinical features of Mets in contrast to normal individuals [25]. Similarly, Chang et al. suggested that compared, the risk of developing renal stones among patients with 5 components of Mets was twice as risky as that among patients without Mets [26]. We also observed that as the number of Mets components increased from 1 to

5, the incidence of bilateral stones increased from 33.0 % to 62.5 %. Based on these findings, we conclude that Mets increased the risk of bilateral upper urinary tract stones formation, and the incidence of bilateral upper urinary tract stones increases with the number of Mets components increased.

Although Mets is associated with bilateral urinary stone formation, each component of Mets has different effects in this process. Curhan et al. reported that excessive sugar, salt, and animal protein intake could increase calcium excretion and accelerate the formation of urinary stones [27]. Borghi reported that hypertension significantly increased the excretion of calcium and oxalate among both men and women, resulting in higher risk of kidney stones [28]. Daudon et al. found that type 2 diabetes contributes to uric acid stones formation [29]. The main pathophysiological mechanism of which was that insulin-resistant impaired the renal ammonium excretion [30,31]. Rosenson et al. illustrated that HDL was vital for cholesterol metabolism in macrophages and can promote the formation of urinary stones mainly through regulating ATP-binding cassette transporter A1 (ABCA1) and ATP-binding cassette transporter G1 (ABCG1) pathways [32]. Unlike previous studies, we further analyzed the association between each component and bilateral upper urinary tract stones formation, results showed that hypertension, diabetes, and low HDL were all independent risk factors for bilateral upper urinary tract stones formation. Therefore, it is necessary to comprehensively monitor and control component of Mets to prevent the formation of bilateral upper urinary tract stones.

We further conducted a subgroup analysis and found significant correlation between Mets and bilateral upper urinary tract stones formation in males rather than in females. This may be due to the several reasons. First, previous studies reported that Chinese males and females had different dietary habits (e.g., meat consumption) and work types (e.g., heavy physical labor) [33,34]. Secondly, the different levels of sexual hormones between males and females may play different roles in the formation of stones. For instance, Heller et al. and Kales et al. found that estrogen inhibited the formation of upper urinary tract stones by affecting the secretion of citric acid and the synthesis of 1,25-dihydroxy vitamin D [35,36]. By contrast, Liang et al. reported that androgen was a risk factor and promoted the formation of upper urinary tract stones [37]. Therefore, for high-risk males with Mets, the most effective and cost-efficient strategy to reduce the formation of bilateral upper urinary tract stones would be to modify their dietary habits and lifestyle.

In addition, patients with metabolic syndrome experience lower quality of life in physiological and social domains compared to those without metabolic syndrome, which can further impact their physical and mental well-being [38]. Furthermore, metabolic syndrome is associated with the occurrence of various complications, such as cardiovascular disease and chronic kidney disease [39,40]. As the prevalence of urinary stones is elevated in individuals with metabolic syndrome, the coexistence of urinary stones in metabolic syndrome patients may contribute to a further decline in their quality of life. In clinical practice, heightened vigilance is essential for patients with concomitant metabolic syndrome, as they may be at an increased risk of developing bilateral ureteral stones. The presence of bilateral upper urinary tract stones can significantly impact renal function. Therefore, prompt lithotripsy is recommended to alleviate obstruction. It is crucial to inform patients with stones and metabolic syndrome that their risk of developing bilateral stones is elevated. Early intervention is advisable to not only reduce the incidence of emergencies but also to improve overall quality of life.

Our study also had some limitations. Firstly, due to the retrospective nature of our study, the causality between the identified risk factors and bilateral upper urinary tract stones formation was not well summarized. Therefore, a larger prospective cohort study is required to confirm the causality in the future. Secondly, we did not include statistical data on daily water consumption of the patients due to the dynamic nature of these variables and the difficulty in recording them in detail. Finally, there are still some unmeasured urine variables information, which should be added and analyzed in future cohort studies. Despite these limitations, our study provided epidemiological evidence to clinical urologists and healthcare physicians for taking better prevention strategies for high-risk populations with bilateral upper urinary tract stones.

Therefore, the results of this study suggest that for individuals at high risk of bilateral urinary tract stones, regular medical examinations are recommended. When necessary, early intervention with medication and surgery is advised. It is believed that this approach can largely reduce the incidence of bilateral urinary tract stones, preserve bilateral kidney function, and decrease the likelihood of undergoing surgical treatment.

6. Conclusion

In this study, the prevalence of bilateral upper urinary tract stones is 36.4 %. Our analysis revealed that high BMI, presence of gout, hyperparathyroidism, uric acid stones, increased 24h urinary calcium, elevated blood uric acid levels, and Mets were all independent risk factors for bilateral upper urinary tract stones. Furthermore, the number of Mets components was found to be positively correlated with the risk of developing bilateral upper urinary tract stones. Among the individual components of Mets, hypertension, diabetes, and low HDL levels all significantly affected the development of bilateral upper urinary tract stones. These findings provided promising strategy for the prevention, screening, and early diagnosis of patients with bilateral upper urinary tract stones.

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Ethical statements

Informed consent was not required for this study because this study is retrospective research. All protocols received approval from

the Ethics Committee of the Second Hospital of Tianjin Medical University (KY2023K156) and were conducted in accordance with its regulations and guidelines.

Data availability

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Zhi Li: Writing – original draft, Data curation, Conceptualization. **Chong Fu:** Writing – review & editing, Software, Investigation, Formal analysis, Conceptualization. **Chuangxin Sun:** Validation, Supervision, Methodology, Conceptualization. **Yong Suo:** Visualization, Data curation. **Kai Li:** Software, Resources. **Shiyong Qi:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:QiShiyong reports financial support was provided by The Second Hospital of Tianjin Medical University.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e31180.

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