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Composition analysis of 1,495 cases of upper urinary tract calculi: the role of age and gender

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Abstract. – OBJECTIVE: This study aimed to quantitatively analyze the calculi components of upper urinary tract calculi and to explore the relationship between calculus components, demographic characteristics, and underlying diseases.

PATIENTS AND METHODS: Clinical data of 1,495 patients with upper urinary tract calculi were retrospectively collected. The calculi were divided into simple calcium oxalate, calcium oxalate mixed, calcium phosphate mixed, uric acid, magnesium ammonium phosphate, and other components. Statistical software SPSS 22.0 was used to analyze the differences between the stone compositions and various factors. The influencing factors ($p < 0.05$) were analyzed using multiple logistic regression analysis.

RESULTS: Among 1,495 patients with upper urinary tract calculi, simple calcium oxalate calculi were the most common component (39.7%), followed by calcium oxalate mixed calculi (30.4%), uric acid calculi (13.6%), calcium phosphate mixed calculi (10.4%), magnesium ammonium phosphate calculi (5.8%) and other component calculi (0.1%). Univariate analysis revealed statistically significant differences in stone composition according to gender, age, and hyperuricemia ($p < 0.05$). Multiple logistic regression analysis showed that compared to men, the odds ratio (OR) values of calcium oxalate mixed stones, calcium phosphate mixed stones, and magnesium ammonium phosphate stones in women were 1.61, 2.50, and 4.17, respectively ($p < 0.001$). Compared with elderly patients, the OR values of calcium phosphate mixed stones in young and middle-aged patients were 3.14 and 2.70, respectively ($p < 0.05$).

CONCLUSIONS: Patients with different stone components had different demographic characteristics, and stone components were significantly different between gender and age. Calcium oxalate mixed stones were more common in females, and calcium phosphate mixed stones and magnesium ammonium phosphate stones were more common in females, young patients, and middle-aged patients.

Key Words:
Urinary calculi, Component analysis, Age, Gender, Diabetes.

Introduction

The prevalence and incidence of urinary calculi have increased in recent years[1]. In addition to gender, age, regional environment, economic and cultural level, and genetics, a variety of metabolic diseases such as hypertension, diabetes, hyperuricemia, and obesity can cause changes in the composition of the blood and urine, affecting the generation and recurrence of stones[2]. Although the application of minimally invasive techniques has improved the treatment of urinary calculi, surgical treatment alone does not change the high postoperative recurrence rate. It has been reported[3] that in the absence of preventive intervention, the postoperative recurrence rate is approximately 6% to 17% after one year, approximately 21% to 53% after 3 to 5 years, and the lifetime recurrence risk is estimated to be 60% to 80%. The key to the prevention and treatment of kidney stones lies in the composition analysis of stone specimens to identify the types of stones and further explore their causes. In recent decades, the composition and demographic characteristics of calculi have changed significantly[4]. To better understand the relationship between stone components and demographic characteristics, we determined the type of stone according to the results of the quantitative analysis of stone

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components and performed multivariate logistic regression analysis to explore the demographic characteristics of patients with different stone components.

Patients and Methods

Data Collection

Data of patients diagnosed with upper urinary tract calculi at our hospital between June 2020 and June 2023 were collected, and 1,495 upper urinary tract calculi samples were obtained by percutaneous nephrolithotomy, ureteroscopic lithotomy, and open or laparoscopic lithotomy for stone composition analysis. Patient data, including gender, age, stone site, body mass index (BMI), hypertension, diabetes, and hyperuricemia, were obtained from the electronic medical record database. Among the 1,495 patients with upper urinary calculi, 857 were males, and 638 were females, aged 18-86 years.

There were 1,067 patients aged 41-66 years, 340 patients aged 18-41 years, and 88 patients aged ≥ 66 years. There were 987 cases of kidney stones, 508 cases of ureteral stones, 450 cases of overweight/obese patients, 503 cases of hypertension, 103 cases of diabetes, and 538 cases of hyperuricemia.

Calculi Analysis Method and Result Judgment

The surface of the stone was cleaned and dried, and the stone samples of 1.0-1.5 mg were mixed with 200-300 mg potassium bromide and crushed to make pressed tablets. An automatic analysis system of the Fourier transform infrared spectrum was used to analyze the composition of the pressed tablets and obtain the results.

Component Analysis and Classification of Calculi

According to the results of the quantitative analysis of stone components, stone components of patients were divided into: (1) simple calcium oxalate stone group (including calcium oxalate monohydrate and calcium oxalate dihydrate); (2) calcium oxalate mixed stone group (the main component is calcium oxalate, containing a small amount of carbonate apatite ≤ 5%); (3) calcium phosphate mixed stone group (containing more than 25% carbonate apatite, the rest calcium oxalate); (4) uric acid stone group (containing any proportion of anhydrous uric acid); (5) magnesium ammonium phosphate stone group (containing any proportion of magnesium ammonium phosphate hexahydrate); and (6) other groups. The World Health Organization standard was used to divide age into young people (18-44 years old), middle-aged people (45-59 years old), and elderly people (≥ 60 years). Age, gender, body mass index (BMI), hypertension, diabetes, and hyperuricemia were analyzed and compared among the different groups.

Statistical Analysis

Statistical software SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. The Chi-square test or Fisher's exact probability method was used for comparisons between groups, and univariate analysis ($p < 0.05$) was included in the multiple logistic regression analysis. Statistical significance was set at $p < 0.05$.

Results

The Distribution of Stone Components

Among 1,495 patients with upper urinary tract calculi, 594 had calcium oxalate alone, 455 had calcium oxalate mixed calculi, 155 had calcium phosphate mixed calculi, 203 had uric acid calculi, 86 had magnesium ammonium phosphate calculi, and 2 had other constituents. Two "other components" were excluded from the comparison between the groups.

Univariate Analysis of Factors Influencing Calculus Composition

There were statistically significant differences in stone composition among the gender, age, and hyperuricemia groups ($p < 0.05$), but there was no significant difference in stone composition between the other groups ($p > 0.05$) (Table I).

Multivariate Logistic Analysis of Influencing Factors of Stone Composition

Using simple calcium oxalate stones as the reference object, disordered multiple logistic regression analysis showed statistically significant differences between stone composition and gender, age, and hyperuricemia ($p < 0.05$). Controlling for other influencing factors, the OR values of calcium oxalate mixed stones, calcium phosphate mixed stones and ammonium magnesium phosphate stones in females were 1.61, 2.50, and 4.17,

Table I. Univariate analysis of factors influencing urinary stone composition (N = 1,493).

Parameter	Total	Stone composition					χ^2	*p*-value
		Simple calcium oxalate stone	Calcium oxalate mixed stone	Calcium phosphate mixed stone	Uric acid stone	Magnesium ammonium phosphate		
Gender							75.065	< 0.001
Male	855	386 (45.0)	239 (28.0)	64 (7.5)	141 (16.5)	25 (2.9)		
Female	638	208 (32.6)	216 (33.9)	91 (14.3)	62 (9.7)	61 (9.6)		
Age							16.273	0.039*
Youth group	339	135 (39.8)	106 (31.3)	41 (12.1)	42 (12.4)	15 (4.4)		
Middle-aged group	1,008	397 (39.4)	314 (31.2)	107 (10.6)	132 (13.1)	58 (5.8)		
Old group	146	62 (42.5)	35 (24.0)	7 (4.8)	29 (19.9)	13 (8.9)		
Hypertension							3.578	0.466
Yes	503	214 (42.5)	142 (28.2)	53 (10.5)	63 (12.5)	31 (6.2)		
No	990	380 (38.4)	313 (31.6)	102 (10.3)	140 (14.1)	55 (5.6)		
Diabetes							7.892	0.096
Yes	103	53 (51.5)	26 (25.2)	6 (5.8)	11 (10.7)	7 (6.8)		
No	1,390	541 (38.9)	429 (30.9)	149 (10.7)	192 (13.8)	79 (5.7)		
Hyperuricemia							26.490	<0.001
Yes	538	236 (43.9)	145 (27.0)	41 (7.6)	94 (17.5)	22 (4.1)		
No	955	358 (37.5)	310 (32.5)	114 (11.9)	109 (11.4)	64 (6.7)		
BMI							9.183	0.327[a]
< 18.5	86	35 (40.7)	22 (25.6)	13 (15.1)	14 (16.3)	2 (2.3)		
18.5-25	957	375 (39.2)	299 (31.2)	104 (10.9)	120 (12.5)	59 (6.2)		
≥ 25	450	184 (40.9)	134 (29.8)	38 (8.4)	69 (15.3)	25 (5.6)		

BMI: body mass index; $*p < 0.05$; [a]: Fisher's exact probability method.

respectively ($p < 0.001$). Compared with elderly patients, the odds ratios (OR) of calcium phosphate mixed stones in young and middle-aged patients were 3.14 and 2.70, respectively ($p < 0.05$) (Table II). Compared with simple calcium oxalate stones, calcium oxalate mixed stones were more common in female patients, and calcium phosphate mixed stones and magnesium ammonium phosphate stones were more common in female, young, and middle-aged patients.

Discussion

Urinary calculus is a common disease in urology that causes kidney colic, urinary tract obstruction, urinary tract infection, and kidney failure. It seriously affects the survival and quality of life of patients and has become an important public health problem worldwide. The incidence of urolithiasis has been steadily increasing in China over the past 20 years, with approximately 1 in 17 adults suffering from kidney stones[5,6]. Performing a good job in the prevention and treatment of calculi has become an urgent problem in the medical field. Analysis of stone components is a method to understand the pathology of stones, which can provide an important basis for the prevention and treatment of urinary calculi. Quantitative analysis of stone components can provide a more scientific classification of stone types, thus compensating for the deficiencies of the qualitative analysis in this study. In this study, the total male-to-female ratio of upper urinary tract calculi was 1.34:1, and most of the patients were male. The ratio of young-to-middle-aged and elderly patients was 2.32:6.9:1, and the proportion of elderly patients was relatively lower than that of young and middle-aged patients.

In this study, the most common stone component was simple calcium oxalate stones (including calcium oxalate monohydrate and calcium oxalate dihydrate), accounting for 39.7%, with significantly more men than females, there was no statistically significant difference in the number of cases at different ages. This was related to the sex hormone levels, diet, and lifestyle habits. Androgens increase serum oxalate levels, leading to increased urinary oxalate excretion and calcium oxalate accumulation, whereas estrogens increase urinary citrate excretion, which inhibits calcium oxalate stone formation[7]. The crystallization degree of calcium oxalate crystal is relatively good, indicating that its precipitation formation process is relatively slow[8]. In addition to simple calcium oxalate stones, calcium oxalate crystals commonly appear in other mixed stones containing calcium oxalate components. Combined with this study, the formation of calcium oxalate crystals is independent and extensive. Simple calcium oxalate stones are considered the basic stone composition.

Table II. Disordered multiple logistic regression analysis of factors influencing calculus composition.

Calculus component	B	Wald	OR (95% CI)	*p*-value
Calcium oxalate mixed stone				
Gender (male *vs*. female)	-0.48	12.70	0.62 (0.48-0.81)	< 0.001
Age (youth *vs*. old)	0.41	2.72	1.51 (0.93-2.47)	0.099
Age (middle-aged *vs*. old)	0.40	3.14	1.50 (0.96-2.33)	0.076
Hyperuricemia (no *vs*. yes)	0.20	2.15	1.22 (0.93-1.60)	0.143
Calcium phosphate mixed stone				
Gender (male *vs*. female)	-0.92	22.39	0.40 (0.27-0.58)	< 0.001
Age (youth *vs*. old)	1.15	6.74	3.14 (1.32-7.46)	0.009*
Age (middle-aged *vs*. old)	0.99	5.67	2.70 (1.19-6.10)	0.017*
Hyperuricemia (no *vs*. yes)	0.33	2.36	1.38 (0.91-2.10)	0.125
Uric acid stone				
Gender (male *vs*. female)	0.16	0.73	1.17 (0.82-1.68)	0.392
Age (youth *vs*. old)	-0.44	2.35	0.64 (0.37-1.13)	0.125
Age (middle-aged *vs*. old)	-0.36	2.16	0.70 (0.43-1.13)	0.141
Hyperuricemia (no *vs*. yes)	-0.23	1.80	0.79 (0.57-1.11)	0.179
Magnesium ammonium phosphate				
Gender (male *vs*. female)	-1.44	29.38	0.24 (0.14-0.40)	< 0.001
Age (youth *vs*. old)	-0.41	0.98	0.66 (0.29-1.50)	0.321
Age (middle-aged *vs*. old)	-0.19	0.30	0.83 (0.42-1.62)	0.585
Hyperuricemia (no *vs*. yes)	0.19	0.48	1.21 (0.71-2.08)	0.487

CI, confidence interval; OR, odds ratio; $^*p < 0.05$.

The second most common stone component was calcium oxalate mixed stones. Because it contains a small amount of calcium phosphate, previous studies[9] have classified it as a calcium oxalate stone. Ohman et al[9] found that even if calcium-containing stones contained only a very small amount of calcium phosphate, urine metabolism abnormalities were significantly different from those of simple calcium oxalate stones, suggesting that the formation of such stones had a more complex etiology than simple calcium oxalate stones. In this study, we found that the number of calcium-containing stones with a calcium phosphate content ≤ 5% was larger; therefore, they were divided into separate groups. The results of the multivariate analysis showed that there was a statistically significant difference in gender between calcium oxalate mixed stones and simple calcium oxalate stones. Calcium oxalate mixed stones are more common in women. We analyzed that the reason for this difference may be that calcium oxalate crystals often coexist with carbonate apatite crystals. Particularly, it is difficult to identify pure calcium oxalate cores in urinary stone cores dominated by calcium oxalate, and its orientation epiphytic mechanism may be the main factor in the formation of calcium oxalate stones, indicating that carbonate apatite plays an important role in the formation of calcium oxalate stones. The detection rate of carbonate apatite in females was significantly higher than in male[10]. In addition, sex hormone levels decrease with age, which affects the promoting effect of androgens on calcium oxalate stones and the protective effect of estrogen on calcium oxalate stones[11,12].

Uric acid stones were the third most common stone component, accounting for 13.6% of the total, consistent with the results reported by the Mayo Clinic[13]. With the improvement of living standards, dietary structure, and lifestyle changes, the proportion of high-purine foods such as meat and beer has increased, and excessive intake of these foods is closely related to the formation of uric acid stones. There has been a significant increase in the prevalence of metabolic syndrome over the past decade[14,15], resulting in a decrease in urinary pH and an increase in uric acid supersaturation, which explains the increase in the incidence of uric acid stones. Although our analysis showed no statistical difference in the proportion of uric acid stones according to gender and age, the detection rate of uric acid stones in males was still higher than in females, and the detection rate of uric acid stones in elderly patients was higher than that in young and middle-aged patients. Studies[16,17] have shown that uric acid stones become more common with age and are thought to be related to age-related changes in renal function associated with aging. In the elderly, renal function decline and renal tubule ammonia secretion function are weakened, while renal acid excretion and ammonium production ability are impaired, resulting in hyperuricuria and low urine pH, and uric acid stones have low solubility in acidic urine, which easily accumulate and precipitate to form uric acid stones[18-20].

Calcium-containing stones with calcium phosphate content higher than 50% were defined as calcium phosphate stones in the literature. However, Tiselius et al[21] compared patients with calcium phosphate content higher than 25% and those with calcium phosphate content lower than 25% and found that the stone recurrence rate and 24-hour urinary calcium secretion of the former were significantly higher than those of the latter. In this study, we found that the calcium phosphate content of some calcium-containing stones was concentrated in the range of 25-90%, with an average content of approximately 40%, so they were grouped into one group. Compared with simple calcium oxalate stones, calcium phosphate mixed stones are more common in women, young people, and middle-aged patients. The degree of crystallization of calcium phosphate crystals is lower than that of calcium oxalate, but the rate of crystal formation is higher than that of calcium oxalate[8]. It has been reported that abnormal accumulation of calcium phosphate components in the renal tubule lumen and sub-epithelium can induce the formation of calcium oxalate stones[22]. Therefore, the rate of stone formation is related to the amount of calcium phosphate in the composition. The higher the calcium phosphate content, the faster the stone formation rate. The main component of calcium phosphate stones is carbonate apatite, which indicates that carbonate apatite plays a key role in the formation of calcium oxalate stones. The formation of carbonate apatite is closely related to urinary tract infection[7], indicating that urinary tract infection may affect the calcium phosphate content in stone components to a large extent. Owing to their different anatomical characteristics, women are more likely to develop tract infections. Second, women generally have a higher urine pH and the theory that calcium phosphate forms in alkaline urine could support our findings regarding differences between genders[23]. In addition, our study found that calcium phosphate stones decreased with age, which may be related to the decrease in urinary calcium and phosphorus concentrations with age[24].

In this study, magnesium ammonium phosphate stones accounted for a relatively small proportion, and the formation of magnesium ammonium phosphate stones was mainly related to Proteus infection in the urine. Proteus can decompose urea in urine to produce ammonia and alkalize urine, resulting in the precipitation of ammonium magnesium phosphate crystals. Urinary tract infections caused by Proteus cause tissue necrosis and shedding, and the shedding necrotic tissue, blood clots, and dead bacterial clumps can become the core of stones, and the stone-forming materials of ammonium magnesium phosphate are continuously deposited around the core to form stones. Urinary tract infections are the main cause of magnesium ammonium phosphate stone formation. Compared to men, women are more prone to urinary tract infections[25], which in turn raises urine pH and promotes the growth of organisms that contain urease[26]. This is an important reason for the high stone detection rate in women. Domestic and foreign literature has shown that the detection rate of magnesium ammonium phosphate stones in women is higher than that in men[7,27-29].

Limitations

This study is one of the few to examine the effects of age and gender on stone composition in Southwest China. However, owing to the retrospective study design, some limitations were evident. First, our data were collected from patients with urolithiasis; therefore, we could not calculate the actual prevalence of upper urinary tract stones in the real world. Second, all stone samples were obtained surgically, leading to bias against the presence of an unknown number of patients with asymptomatic stones or patients with spontaneous stone passing. Third, our department mostly treated adult patients, which could also lead to a bias in the assessment of children. Finally, since this was a retrospective study, we were unable to collect 24-hour urine analysis and other information. Further multicenter studies are required to elucidate the mechanisms underlying these differences. However, quantitative analysis of stone composition can provide basic information about the factors that influence stone formation. The present study presents a series of relatively large analyses of upper urinary tract stones in Southwest China, providing valuable information on the distribution of upper urinary tract stone types and gender and age-related susceptibility to stone formation, which should provide clues to the mechanisms and activities of stone formation processes.

Conclusions

This study demonstrated that patients with different stone types had different demographic characteristics and significant differences in gender and age. Calcium oxalate mixed stones are more common in females, calcium phosphate mixed stones are more common in female, young, and middle-aged patients, and magnesium ammonium phosphate stones are more common in women. With the increase in the prevalence and incidence of urinary calculi worldwide, the composition of calculi has changed in terms of gender and age structure[28,29], and the prevention and treatment of calculi are faced with a severe test. Doctors should combine the results of stone component analyses to determine the cause of stone formation and formulate preventive measures and health education.

Ethics Approval

This study was approved by the Ethics Committee of Chengdu Second People's Hospital (Number: 2023LP1062).

Informed Consent

All patients included in this study and their families signed informed consent forms for the use of their anonymized data in research.

Date Availability

The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

Conflict of Interest

The authors state no conflict of interest.

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Authors' Contributions

XT proposed the study design and contributed to manuscript drafting; XYZ was responsible for data collection; XXB and CYH were responsible for the revision of the manuscript for important intellectual content; and all authors issued final approval for the version to be submitted.

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