Journal of Pharmaceutical and Medical Research
Print ISSN: 2663-1954
Online ISSN: 2663-1962
DOI: https://doi.org/10.61784/jpmr3101

ASSOCIATION OF METABOLIC SYNDROME AND ITS COMPONENT BURDEN WITH UPPER URINARY TRACT STONE COMPOSITION: A RETROSPECTIVE OBSERVATIONAL STUDY

FangMing Xu[1#], ZiLe Pan[2#], KaiLu Wei[1], Min Xiong[1], JiaQiang Pan[1*]
[1]*The Second Affiliated Hospital of Guilin Medical University, Guilin 541199, Guangxi, China.*
[2]*School of Basic Medical Sciences, Hebei North University, Zhangjiakou 075000, Hebei, China.*
[#] *FangMing Xu and ZiLe Pan are both the first authors.*
[*]*Corresponding Author: JiaQiang Pan*

Abstract: Upper urinary tract stones are chemically heterogeneous, with compositions that reflect distinct underlying metabolic perturbations. Metabolic syndrome (MetS) comprises a cluster of interconnected metabolic abnormalities, but the relationship between the cumulative burden of these components and specific stone phenotypes remains incompletely characterized in Chinese populations. This study aimed to investigate the associations of MetS and the number of its components with upper urinary tract stone composition, with a particular focus on uric acid stones. This retrospective observational study included 800 patients with upper urinary tract stones and infrared spectroscopic stone-composition analysis at the Second Affiliated Hospital of Guilin Medical University. Patients were stratified by metabolic syndrome (MetS) status, and predominant stone composition was categorized as calcium oxalate, calcium phosphate, struvite, uric acid, or other. Overall composition differences were assessed by a chi-square test with Monte Carlo resampling. Logistic regression examined associations with uric acid stone composition after sequential adjustment for age, the female/male classification, and serum creatinine. Metabolic component burden was assessed using both categorical and linear terms; Firth penalized logistic regression was used in sensitivity analyses. Among 800 patients, 280 (35.0%) were classified as having MetS. Stone-composition distributions differed by MetS status (Monte Carlo P = 0.0058), and uric acid stones accounted for 13.2% of stones in the MetS group versus 5.6% in the non-MetS group. In the fully adjusted model, MetS was associated with greater odds of uric acid stone composition (OR = 2.65, 95% CI 1.57–4.50; P = 0.00028). Compared with the zero-component group, patients with two, three, and four components showed elevated odds of uric acid composition. The category-specific point estimate was highest in the three-component group (OR = 6.06, 95% CI 2.46–18.31); the categorical specification fitted better than the linear term (likelihood ratio P = 0.040). Firth estimates were directionally similar. Among patients with confirmed upper urinary tract stones, MetS was associated with increased odds of uric acid stone composition. A categorical analysis suggested that the association varied across metabolic component counts, although sparse events in some groups warrant cautious interpretation. These findings merit confirmation in independent patient cohorts with more complete metabolic profiling.
Keywords: Upper urinary tract stones; Metabolic syndrome; Stone composition; Uric acid stones; Dose-response relationship; Firth penalized logistic regression

1 INTRODUCTION

Upper urinary tract stone disease is an important clinical condition with a substantial and geographically variable population burden [1-2]. Stone composition reflects interactions among urinary chemistry, metabolic characteristics, dietary exposures, and inherited susceptibility [3-4]. Calcium-based stones constitute a major proportion of urinary calculi, whereas uric acid stones are particularly relevant to metabolic and urinary-acidification abnormalities [3]. Identifying relationships between clinical features and stone composition may inform appropriate metabolic evaluation and prevention.

Metabolic syndrome (MetS), characterized by clustered abnormalities in body habitus, glucose regulation, blood pressure, and lipids, has been associated with nephrolithiasis in epidemiologic research [5-6]. Prior stone-composition studies have also examined differences between patients with and without MetS, particularly for uric acid calculi [7-10]. Low urinary pH, linked in part to insulin resistance and altered ammonium buffering, provides a plausible metabolic pathway [11-12]. However, the association between the number of metabolic abnormalities and specific stone-composition categories may be inadequately characterized by a simple linear term.

Earlier investigations have addressed MetS and urinary stone composition [7-10], including recent research in Chinese patients [10]. The present study focuses on a different but related question: within a cohort of patients with stones of known composition, does the number of metabolic abnormalities show a linear or non-linear association with uric acid stone composition? Sparse uric acid events in some component strata also make sensitivity analyses relevant.

Accordingly, we evaluated MetS status and four-component burden in relation to infrared spectroscopy-based stone classification at a single center in southern China. We compared categorical and linear component-count models and performed Firth penalized logistic regression to assess sensitivity to sparse uric acid events.

© By the Author(s) 2026, under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0).

2 METHODS

2.1 Study Design and Study Population

This retrospective observational study was conducted at the Second Affiliated Hospital of Guilin Medical University, a tertiary teaching hospital in Guangxi, southern China. We consecutively enrolled patients diagnosed with upper urinary tract stones who underwent stone composition analysis between January 2023 and December 2025.
Inclusion criteria:
Radiologically confirmed upper urinary tract stones (kidney or ureteral stones)
Stone composition analyzed by Fourier-transform infrared spectroscopy
Complete clinical and laboratory data available for MetS component assessment
Age ≥ 18 years
Exclusion criteria:
Secondary stones due to urinary tract malformation, neurogenic bladder, urinary tract tumor, or chronic infection
History of inherited metabolic stone disease (e.g., cystinuria, primary hyperoxaluria)
Incomplete clinical or laboratory data
Malignancy, severe hepatic dysfunction, or end-stage renal disease
A total of 800 eligible patients were included in the final analysis. The study was approved by the Ethics Committee of the Second Affiliated Hospital of Guilin Medical University (approval No.QWJW-2024018) and was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. The requirement for written informed consent was waived due to the retrospective design and fully anonymized data processing.

2.2 Definition of Metabolic Syndrome and Component Count

MetS was operationalized using four component categories derived from the 2004 Chinese Diabetes Society (CDS) proposal [13]. The thresholds used in the analysis are listed below; the availability and coding of treatment history and 2-hour glucose results must be verified against the original patient-level dataset before submission.
Overweight/obesity: body mass index (BMI) ≥ 25.0 kg/m²
Hypertension: systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or previously diagnosed hypertension on treatment
Dysglycemia: fasting plasma glucose ≥ 6.1 mmol/L, or previously diagnosed type 2 diabetes on treatment
Dyslipidemia: triglycerides ≥ 1.7 mmol/L, high-density lipoprotein cholesterol < 0.9 mmol/L in men / < 1.0 mmol/L in women, or on lipid-lowering treatment
Patients with ≥ 3 components were classified as having MetS. The number of metabolic components was categorized into five ordinal groups: 0, 1, 2, 3, or 4 components.

2.3 Stone Composition Classification

Stone composition was determined by Fourier-transform infrared spectroscopy in the hospital's central laboratory. Stones were classified into five mutually exclusive categories based on the predominant chemical component:
Calcium oxalate (CaOx)
Calcium phosphate (CaP)
Struvite (magnesium ammonium phosphate)
Uric acid (UA)
Other compositions

2.4 Outcome and Covariates

The primary outcome was the presence of uric acid stones, coded as a binary variable (1 = uric acid stone, 0 = other stone types). The primary exposure variable was MetS status (binary). Secondary exposure was the number of metabolic components, modeled as both a categorical variable (with 0 components as the reference) and a continuous variable for linear trend testing.
Covariates included age (years), the female/male classification, and serum creatinine (μmol/L). Age and the female/male classification were selected as baseline covariates, and creatinine was examined in the fully adjusted model as an additional marker of renal function. Because observational adjustment cannot eliminate all confounding, the estimates are interpreted as associations rather than causal effects.

2.5 Statistical Analysis

Categorical variables are presented as counts and percentages, and continuous variables as means ± standard deviations. The overall difference in stone-composition distribution between MetS and non-MetS groups was examined using a chi-square statistic with Monte Carlo resampling (10,000 replicates) in view of the sparse counts for uncommon stone categories [14].

Binary logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between MetS and uric acid stones. Three sequential models were constructed:
Model 1: Crude model, unadjusted
Model 2: Adjusted for age and the female/male classification
Model 3: Fully adjusted for age, the female/male classification, and serum creatinine
For the component-count analysis, two logistic regression models were built, both adjusted for age and the female/male classification
:
Categorical model: component count as a 5-level factor variable (0 = reference)
Linear trend model: component count as a continuous variable
A likelihood ratio test was used to compare the fit of the categorical and linear models to evaluate nonlinearity in the dose-response relationship. The overall association of component count with uric acid stones was tested by comparing the categorical model with a base model containing only covariates.
Firth penalized logistic regression was used as a sensitivity analysis to address potential small-sample bias caused by few uric acid events in some strata [15-17]. This method modifies the likelihood and can yield finite estimates in separation-prone settings.
Model diagnostics included convergence checks, Cook's distance, and assessment of collinearity. Statistical analyses were conducted in R version 4.5.3 (R Foundation for Statistical Computing, Vienna, Austria); two-sided $P < 0.05$ was used as the conventional significance threshold. Reporting was informed by STROBE recommendations [18].

3 RESULTS

3.1 Baseline Characteristics of the Study Cohort

The study cohort comprised 800 patients, including 520 (65.0%) in the non-MetS group and 280 (35.0%) in the MetS group. The mean age of the overall cohort was 51.9 ± 13.4 years, and 63.9% were male. The MetS group had a higher mean age, higher BMI, and higher blood pressure compared with the non-MetS group, consistent with the definition of MetS. Detailed baseline characteristics are presented in Table 1.

Table 1 Descriptive Characteristics of the Study Cohort by MetS Status

Characteristic	Non-MetS (n = 520)	MetS (n = 280)
Age, years	50.0 ± 13.9	55.4 ± 11.7
Male, n (%)	335 (64.4)	176 (62.9)
BMI, kg/m²	24.4 ± 2.7	27.2 ± 2.3
Systolic blood pressure, mmHg	130.5 ± 13.2	145.7 ± 11.8
Diastolic blood pressure, mmHg	81.2 ± 9.1	91.9 ± 7.6

Note: All values are presented as mean ± standard deviation or n (%).

3.2 Stone Composition Distribution by MetS Status

The overall distribution of stone composition differed significantly between the MetS and non-MetS groups (Monte Carlo P = 0.0058). Calcium oxalate was the most common stone type in both groups, accounting for 76.7% of cases in the non-MetS group and 71.1% in the MetS group. The proportion of uric acid stones was markedly higher in the MetS group (13.2%) than in the non-MetS group (5.6%). The proportions of calcium phosphate and struvite stones were similar between the two groups. Stone composition distributions are detailed in Table 2.

Table 2 Stone Composition Distribution by MetS Status

Stone composition	Non-MetS (n = 520), n (%)	MetS (n = 280), n (%)
Calcium oxalate	399 (76.7)	199 (71.1)
Calcium phosphate	63 (12.1)	29 (10.4)
Struvite	27 (5.2)	13 (4.6)
Uric acid	29 (5.6)	37 (13.2)
Other	2 (0.4)	2 (0.7)
Total	520 (100.0)	280 (100.0)

Note: The overall between-group comparison was performed using a Monte Carlo–adjusted chi-square test (P = 0.0058).

3.3 Association Between MetS and Uric Acid Stones

The association between MetS and uric acid stone composition was directionally similar across three models (Table 3). The crude OR was 2.58 (95% CI 1.55–4.32; $P < 0.001$), and the age- and the female/male classification-adjusted OR was 2.54 (95% CI 1.52–4.31; P = 0.00044). After additional adjustment for serum creatinine, the OR was 2.65 (95% CI 1.57–4.50; P = 0.00028). The outcome denotes uric acid composition among patients with stones, not incident kidney stone risk in the general population.
The sequential-adjustment results are visualized in Figure 1.

Table 3 Logistic Regression Models for the Association between MetS and Uric Acid Stones

Model	Adjustment variables	OR for MetS	95% CI	P value
Model 1	None	2.58	1.55–4.32	0.00027
Model 2	Age, the female/male classification	2.54	1.52–4.31	0.00044
Model 3	Age, the female/male classification, serum creatinine	2.65	1.57–4.50	0.00028

Abbreviations: OR, odds ratio; CI, confidence interval. Note: All estimates are derived from binary logistic regression with binomial family.

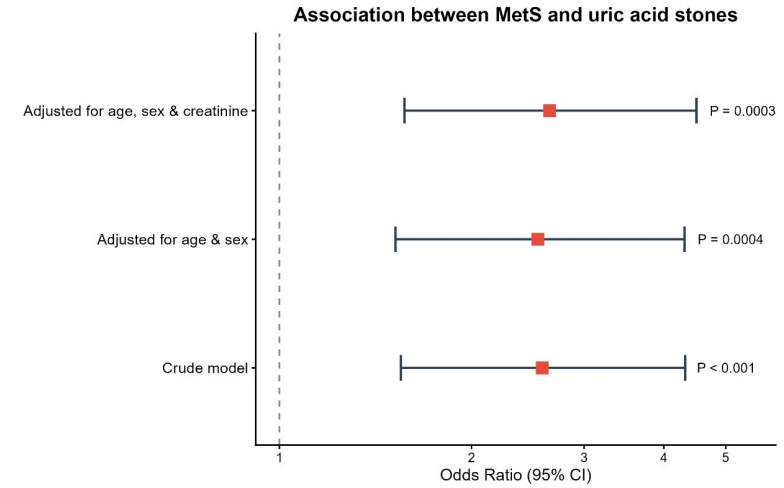


Figure 1 Odds Ratios for the Association between MetS and Uric Acid Stones across Sequential Adjustment Models

3.4 Number of Metabolic Components and Uric Acid Stones

The component-count groups included 180 patients with 0 components, 180 with 1 component, 160 with 2 components, 180 with 3 components, and 100 with 4 components. The prevalence of uric acid stones increased with component count up to 3 components, reaching 15.0% in the 3-component group, and then decreased slightly to 10.0% in the 4-component group (Figure 2).

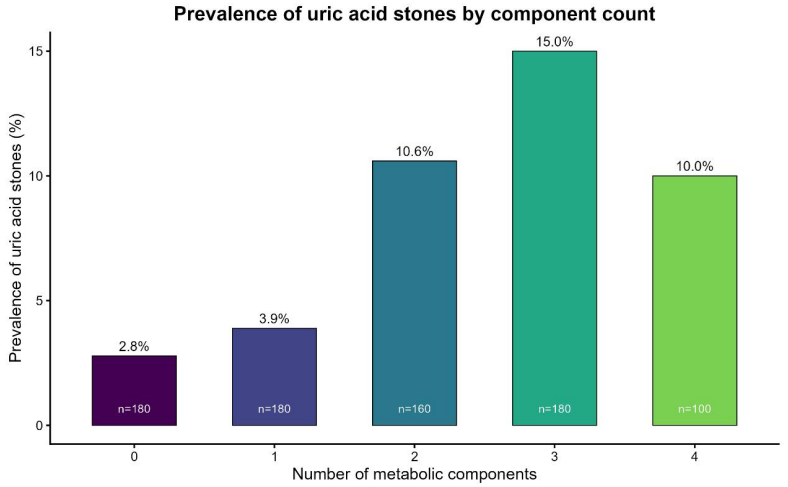


Figure 2 Prevalence of Uric Acid Stones According to Number of Metabolic Components

The overall association between component count and uric acid stones was statistically significant after adjustment for age and the female/male classification (likelihood ratio test: $\chi^2 = 24.64$, df = 4, $P < 0.001$). In the categorical model (Table 4), compared with the 0-component reference group, the odds of uric acid stones were significantly higher in the 2-component (OR = 4.19, 95% CI = 1.61–13.00, P = 0.006), 3-component (OR = 6.06, 95% CI = 2.46–18.31, P < 0.001), and 4-component groups (OR = 3.78, 95% CI = 1.29–12.49, P = 0.019). The 1-component group did not show a statistically significant difference (OR = 1.41, 95% CI = 0.44–4.83, P = 0.567).

When metabolic component count was entered as a linear term, the odds ratio per additional component was 1.49 (95% CI 1.22–1.83; P < 0.001). Nevertheless, the categorical model improved fit relative to the linear specification (likelihood ratio $\chi^2 = 8.33$, df = 3, P = 0.040). Observed proportions were not monotonically increasing, and uncertainty was substantial in the groups with the fewest uric acid events. These results support retaining categorical estimates rather than interpreting the trend coefficient as a uniform increment at every level (Figure 3).

Table 4 Association between Number of Metabolic Components and Uric Acid Stones (Age- and the female/male classification -Adjusted)

Number of components	Total records	Uric acid stones, n (%)	Adjusted OR	95% CI	P value
0	180	5 (2.8)	1.00	Reference	—
1	180	7 (3.9)	1.41	0.44–4.83	0.567
2	160	17 (10.6)	4.19	1.61–13.00	0.006
3	180	27 (15.0)	6.06	2.46–18.31	< 0.001
4	100	10 (10.0)	3.78	1.29–12.49	0.019

Note: ORs and P values are adjusted for age and the female/male classification. The reference group is the 0-component group.

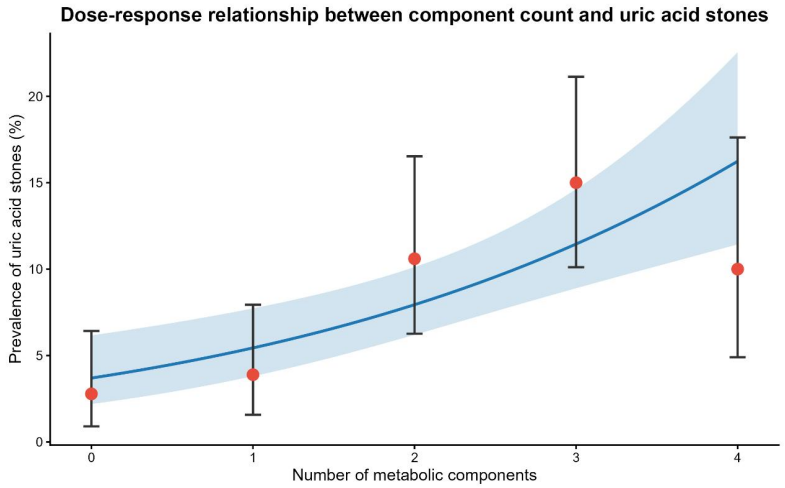


Figure 3 Dose-Response Relationship between Number of Metabolic Components and Prevalence of Uric Acid Stones
Observed values are shown as red points with 95% exact binomial confidence intervals; the blue line represents the linear model fit with 95% confidence band.

3.5 Sensitivity Analysis: Firth Penalized Logistic Regression

Firth penalized logistic regression produced estimates that were broadly consistent with those from conventional logistic regression (Table 5). The ORs were slightly attenuated compared with the conventional model, but the direction and statistical significance of the associations remained unchanged. Specifically, the 2-component (OR = 3.91, 95% CI = 1.55–11.51, P = 0.003), 3-component (OR = 5.58, 95% CI = 2.33–15.99, P < 0.001), and 4-component groups (OR = 3.58, 95% CI = 1.27–11.21, P = 0.016) remained significantly associated with higher odds of uric acid stones. The 1-component group remained nonsignificant.

A side-by-side comparison of conventional and Firth regression estimates is presented in Figure 4.

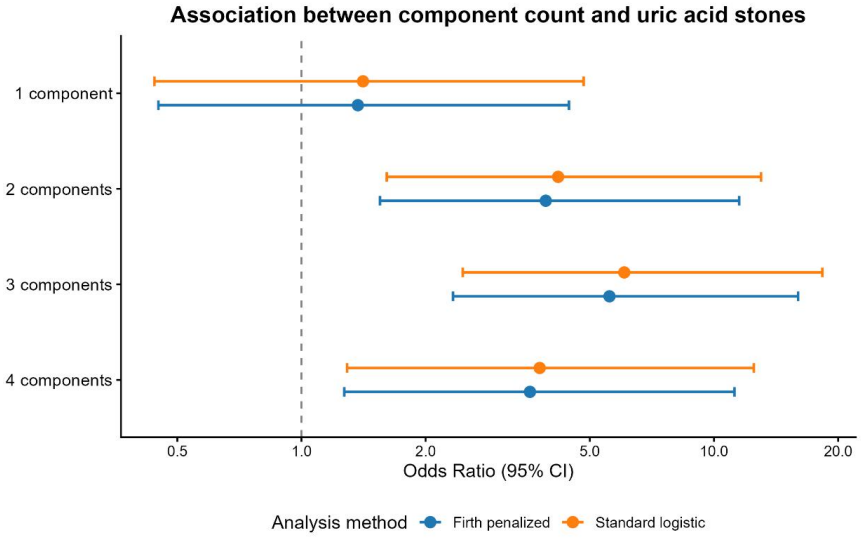


Figure 4 Forest Plot Comparing Conventional and Firth Penalized Logistic Regression Estimates for Component Count Associations with Uric Acid Stones

Table 5 Sensitivity Analysis: Comparison of Conventional and Firth Penalized Logistic Regression Results

Component count	Conventional logistic regression		Firth penalized logistic regression	
	OR (95% CI)	P value	OR (95% CI)	P value
0	1.00 (Reference)	—	1.00 (Reference)	—
1	1.41 (0.44–4.83)	0.567	1.37 (0.45–4.45)	0.579
2	4.19 (1.61–13.00)	0.006	3.91 (1.55–11.51)	0.003
3	6.06 (2.46–18.31)	< 0.001	5.58 (2.33–15.99)	< 0.001
4	3.78 (1.29–12.49)	0.019	3.58 (1.27–11.21)	0.016

Note: Both models are adjusted for age and the female/male classification.

3.6 Model Diagnostics

The logistic models converged. The maximum reported Cook's distance was 0.035, and estimated variance inflation factors were below 1.06, suggesting little evidence of multicollinearity among included terms. Fitted probabilities ranged from approximately 0.023 to 0.182. These checks do not exclude residual confounding or uncertainty arising from sparse uric acid events.

4 DISCUSSION

4.1 Summary of Key Findings

In the analyzed cohort of 800 upper urinary tract stone patients, MetS was associated with higher odds of uric acid rather than other stone composition (fully adjusted OR 2.65). The estimated association varied across categories of metabolic component burden, with the largest point estimate in the three-component group. Because the zero-component reference group contained only five uric acid events and the four-component group contained ten, the apparent peak at three components should be regarded as exploratory rather than evidence of a biological threshold. Firth estimates were broadly consistent with standard logistic regression.

4.2 Context of Existing Literature

Previous investigations provide relevant comparators. Cho et al. reported a higher proportion of uric acid calculi among patients with MetS in a multicenter Korean stone-composition study [7]. Kadlec et al. [8] and Valente et al. [9] also examined metabolic traits and stone composition. More recently, Bu et al. studied MetS components, complex renal calculi, and composition in a Chinese surgical cohort [10]. These reports indicate that both MetS status and its component features have been studied previously; the added contribution of the present work is the comparison of alternative component-count specifications in a regionally defined population.

The category-specific prevalence of uric acid stones increased between zero and three components but was lower in the four-component group. This descriptive pattern and the model comparison (P = 0.040) suggest that a single linear trend may not fully summarize the data. The small number of uric acid events in the reference and highest-burden categories, however, limits precision. Medication exposure, dietary patterns, and urinary pH were not incorporated, so the decline at four components cannot be attributed to treatment effects or biologic saturation. Insulin resistance and low urinary pH remain plausible explanations for the broader MetS–uric acid association [11-12, 19-20].

Firth penalization was used to examine the stability of estimates in the presence of relatively sparse uric acid outcomes. Its methodological basis and advantages in small or separation-prone logistic models are established [15-17]. The similarity between conventional and penalized point estimates is reassuring for this particular modeling specification but does not by itself verify data provenance or eliminate selection bias.

Uric acid calculi represented 66 of 800 stones (8.3%) in this cohort. Because patients were selected on the basis of available stone-composition analyses, this percentage should not be interpreted as representative of all stone patients in Guangxi or of the wider population. The predominance of calcium oxalate stones and the positive association of MetS with uric acid composition are broadly consistent with established stone-composition literature [3, 7-10].

4.3 Clinical Implications

The clinical relevance is primarily in supporting comprehensive metabolic evaluation among stone-forming patients. MetS status and component burden may help prompt consideration of urine pH and other metabolic risk factors, although they cannot replace direct stone analysis. Uric acid stones may be amenable to urinary alkalinization in appropriate patients, whereas urate-lowering therapy is reserved for specific indications rather than used solely on the basis of stone type [21-22]. The observed association is not sufficient to recommend a new risk score or to infer that treating individual MetS components would directly change stone composition.

4.4 Limitations

This study has limitations. First, its single-center retrospective design and inclusion of patients with available infrared spectroscopy may introduce selection bias. Second, the models adjusted for age, the female/male classification, and serum creatinine but did not address important potential confounders such as urine pH, diet, urinary citrate, and relevant

medications. Third, mixed calculi were classified by the predominant component. Fourth, the zero-component stratum contained only five uric acid events, and the four-component group included ten, limiting the precision of category-specific contrasts and the interpretation of apparent nonlinearity. Finally, because MetS and composition were assessed observationally, temporality and causation cannot be established.

Future multicenter prospective studies with larger sample sizes and comprehensive metabolic profiling are warranted to validate our findings and elucidate the underlying mechanisms.

5 CONCLUSION

In patients with analyzed upper urinary tract stones, MetS was associated with higher odds of uric acid stone composition. Although a categorical model fit better than a simple linear component-count term, sparse outcomes warrant caution in interpreting the apparent maximum at three components. External replication using verified patient-level records and more complete metabolic and treatment data is needed before drawing stronger clinical or mechanistic conclusions.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

FUNDING

This research was supported by the Guilin Municipal Scientific Research and Technological Development Program (Grant No. 2020011205-5). The funding body played no role in the study design, data collection and analysis, manuscript writing, or the decision to submit the work for publication.

ETHICS APPROVAL

This retrospective observational study was reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Guilin Medical University (approval No.QWJW-2024018). All procedures were performed in accordance with the ethical standards of the institutional research committee and the 1964 Declaration of Helsinki and its later amendments.

CONSENT TO PARTICIPATE

The requirement for written informed consent was waived by the Ethics Committee of the Second Affiliated Hospital of Guilin Medical University, given the retrospective design of the study and the fully anonymized processing of all patient clinical data.

DATA AVAILABILITY

The datasets generated and analyzed during this study are not publicly available due to institutional medical data privacy regulations, but can be obtained from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

Fangming Xu: Methodology, data curation, formal analysis, visualization, and writing – original draft.
Zile Pan: Investigation, data collection, data curation, formal analysis, and writing – original draft.
Min Xiong and Kailu Wei: Data collection, data curation, writing – review and editing.
Jiaqiang Pan: Conceptualization, supervision, project administration, funding acquisition, and writing – review and editing.
Fangming Xu and Zile Pan contributed equally to this work and share first authorship. All authors reviewed and approved the final manuscript.

REFERENCES

[1] Ma C, Chen L. Temporal trends and global burden of urolithiasis: a comparative analysis of incidence, prevalence, mortality, and disability-adjusted life years in China and globally from 1990 to 2021. Frontiers in Epidemiology, 2025, 5: 1623575. DOI: 10.3389/fepid.2025.1623575.
[2] Zeng G, Mai Z, Xia S, et al. Prevalence of kidney stones in China: an ultrasonography based cross-sectional study. BJU International, 2017, 120: 109-116. DOI: 10.1111/bju.13828.
[3] Khan S R, Pearle M S, Robertson W G, et al. Kidney stones. Nature Reviews Disease Primers, 2017, 3: 17001. DOI: 10.1038/nrdp.2017.1.
[4] Sorokin I, Mamoulakis C, Miyazawa K, et al. Epidemiology of stone disease across the world. World Journal of Urology, 2017, 35: 1301-1320. DOI: 10.1007/s00345-017-2008-6.

[5] West B, Luke A, Durazo-Arvizu R A, et al. Metabolic Syndrome and Self-Reported History of Kidney Stones: The National Health and Nutrition Examination Survey (NHANES III) 1988-1994. American Journal of Kidney Diseases, 2008, 51: 741-747. DOI: 10.1053/j.ajkd.2007.12.030.
[6] Dassanayake S N, Lafont T, Somani B K. Association and risk of metabolic syndrome and kidney stone disease: outcomes from a systematic review and meta-analysis. Current Opinion in Urology, 2025, 35: 377-384. DOI: 10.1097/MOU.0000000000001227.
[7] Cho S T, Jung S I, Myung S C, et al. Correlation of metabolic syndrome with urinary stone composition. International Journal of Urology, 2013, 20: 208-213. DOI: 10.1111/j.1442-2042.2012.03131.x.
[8] Kadlec A O, Greco K, Fridirici Z C, et al. Metabolic Syndrome and Urinary Stone Composition: What Factors Matter Most? Urology, 2012, 80: 805-810. DOI: 10.1016/j.urology.2012.05.011.
[9] Valente P, Castro H, Pereira I, et al. Metabolic syndrome and the composition of urinary calculi: is there any relation? Central European Journal of Urology, 2019. DOI: 10.5173/ceju.2019.1885.
[10] Bu S, Zhang T, Xu H, et al. Associations of metabolic syndrome and its components with complex renal calculi and stone composition: a cross-sectional study. European Journal of Medical Research, 2025, 30: 1089. DOI: 10.1186/s40001-025-03349-x.
[11] Maalouf N M, Cameron M A, Moe O W, et al. Low Urine pH: A Novel Feature of the Metabolic Syndrome. Clinical Journal of the American Society of Nephrology, 2007, 2: 883-888. DOI: 10.2215/CJN.00670207.
[12] Maalouf N M, Cameron M A, Moe O W, et al. Metabolic Basis for Low Urine pH in Type 2 Diabetes. Clinical Journal of the American Society of Nephrology, 2010, 5: 1277-1281. DOI: 10.2215/CJN.08331109.
[13] Metabolic Syndrome Research Collaborative Group, Chinese Diabetes Society. Recommendations of the Chinese Diabetes Society regarding metabolic syndrome. Chinese Journal of Diabetes, 2004: 5-10.
[14] Hope A C A. A Simplified Monte Carlo Significance Test Procedure. Journal of the Royal Statistical Society Series B: Statistical Methodology, 1968, 30: 582-598. DOI: 10.1111/j.2517-6161.1968.tb00759.x.
[15] Firth D. Bias reduction of maximum likelihood estimates. Biometrika, 1993, 80: 27-38. DOI: 10.1093/biomet/80.1.27.
[16] Heinze G, Schemper M. A solution to the problem of separation in logistic regression. Statistics in Medicine, 2002, 21: 2409-2419. DOI: 10.1002/sim.1047.
[17] Puhr R, Heinze G, Nold M, et al. Firth's logistic regression with rare events: accurate effect estimates and predictions? Statistics in Medicine, 2017, 36: 2302-2317. DOI: 10.1002/sim.7273.
[18] Von Elm E, Altman D G, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. PLoS Medicine, 2007, 4: e296. DOI: 10.1371/journal.pmed.0040296.
[19] Abate N, Chandalia M, Cabo-Chan A V, et al. The metabolic syndrome and uric acid nephrolithiasis: Novel features of renal manifestation of insulin resistance. Kidney International, 2004, 65: 386-392. DOI: 10.1111/j.1523-1755.2004.00386.x.
[20] Sakhaee K, Maalouf N M. Metabolic Syndrome and Uric Acid Nephrolithiasis. Seminars in Nephrology, 2008, 28: 174-180. DOI: 10.1016/j.semnephrol.2008.01.010.
[21] Pearle M S, Goldfarb D S, Assimos D G, et al. Medical Management of Kidney Stones: AUA Guideline. Journal of Urology, 2014, 192: 316-324. DOI: 10.1016/j.juro.2014.05.006.
[22] European Association of Urology. EAU Guidelines on Urolithiasis: Metabolic Evaluation and Recurrence Prevention. European Association of Urology, 2026.