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ORIGINAL RESEARCH

CT-Detected Arterial Calcification and Ischemic Cardiovascular Risk Assessment in Patients with Upper Urinary Tract Calculi: A Case-Control Study

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Objective: Arterial calcification (AC) is frequently observed in computed tomography (CT) scans of patients with upper urinary tract calculi (UUTC). This study aimed to investigate the relationship between AC detected by CT in UUTC patients and the risk of ischemic cardiovascular diseases (ICVD).

Methods: In this retrospective case-control study, clinical data of 596 patients were collected. Bone mineral density (BMD) of L1 vertebra and calcification of major/medium arteries were analyzed. Differences in clinical data, CT images and 10-year ICVD risk scores were compared between groups. Univariate analysis and multivariate logistic regression identified independent risk factors for AC in UUTC patients. A scoring system to assess concurrent AC risk in UUTC patients was developed and validated.

Results: A total of 396 UUTC patients and 200 controls were included. AC prevalence was higher in UUTC group (71.7% vs 63.5%, $P = 0.041$), remained valid after controlling for specific confounding factors. UUTC patients exhibited lower BMD of L1 vertebra. Their 10-year ICVD risk scores were elevated (male: OR = 2.450, 95% CI = 1.262–4.758, $P = 0.007$; female: OR = 4.340, 95% CI = 2.203–8.550, $P < 0.001$). Multivariate analysis confirmed L1 vertebra BMD < 160 Hounsfield units (OR = 3.660, 95% CI = 2.107–6.358, $P < 0.001$) as an independent AC risk factor. The presence of AC was associated with a 13.7-fold increased odds of high-risk group classification (OR = 13.689, 95% CI = 8.021–23.346, $P < 0.001$).

Conclusion: AC and the risk of ICVD are associated with UUTC. Our study establishes an innovative integration of UUTC with CT-based AC assessment and ICVD risk stratification, highlighting the need for cardiovascular surveillance in UUTC-affected individuals.

Keywords: upper urinary tract calculi, arterial calcification, ischemic cardiovascular diseases, computed tomography, bone mineral density

Introduction

Upper urinary tract calculi (UUTC) is among the most common urological diseases, affecting over 10% of adults in the United States,[1] with complications extending beyond renal colic to renal insufficiency and urothelial tumors.[2] Prior studies focused predominantly on stone composition or local renal effects, often neglecting the systemic implications of UUTC. Intriguingly, in UUTC patients' computed tomography (CT) images, abnormal arterial calcification (AC) — defined as the pathological deposition of calcium-phosphate crystals in arterial walls — is often observed. While shared metabolic

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imbalance pathways such as hypercalciuria, hyperoxaluria — which are related to osteoporosis — have been proposed,[3,4] the clinical significance of this association has been barely studied before.

AC fundamentally alters vascular biomechanics. A certain degree of elasticity and the ability to maintain hemodynamic stability during diastole is important for artery, but AC increases vessel wall stiffness and decreases the compliance of vessel walls, which causes vasomotor dysfunction.[3,5] Biomechanical model analysis indicates that focal calcium deposits in arteries could result in compliance mismatch and the failure stress in regions subjected to the principal stress direction during vasodilation, thereby predisposing to plaque rupture and subsequently increasing the risk of catastrophic cardiovascular events.[6] Clinically, AC significantly promotes adverse clinical effects, including critical systolic hypertension, left ventricular hypertrophy, coronary ischemia, congestive heart failure, plaque rupture, thrombosis, and myocardial infarction. Therefore, it is necessary to elucidate the relationship between UUTC and AC, which is vital for developing targeted interventions to protect the cardiovascular health in UUTC patients.

Therefore, we hypothesize that UUTC patients demonstrate a significantly higher burden of AC compared to matched controls, with reduced bone mineral density (BMD) identified as independent associated factors in this population. Our retrospective case-control study conducted a comparative analysis of clinical data of UUTC patients and controls, elucidated the incidence of AC in UUTC patients and the causal relationship between UUTC and AC. We aim to (1) quantify AC prevalence in UUTC patients compared with matched controls, (2) characterize modifiable risk factors contributing to AC, and (3) assess the comparative risk of ischemic cardiovascular disease (ICVD) in UUTC patients versus matched controls, thereby enabling the identification of high-risk individuals who require intensified surveillance and targeted interventions.

Materials and Methods

Diagnostic confirmation of UUTC required calculi in the renal pelvis or ureter visualized through non-contrast abdominal and pelvic CT examination. Our study reviewed clinical records of 524 hospitalized patients diagnosed with UUTC between March 2018 and June 2020 at Peking University People's Hospital. In addition, clinical data of 268 hospitalized patients with renal cysts during the same period and same confirmed free from UUTC by non-contrast CT showing no calculi in the renal pelvis or ureter, and age- and sex-matched, were assigned to the control group. The following clinical data were retrieved: demographics, medical history, smoking status, physical examination findings, laboratory parameters, and CT images. Exclusion criteria were: (1) Deficiency of critical clinical data (including incomplete demographic records, missing laboratory results, or unavailable CT images). (2) Congenital urinary tract malformation (eg, stenosis of the ureteral junction, polycystic kidney). (3) Age < 18 or > 75 years. (4) Active malignant tumor. (5) History of hereditary non-calcium stones (such as cystine stones). (6) History of anatomically disruptive urinary tract surgical procedures (eg, ureterostomy). After exclusions, a total of 396 UUTC patients and 200 controls were included in the final analysis. This study was approved by the Ethical Review Committee of Peking University People's Hospital (2020PHB177-01).

The 10-year ICVD risk score was assessed using validated gender-specific prediction models.[7] AC and BMD of L1 vertebra were assessed using established protocols.[8] The images of non-contrast 64-slice CT (slice thickness 1 mm) were manually analyzed to quantify calcifications in the thoracic aorta, abdominal aorta, bilateral renal arteries, bilateral iliac arteries, and BMD of L1 vertebra. AC was defined as vessel wall calcification occupying ≥ 1 mm² with CT attenuation ≥ 130 Hounsfield units (HU) on non-contrast CT imaging (Figure 1). We assessed BMD of the L1 vertebra by measuring mean CT attenuation at four anatomical corners of the vertebral body on a randomly selected axial slice of non-contrast abdominal CT. All of the diagnostic CT imaging was performed using calibration-certified equipment following standardized protocols, documented by certified radiologists in Peking University People's Hospital. According to presence or absence of AC, UUTC patients were further stratified into AC-positive and AC-negative groups.

Continuous variables were dichotomized using receiver operating characteristic (ROC) curve-derived optimal cutoffs, with maximum Youden index (sensitivity + specificity − 1) as selection criteria. Univariate analyses comparing UUTC and control groups, as well as AC-positive and AC-negative groups, were performed using χ^2 test. When stratified analysis is required, the Cochran-Mantel-Haenszel test is employed. In univariate analysis between AC-positive and AC-negative groups, variables with $P < 0.10$ were incorporated into the multivariate binary logistic regression. To

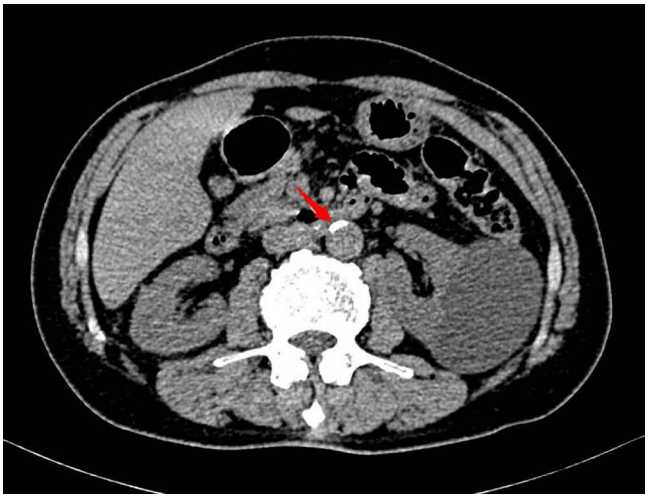

Figure 1 The CT image shows AC (the arrow) in abdominal aorta.

comprehensively adjust for potential confounders, a backward stepwise selection method was applied to establish the regression model. After obtaining independent risk factors for AC in UUTC patients, risk stratification protocol was further developed using logistic regression coefficients scaled into point scores, validated via ROC curve analysis with Youden-index optimized cutoff, and assessed with odds ratios demonstrating high-risk group discrimination. Two-tailed *P* values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS Statistics version 25.0 (IBM Corp.).

Results

The study cohort comprised 396 UUTC patients. The baseline demographic characteristics of UUTC patients were not significantly different compared with 200 controls. Table 1 comprehensively presents baseline clinical characteristics of UUTC patients and controls, with Table 2 specifically detailing these parameters in AC and non-AC subgroups within UUTC patients.

Key clinical parameters were compared between the UUTC patients and controls (Table 3). Regarding the CT images, the prevalence of AC in UUTC group was significantly higher compared with control group (71.7% vs 63.5%, $\chi^2 = 4.192$,

Table 1 Comparison of Clinical Characteristics Between the UUTC Group and Control Group

	UUTC (n = 396)	Control (n = 200)	*P*
Age (years)	53.5 ± 13.4	53.9 ± 13.4	0.441
Sex			0.173
Male (%)	296 (74.7)	139 (69.5)	
Female (%)	100 (25.3)	61 (30.5)	
BMI (m^2/kg)	25.69 ± 3.40	24.96 ± 3.32	0.004
Systolic pressure (mmHg)	130.5 ± 14.7	128.7 ± 16.1	0.002
Diastolic pressure (mmHg)	80.9 ± 9.7	80.4 ± 10.3	0.003
Hypertension (%)	140 (35.4)	78 (36.0)	0.383
Diabetes mellitus (%)	83 (21.0)	21 (10.5)	0.001
Coronary heart disease (%)	30 (7.5)	13 (7.5)	0.632
Cerebrovascular disease (%)	18 (4.5)	5 (2.5)	0.692
Smoking (%)	89 (22.4)	32 (16.0)	0.064
Serum glucose (mmol/L)	5.97 ± 1.91	5.63 ± 1.47	0.028
Serum uric acid (μmol/L)	384.4 ± 100.7	357.4 ± 89.9	0.003
Serum LDL (mmol/L)	3.05 ± 0.80	2.78 ± 0.78	< 0.001

(*Continued*)

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Table 1 (Continued).

	UUTC (n = 396)	Control (n = 200)	*P*
TC (mmol/L)	4.69 ± 1.05	4.54 ± 1.00	0.024
TG (mmol/L)	1.75 ± 1.02	1.72 ± 0.96	0.094
Cr (μmol/L)	96.4 ± 57.8	80.6 ± 21.7	< 0.001
eGFR (mL/min*1.73m^2)	81.89 ± 24.78	88.01 ± 19.40	< 0.001
BMD of L1 (HU)	141.0 ± 39.5	149.6 ± 36.8	0.046
AC (%)	284 (71.7)	127 (63.5)	0.041
ICVD score			
Male	5.7 ± 3.7	5.6 ± 3.7	0.007
Female	6.4 ± 3.6	4.3 ± 3.4	< 0.001

Table 2 Comparison of Clinical Characteristics Between AC and Non-AC Subgroups within the UUTC Group

	AC (n = 284)	Non-AC (n = 112)	*P*
Age (years)	58.4 ± 10.4	41.1 ± 12.0	< 0.001
Sex			0.742
Male (%)	211 (74.3)	85 (75.9)	
Female (%)	73 (25.7)	27 (24.1)	
BMI (m^2/kg)	25.74 ± 3.43	25.58 ± 3.36	0.172
Systolic pressure	132.0 ± 14.9	126.5 ± 13.6	0.002
Diastolic pressure	81.0 ± 10.1	80.4 ± 8.7	0.469
Hypertension (%)	126 (44.4)	14 (12.5)	< 0.001
Diabetes mellitus (%)	73 (25.7)	10 (8.9)	< 0.001
Hyperlipidemia (%)	26 (9.2)	2 (1.8)	0.010
Coronary heart disease (%)	30 (10.6)	0 (0)	< 0.001
Cerebrovascular disease (%)	18 (6.3)	0 (0)	0.003
Smoking (%)	74 (26.1)	15 (13.4)	0.007
Serum glucose (mmol/L)	6.14 ± 2.03	5.55 ± 1.47	0.001
Serum uric acid (μmol/L)	385.1 ± 104.4	382.7 ± 90.9	0.185
Serum LDL (mmol/L)	3.08 ± 0.84	2.97 ± 0.68	0.022
TC (mmol/L)	4.75 ± 1.10	4.54 ± 0.91	0.024
TG (mmol/L)	1.76 ± 0.96	1.75 ± 1.18	0.035
Cr (μmol/L)	97.2 ± 54.3	94.6 ± 66.0	0.120
eGFR (mL/min*1.73m^2)	77.48 ± 22.51	93.09 ± 26.77	< 0.001
BMD of L1 (HU)	130.8 ± 34.8	166.9 ± 39.1	< 0.001
ICVD score			
Male	6.8 ± 3.4	2.8 ± 2.7	< 0.001
Female	7.6 ± 2.9	3.2 ± 3.2	< 0.001

OR = 1.458, 95% CI = 1.015–2.092, $P = 0.041$). This conclusion remained valid after controlling for confounding factors (age, hypertension, and hyperlipidemia) through stratified analysis (Table 4). BMD of L1 vertebral was markedly reduced in UUTC group (64 vs 166, $\chi^2 = 3.986$, OR = 1.425, 95% CI = 1.006–2.018, $P = 0.046$). Sex-stratified analysis demonstrated elevated 10-year ICVD risk scores in UUTC patients (males: 5.7 ± 3.7 vs 5.6 ± 3.7, $\chi^2 = 7.360$, OR = 2.450, 95% CI = 1.262–4.758, $P = 0.007$; females: 6.4 ± 3.6 vs 4.3 ± 3.4, $\chi^2 = 18.953$, OR = 4.340, 95% CI = 2.203–8.550, $P < 0.001$). AC distribution analysis in UUTC patients revealed, that the most common site of AC was iliac arteries (63.34%), followed by abdominal aorta (62.88%), renal arteries (21.97%) and thoracic aorta (15.40%).

Table 3 Univariate Analysis of Key Clinical Parameters Between the UUTC Group and Control Group

	Control (n = 200)	UUTC (n = 396)	χ^2	OR	95% CI	*P*
AC (%)	127 (63.5)	284 (71.7)	4.192	1.458	1.015–2.092	0.041
BMD of L1 < 130 HU (%)	64 (32.0)	166 (41.9)	3.986	1.425	1.006–2.018	0.046
ICVD score						
Male ≥ 1 (%)	119 (85.6)	277 (93.6)	7.360	2.450	1.262–4.758	0.007
Female ≥ 6 (%)	22 (36.1)	71 (71.0)	18.953	4.340	2.203–8.550	< 0.001

Table 4 Stratified Analysis of UUTC-AC Association: Age Stratification (< 50 vs ≥ 50 Years), Hypertension Status, and Hyperlipidemia Status

Subgroups	OR	95% CI	*P*
Age			0.002
≥ 50 years	1.623	0.849–3.103	
< 50 years	2.800	1.407–5.574	
Hypertension			0.021
Yes	2.143	0.974–4.715	
No	1.461	0.945–2.259	
Hyperlipidemia			0.042
Yes	0.867	0.072–10.382	
No	1.508	1.041–2.185	

Univariate analysis of UUTC patients (Table 5) demonstrated significant associations with AC across multiple clinical categories. In demographic parameters, age distribution showed profound disparity (23 vs 224, $\chi^2 = 116.478$, OR = 14.446, 95% CI = 8.421–24.784, $P < 0.001$). Regarding medical history, smoking exposure emerged as a significant risk factor (15 vs 74, $\chi^2 = 7.393$, OR = 2.279, 95% CI = 1.244–4.173, $P = 0.007$), alongside diabetes mellitus (10 vs 73, $\chi^2 = 13.645$, OR =

Table 5 Univariate Analysis of Key Clinical Parameters Between the AC and Non-AC Subgroups within the UUTC Group

	Non-AC (n = 112)	AC (n = 284)	χ^2	OR	95% CI	*P*
Age ≥ 50 years old (%)	23 (20.5)	224 (78.9)	116.478	14.446	8.421–24.784	< 0.001
Sex			0.109	–	–	0.742
Male (%)	85 (75.9)	211 (74.3)				
Female (%)	27 (24.1)	73 (25.7)				
BMI ≥ 23.5 m^2/kg	77 (68.8)	213 (75.0)	1.867	–	–	0.172
Systolic pressure ≥ 135 mmHg (%)	30 (26.8)	125 (44.0)	10.009	2.149	1.331–13.470	0.002
Diastolic pressure ≥ 85 mmHg (%)	34 (30.4)	97 (34.2)	0.523	–	–	0.469
Hypertension (%)	14 (12.5)	126 (44.4)	35.688	5.582	3.042–10.243	< 0.001
Diabetes mellitus (%)	10 (8.9)	73 (25.7)	13.645	3.529	1.749–7.120	< 0.001
Hyperlipidemia (%)	2 (1.8)	26 (9.2)	6.638	5.543	1.293–23.758	0.010
Coronary heart disease (%)	0 (0)	30 (10.6)	–	–	–	< 0.001
Cerebrovascular disease (%)	0 (0)	18 (6.3)	–	–	–	0.003
Smoking (%)	15 (13.4)	74 (26.1)	7.393	2.279	1.244–4.173	0.007
Serum glucose ≥ 5.5 mmol/L (%)	33 (29.5)	138 (48.6)	11.977	2.263	1.417–3.614	0.001
Serum uric acid ≥ 450 μmol/L (%)	21 (18.8)	71 (25.0)	1.759	–	–	0.185
Serum LDL ≥ 3 mmol/L (%)	32 (28.6)	214 (75.4)	5.253	1.672	1.075–2.600	0.022
Total cholesterol ≥ 4.8 mmol/L (%)	37 (33.0)	129 (45.4)	5.062	1.687	1.067–2.667	0.024
TG ≥ 1.05 mmol/L (%)	78 (69.6)	226 (79.6)	4.445	1.698	1.035–2.788	0.035
Cr ≥ 100 μmol/L (%)	27 (23.9)	91 (32.0)	2.418	–	–	0.120

(*Continued*)

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Table 5 (Continued).

	Non-AC (n = 112)	AC (n = 284)	χ^2	OR	95% CI	*P*
eGFR < 105 mL/min*1.73m^2 (%)	67 (59.8)	263 (92.6)	62.159	8.412	4.694–15.073	< 0.001
BMD of L1 < 160 HU (%)	54 (48.2)	236 (83.1)	49.864	5.281	3.257–8.563	< 0.001
ICVD score						
Male ≥ 4 (%)	28 (32.9)	175 (82.9)	70.292	9.896	5.556–17.626	< 0.001
Female ≥ 6 (%)	8 (29.6)	63 (86.3)	30.744	14.963	5.174–43.266	< 0.001

3.529, 95% CI = 1.749–7.120, $P < 0.001$), hypertension (14 vs 126, $\chi^2 = 35.688$, OR = 5.582, 95% CI = 3.042–10.243, $P < 0.001$), hyperlipidemia (2 vs 26, $\chi^2 = 6.638$, OR = 5.543, 95% CI = 1.293–23.758, $P = 0.010$), coronary heart disease (0 vs 30, $P < 0.001$), and cerebrovascular disease (0 vs 18, $P = 0.006$). Physical examination findings revealed systolic blood pressure differences (30 vs 125, $\chi^2 = 10.009$, OR = 2.149, 95% CI = 1.331–13.470, $P = 0.002$). Laboratory investigations identified renal function impairment through eGFR (67 vs 263, $\chi^2 = 62.159$, OR = 8.412, 95% CI = 4.694–15.073, $P < 0.001$) and metabolic dysregulation evidenced by serum glucose (33 vs 138, $\chi^2 = 11.977$, OR = 2.263, 95% CI = 1.417–3.614, $P = 0.001$), triglycerides (78 vs 226, $\chi^2 = 4.445$, OR = 1.698, 95% CI = 1.035–2.788, $P = 0.035$), LDL (32 vs 214, $\chi^2 = 5.253$, OR = 1.672, 95% CI = 1.075–2.600, $P = 0.022$), and total cholesterol (37 vs 129, $\chi^2 = 5.062$, OR = 1.687, 95% CI = 1.067–2.667, $P = 0.024$). BMD of the L1 vertebra displayed marked divergence (54 vs 236, $\chi^2 = 49.864$, OR = 5.281, 95% CI = 3.257–8.563, $P < 0.001$). The 10-years ICVD risk scores demonstrated pronounced divergence between AC and non-AC patients across sex subgroups with male and female patients showing significantly elevated risk (male: 28 vs 175, $\chi^2 = 70.292$, OR = 9.896, 95% CI = 5.556–17.626, $P < 0.001$; female: 8 vs 63, $\chi^2 = 30.744$, OR = 14.963, 95% CI = 5.174–43.266, $P < 0.001$).

Multivariable logistic regression analysis was subsequently conducted. Following adjustment for potential confounders (systolic pressure, diabetes mellitus, hyperlipidemia, coronary heart disease, cerebrovascular disease, serum glucose, total cholesterol, TG, and eGFR), we identified five independent predictors of AC in UUTC patients (Table 6): age ≥ 50 years (OR = 5.917, 95% CI = 3.093–11.320, $P < 0.001$), hypertension (OR = 4.437, 95% CI = 2.289–8.600, $P < 0.001$), smoking (OR = 2.096, 95% CI = 1.031–4.263, $P = 0.041$), LDL ≥ 3 mmol/L (OR = 2.190, 95% CI = 1.279–3.751, $P = 0.004$), BMD of the L1 vertebra < 160 HU (OR = 3.660, 95% CI = 2.107–6.358, $P < 0.001$).

The scoring system for evaluating the rick of AC in UUTC patients was developed by assigning 2 points to the variable with the smallest partial regression coefficient (PRC), also known as the β value. Subsequent variable scores were calculated as the ratio of each β coefficient to this reference β value (Table 6). Following unit standardization, a composite risk score (range: 0–17) was generated by summing scores from the five variables to assess the risk of concurrent AC in UUTC patients. The ROC curve (Figure 2) was constructed to evaluate the diagnostic performance of the evaluating system, identifying an optimal cutoff of 7 points (AUC = 0.848, 95% CI = 0.807–0.889). This threshold maximized the Youden index, yielding 78.9% sensitivity and 78.6% specificity. Based on this threshold, patients were stratified into low-risk (0–6 points; n = 148, 37.4%) and high-risk (7–17 points; n = 248, 62.6%) groups. Patients with AC had approximately 13.7 times higher odds of being in the high-risk group compared to those without AC (OR = 13.689, 95% CI = 8.021–23.346, $P < 0.001$).

Table 6 Multivariate Analysis and Predictive Risk Scoring System for AC in UUTC Patients

	PRC	*P*	OR	95% CI	Score
Age ≥ 50 years	1.778	< 0.001	5.917	3.093–11.320	5
Hypertension	1.298	< 0.001	4.437	2.289–8.600	4
Smoking	0.740	0.041	2.096	1.031–4.263	2
Serum LDL ≥ 3 mmol/L	0.784	0.004	2.190	1.279–3.751	2
BMD of L1 < 160 HU	1.277	< 0.001	3.660	2.107–6.358	4

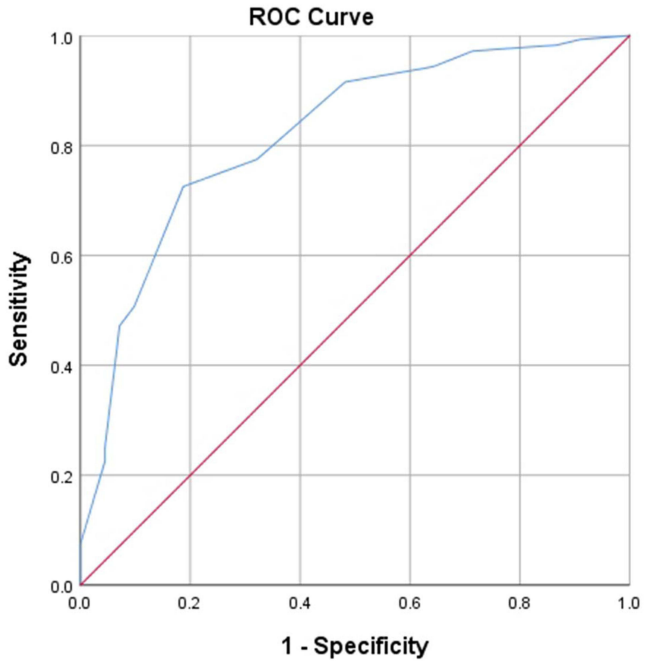

Figure 2 The ROC curve of the score evaluating system for UUTC patients with AC.

Discussion

Major arteries calcification is a well-established marker for cardiovascular morbidity. Bengtsson et al found that elderly subjects with carotid artery calcifications detected in radiographs had a significantly higher risk of stroke and ischemic heart disease.[9] In a cohort of 139 participants, Blomberg et al quantified the 10-year cardiovascular disease progression risks in 139 subjects, demonstrating a significant association between thoracic aorta calcification detected via radiography and elevated cardiovascular disease risk.[10] In addition, previous studies established coronary artery calcification as a strong predictor of acute cardiovascular events.[11,12] Yun et al demonstrated that radiographically detected vascular calcification was a significant predictor of cardiovascular mortality in hemodialysis patients.[13]

Emerging evidence highlights the association between UUTC and AC. Kim et al found patients with nephrolithiasis had a higher prevalence of coronary calcification than those without,[14] while Tanaka et al reported elevated aortic calcification scores in kidney stone patients, independent of age.[15] Reinforced by Chen's cross-sectional data showing marked AC increases in urolithiasis patients,[16] these findings collectively suggest a UUTC-AC pathophysiological link. Our study demonstrated a higher prevalence of AC in UUTC patients after controlling for confounding factors (age, hypertension, and hyperlipidemia) through stratified analysis, showing consistency with previous epidemiological investigations. However, the clinical implications of AC was barely studied in UUTC patients.

To address this gap, our nested case-control study further provides novel insights into the long-term cardiovascular disease risk stratification in UUTC patients — an area previously receiving scant attention in clinical research — based on the 10-year ICVD risk score for Chinese population. We revealed significantly elevated risks of 10-year ICVD in UUTC patients, not only validates previous findings in nephrolithiasis cohorts,[17] but also reveals an elevated cardiovascular risk profile specifically in UUTC patients, suggesting they may need additional cardiovascular disease evaluation. Notably, only a subset of UUTC patients demonstrate AC and higher ICVD risk, highlighting the clinical necessity of differentiated clinical management. A clinically significant proportion of UUTC patients do not routinely undergo diagnostic imaging modalities capable of detecting major arterial calcification, such as thoraco-abdomino-pelvic CT. We suggest that these patients undergo systematic evaluation via our risk stratification protocol to access their AC risk. This can help avoid both overutilization of unnecessary cardiovascular screening procedures and underrecognition of occult cardiovascular risk.

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Emerging evidence suggests UUTC may be associated with multiple metabolic diseases, such as hyperuricemia, diabetes, and osteoporosis.[18,19] Our multivariable regression analysis revealed decreased BMD as an independent risk factor for AC in UUTC patients. In a meta-analysis investigating BMD and fracture susceptibility in nephrolithiasis patients, Lucato et al demonstrated significantly lower BMD values across multiple skeletal sites compared with healthy controls.[20] UUTC-associated osteoporosis often induces hyperphosphatemia, which stimulates osteocyte activation and may consequently drive AC through both direct and indirect mechanisms.[21] As prevalent complication of UUTC, osteoporosis likely exacerbates cardiovascular risks through this calcification pathway in UUTC patients.

The association between UUTC and arterial calcification (AC) may be mediated by inflammation. Sega et al highlighted that pro-inflammatory cytokines promote vascular smooth muscle cell osteogenic differentiation, thereby driving AC pathogenesis.[22] Khan et al demonstrate that pro-inflammatory M1 macrophage polarization can trigger Randall's plaque development through shared vascular calcification pathways (osteopontin and matrix Gla protein), so as to promote the formation of calcium oxalate stones.[23] These inflammatory cascades could synergistically link UUTC to AC by amplifying oxidative stress and mineral dysregulation.

Our study identified a significant association between UUTC and ICVD risk, while establishing the clinical relevance of AC detected through CT imaging. This study not only provides a mechanistic framework for further exploring the mechanism of UUTC-associated systemic metabolic dysregulation, but also holds essential clinical significance for cardiovascular health monitoring in UUTC patients. However, our study has some limitations. The single-center retrospective design limits the generalizability of our study, necessitating validation through multicenter prospective cohorts. Additionally, while demonstrating tripartite associations among UUTC, AC, and ICVD, the precise pathophysiological cascade requires elucidation through targeted molecular studies in the future.

Conclusion

This study demonstrated that AC and increased ICVD risk are significantly associated with UUTC, suggesting systemic metabolic alterations may critically influence UUTC pathogenesis. While the specific mechanisms underlying this association require further investigation, our findings underscore the clinical importance of incorporating AC evaluation in routine CT examination and implementing cardiovascular risk stratification for UUTC patients.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethical Review Committee of Peking University People's Hospital (2020PHB177-01). This study was conducted in accordance with the declaration of Helsinki. Due to the retrospective nature of the study, the requirement of patient consent for inclusion was waived. All patient data were treated with strict confidentiality. Data presented in this manuscript have been aggregated and anonymized to prevent individual patient identification.

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Disclosure

The authors declare that they have no competing interests in this work.

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