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Analysis of risk factors for abnormal renal function in patients with gout in Southwest China: a cross-sectional study

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Abstract

Objective: To analyse the associations between renal function and clinical laboratory indicators and explore the renal function abnormality risk factors for gout patients in Southwest China.

Methods: Outpatient and hospitalized gout patients ($n = 4384$) at the First Affiliated Hospital of Chengdu Medical College between January 2017 and December 2020 were divided into normal ($n = 2393$) and abnormal ($n = 1991$) renal function groups according to their eGFR. The relationships between clinical laboratory indicators and the eGFR were analysed, and a logistic regression model was fit to identify significant risk factors.

Results: Sex, age, absolute lymphocyte count (ALC), cystatin C (CysC), homocysteine (Hcy) and thyroid stimulating hormone (TSH) were associated with renal function abnormalities ($P < 0.05$), whereas age [odds ratio (95% CI) = 1.06 (1.05–1.08), $P < 0.001$], Hcy [1.02 (1.00–1.04), $P = 0.028$], CysC [1.72 (1.54–1.92), $P < 0.001$], ALC [0.71 (0.52–0.97), $P = 0.03$] and TSH [1.08 (1.00–1.17), $P = 0.049$] were abnormal renal function risk factors for gout patients. After stratification by UA, binary logistic regression analysis identified the following risk factors: Q1 age [1.06 (1.02–1.11), $P = 0.003$], CysC [1.67 (1.30–2.16), $P < 0.001$]; Q2 age [1.09 (1.06–1.12), $P < 0.001$], CysC [1.55 (1.28–1.88), $P < 0.001$], FT3 [0.66 (0.46–0.96), $P = 0.029$]; Q3 age [1.06 (1.03–1.09), $P < 0.001$], CysC [1.75 (1.41–2.18), $P < 0.001$], Hcy [1.04 (1.00–1.08), $P = 0.047$], ALC [0.35 (0.18–0.69), $P = 0.002$]; Q4 age [1.05 (1.02–1.09), $P = 0.004$], CysC [1.79 (1.40–2.30), $P < 0.001$].

Conclusion: ALC and levels of TSH and serum Cys could be used for monitoring for abnormal renal function in patients with gout.

Lay Summary

What does this mean for patients?

In people with gout, monosodium urate crystals are deposited in joints or other tissues. Research has shown that gout is closely related to the occurrence of heart disease, diabetes, hypertension, obstructive sleep apnoea syndrome, hyperuricaemia, obesity, kidney disease and hyperlipidaemia. Gout is particularly closely related to kidney damage. There is a strong association between poor kidney function and the risk of developing gout. In our study, we found that age and levels of homocysteine, cystatin C and thyrotropin (which are measured to help determine kidney function) were associated with abnormal kidney function in people with gout. We suggest that homocysteine, cystatin C and thyrotropin could be measured to help monitor kidney function in people with gout.

Keywords: gout, renal function, glomerular filtration rate, risk factors, cross-section.

Key messages

- Age, Hcy, CysC and TSH were independent abnormal renal function risk factors for gout.
- ALC is independently and inversely associated with renal dysfunction in gout patients.
- ALC, TSH and CysC could be used for monitoring for abnormal renal function in patients with gout.

Introduction

Gout is the precipitation and deposition of MSU crystals in joints or other tissues due to impaired purine metabolism and/or reduced serum urate (UA) excretion and continuous elevation of blood UA levels. Gout is a metabolic and inflammatory/immune disease [1]. Many studies have shown that gout is closely related to the occurrence of heart disease, diabetes mellitus, hypertension, obstructive sleep apnoea syndrome, hyperuricaemia, obesity, renal disease (including renal insufficiency) and hyperlipidaemia [2, 3], among which gout is particularly closely related to the occurrence of kidney

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damage. There is a strong dose–response association between impaired renal function and the risk of developing gout [4], and the association between a lower estimated glomerular filtration rate (eGFR) and a greater risk of developing gout persists [5]. The kidney is an important organ for UA excretion and is responsible for approximately 70% of UA excretion in the human body [6]. Previous studies have demonstrated that decreased eGFR and proteinuria are closely associated with the risk of developing hyperuricaemia [7]. However, in the early stage of renal function impairment, patients often have no specific manifestations [8]. In previous studies on the relationship between gout/UA levels and renal function, chronic kidney disease (CKD; GFR <60 ml/min/1.73 m^2) was used as the dependent variable, but the patients had already entered CKD stage 3a, even if the urinary albumin/creatinine ratio was normal or slightly increased, and the risk stratification of CKD was medium risk [9]. Therefore, we define eGFR <90 ml/min/1.73 m^2 as abnormal renal function. Therefore, in this study, we aimed to analyse the incidence and severity of renal impairment at different UA concentrations in patients with gout and to identify relevant risk factors that may predict renal impairment in patients with gout.

Data and methods

Patient inclusion and data information

The diagnosis and treatment information of gout patients at the First Affiliated Hospital of Chengdu Medical College was collected from the information management system from January 2017 to December 2020. The information management system contains the basic information of patients, test items, test results, diagnoses, comorbidities, treatment methods and various costs and other information. The inclusion criteria for gout patients were as follows: (1) complete diagnosis and treatment records; (2) met the 2015 American College of Rheumatology/European Alliance criteria [10]; (3) aged 18–85 years; and (4) no use of nonsteroidal anti-inflammatory drugs, hormones, UA-lowering drugs, Chinese medicine or diuretics that affect renal function in the past 3 months. The above information was obtained from current or previous visit records. The exclusion criteria were as follows: (1) secondary gout caused by trauma, burns, dialysis, myeloproliferative diseases, posttumour chemoradiation, or blood system diseases; (2) kidney disease [chronic glomerulonephritis, nephrotic syndrome, chronic kidney failure, kidney stones, kidney cyst (polycystic kidney), diabetic nephropathy, hypertensive kidney disease, purpura nephritis and lupus nephritis], hypertension, diabetes (diabetes and hypertension may have an influence on renal function. Considering that this project is a cross-sectional study, it is unable to longitudinally observe the effect of blood pressure or blood sugar on renal function. Therefore, this study excludes hypertension and diabetes); (3) rheumatoid arthritis, reactive arthritis, psoriatic arthritis, spinal arthritis or other autoimmune diseases; (4) severe heart and liver diseases, vasculitis and other infectious diseases; (5) history of urinary surgery or recent use of contrast agents affecting renal excretion and (6) other severe lesions affecting the investigation. The above information was obtained from current or previous visit records (Fig. 1). This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Chengdu Medical College (2019CYFYHEC-BA-35).

Data collection

Demographic characteristics (age, sex) and laboratory examination indicators were included in the analysis. The above information was obtained from the information management system of the outpatient and inpatient departments of the First Affiliated Hospital of Chengdu Medical College.

The laboratory examination indicators included white blood cell count (WBC), red blood cell count (RBC), haemoglobin (HGB), platelet count (PLT), neutrophilic granulocyte percentage (NE%), percentage of lymphocytes (LY%), percentage of monocytes (MO%), eosinophil percentage (EO%), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), monocyte count (MONO), eosinophil count (EOS), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin content (MCH), mean corpuscular haemoglobin concentration (MCHC), alanine transaminase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), UA, cystatin C (CysC), triglycerides (TG), cholesterol (CHOL), high-density lipoprotein cholesterol (HDLC), low-density lipoprotein cholesterol (LDLC), apolipoprotein A (APOA), apolipoprotein B (APOB), lipoprotein A (LPA), homocysteine (Hcy), RF, antistreptolysin 'O' (ASO), anti-cyclic citrullinated peptide antibody (CCP), serum-free triiodothyronine (FT3), serum-free tetraiodothyronine (FT4) and thyroid stimulating hormone (TSH). The eGFR was calculated via the CKD-EPI formula.

Grouping of UA levels

UA levels were divided into four groups according to the gout classification criteria (Supplementary Table S1, available at *Rheumatology Advances in Practice* online): Q1: UA ≤ 360 μmol/l; Q2: 360 μmol/l ≤ UA < 480 μmol/l; Q3: 480 μmol/l ≤ UA < 600 μmol/l; and Q4: UA ≥ 600 μmol/l.

Definition of abnormal renal function

The GFR was estimated from the serum creatinine (SCr) level, and an eGFR < 90 ml/min/1.73 m^2 was defined as abnormal renal function [11]. The GFR is the best indicator for assessing human renal function [12, 13]. The primary screening for renal disease includes the GFR estimated by the SCr level and the albuminuria level assessed by the urinary albumin–creatinine ratio [11]. In this study, the CKD-EPI formula was used to estimate the eGFR to assess renal function in patients [14, 15]: a × (SCr/b)c × (0.993) age.

1) Female: a = 144, b = 0.7, c = −0.329 when SCr ≤ 0.7 mg/dL, c = −1.209 when SCr > 0.7 mg/dL;
2) Male: a = 141, b = 0.9, c = −0.411 at SCr ≤ 0.9 mg/dL, c = −1.209 at SCr > 0.9 mg/dL.

Statistical analysis

The data were statistically analysed via IBM SPSS 26.0 software (IBM Corporation, Armonk, NY, USA). Categorical variables are presented as counts or percentages, and continuous variables are presented as the mean ± standard deviation ($\bar{x} \pm s$). For the univariate analysis, we used *t*-tests or chi-square tests ($P < 0.05$). Based on the results of univariate analysis, with renal function abnormality as the dependent

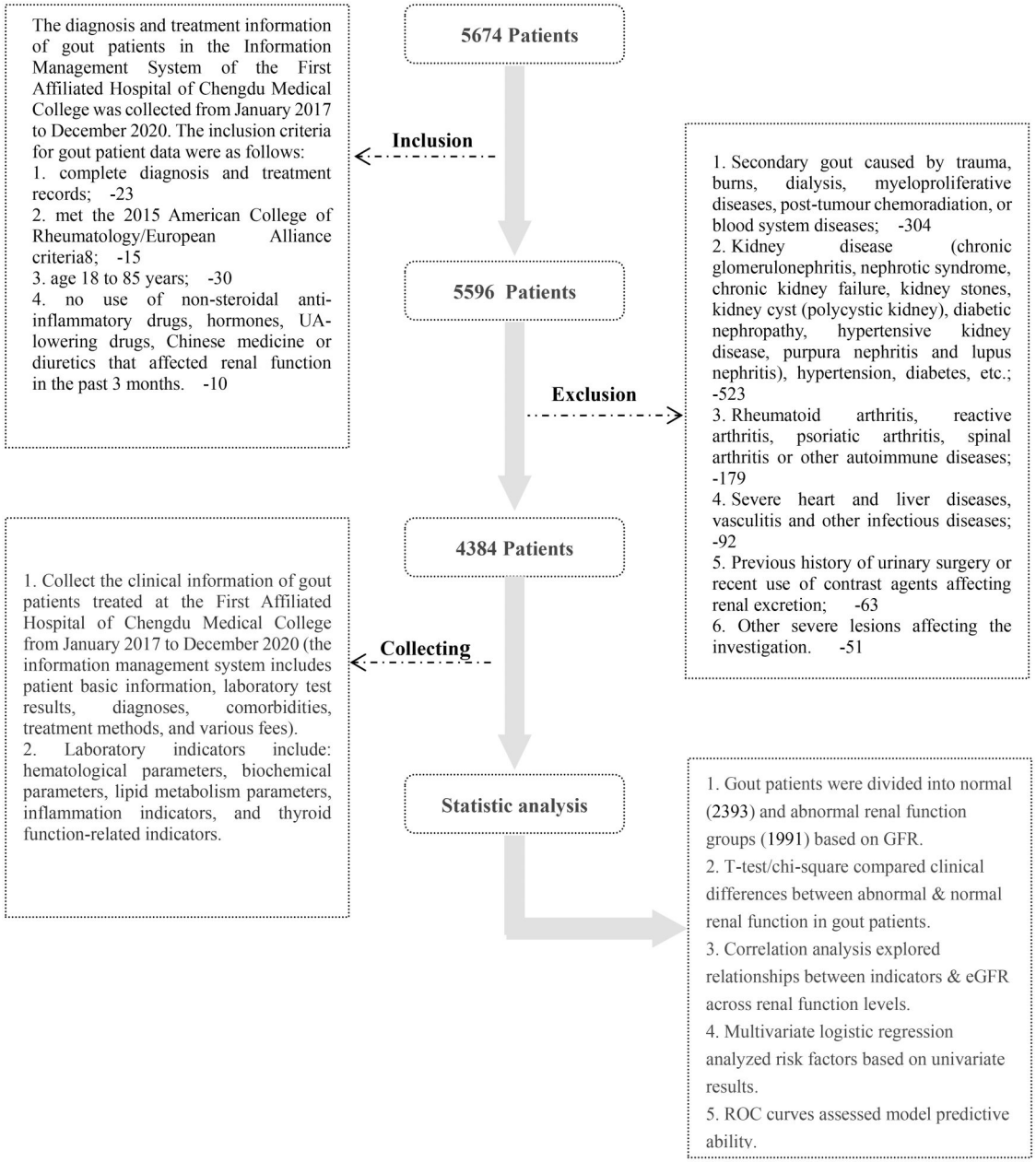

Figure 1. Flow chart of the included patients

variable and relevant indicators as independent variables, where multicategorical variables are used in dummy variable form, they are included in the logistic regression model. Stepwise regression method was used for model fitting, and the receiver operating characteristic (ROC) curve was employed to evaluate the predictive performance of the model. Combining the number and expertise of the included factors, the threshold for retaining biomarkers in multivariate analysis is $P < 0.05$. For the issue of collinearity indicators, we eliminate them by calculating the variance inflation factor (VIF), and any indicator with a VIF value greater than 10 is removed. The *X*-axis of the ROC curve represents 1-specificity, while the *Y*-axis represents sensitivity. The accuracy of the model's predictions determines the area under the ROC curve. The statistical significance was set at 0.05.

Results

General patient data

Overall, 4384 patients were included in the statistical analysis, including their age, sex, routine blood test indicators, biochemical indicators, lipid metabolism indicators,

immunologically related indicators, and thyroid function indicators (Supplementary Table S2, available at *Rheumatology Advances in Practice* online).

Comparison of clinical characteristics and laboratory indicators between the groups with normal and abnormal renal function among patients with gout

RBC, HGB, PLT, LY%, ALC, HCT, MCH, MCHC, ALT, TG, CHOL, LDLC, APOA, APOB and FT3 were significantly lower among the patients in the abnormal renal function group than among those in the normal renal function group ($P < 0.05$); female sex, age, NE%, MO%, ANC, MONO, MCV, BUN, UA, CysC, LPA, Hcy, FT4 and TSH were significantly greater among the patients in the abnormal renal function group than among those in the normal renal function group ($P < 0.05$; Table 1).

Risk factor analysis of patients with gout

Following the univariate analysis and exclusion of collinearity indicators, renal function was used as the dependent variable, with sex, age, HGB, PLT, NE%, LY%, MO%, ANC, ALC, ALC, MCH, MCHC, ALT, BUN, UA, CysC, TG, CHOL, LDLC, APOA, APOB, LPA, Hcy, FT3, FT4 and TSH as the independent variables, and the qualitative factors were included in the multivariate logistic regression model and model fitting by stepwise regression. Age, ALC, CysC, Hcy and TSH remained risk factors for abnormal renal function in gout patients; age, CysC, Hcy and TSH were risk factors for abnormal renal function in gout patients and ALC was a protective factor (Fig. 2).

After applying age, ALC, CysC, Hcy and TSH individually or in combination for the identification of renal dysfunction in gout patients, the combined prediction had greater value. The area under the ROC curve (AUC) was 0.912, with a sensitivity of 77.5% and a specificity of 90.9% (Fig. 3).

Risk factor analysis of gout patients with renal function abnormalities in subgroups with different UA levels

The gout patients were divided into four groups according to the quartiles of their UA levels, and the average eGFRs in the Q1–Q4 groups were 95.07 ml/min/1.73 m^2, 90.06 ml/min/1.73 m^2, 88.79 ml/min/1.73 m^2, and 85.21 ml/min/1.73 m^2, respectively. The analysis results revealed that the eGFR of the Q1 group was significantly greater than that of the other three groups and that the eGFR of the Q4 group was significantly lower than that of the other three groups ($P < 0.001$). There was no significant difference in the eGFR between the Q2 and Q3 groups ($P > 0.05$). The proportions of patients with abnormal renal function in the Q1–Q4 groups were 35.2%, 45.2%, 47% and 51.1%, respectively. The χ^2 results revealed that the proportion of patients with abnormal renal function in the Q1 group was significantly lower than that in the Q2, Q3 and Q4 groups ($P < 0.001$). There were no significant differences among the Q2, Q3 and Q4 groups ($P > 0.05$). The proportion of patients with abnormal renal function generally increased with increasing UA levels (Fig. 4).

According to the univariate results and excluding collinearity indicators, multivariate binary logistic regression analysis was conducted for the Q1–Q4 groups. The results revealed that age and CysC were risk factors for gout combined with abnormal renal function in the Q1 group. In the Q2 group, age and CysC were risk factors for gout combined with abnormal renal function, and FT3 was a protective factor. In the Q3 group, age, CysC and Hcy were risk factors for gout associated with abnormal renal function, and ALC was a protective factor. In the Q4 group, age and CysC were risk factors for gout combined with abnormal renal function (Fig. 5).

Table 1. Comparison of clinical characteristics between the NRF and the ARF

Categories	NRF (2393) $\bar{x} \pm s$(%)	ARF (1991) $\bar{x} \pm s$(%)	t/χ^2	*P*
Gender			**16.15**	**<0.001**
Female	8.80%	12.60%		
Male	91.20%	87.40%		
Age	**42.54 ± 13.55**	**62.62 ± 14.74**	**−46.95**	**<0.001**
WBC	7.98 ± 2.86	8.03 ± 3.29	−0.424	0.671
RBC	**4.95 ± 0.7**	**4.44 ± 0.84**	**17.427**	**<0.001**
HGB	**147.05 ± 20.6**	**130.96 ± 25.74**	**21.632**	**<0.001**
PLT	**199.43 ± 72.88**	**177.50 ± 80**	**7.545**	**<0.001**
NE%	**65.91 ± 10.95**	**70.19 ± 17.22**	**−9.248**	**<0.001**
LY%	**24.62 ± 9.76**	**20.30 ± 9.87**	**13.877**	**<0.001**
MO%	**7.30 ± 2.11**	**7.55 ± 2.44**	**−3.404**	**0.001**
EO%	1.77 ± 1.6	1.89 ± 2.25	−1.948	0.052
ANC	**5.43 ± 2.71**	**5.89 ± 3.28**	**−4.809**	**<0.001**
ALC	**1.82 ± 0.71**	**1.50 ± 0.73**	**14.293**	**<0.001**
MONO	**0.58 ± 0.26**	**0.60 ± 0.29**	**−2.434**	**0.015**
EOS	0.13 ± 0.11	0.14 ± 0.17	−1.804	0.071
HCT	**44.01 ± 5.65**	**39.91 ± 7.21**	**19.852**	**<0.001**
MCV	**90.38 ± 6.98**	**91.46 ± 7.95**	**−4.549**	**<0.001**
MCH	**30.18 ± 2.86**	**29.98 ± 3.18**	**2.102**	**0.036**
MCHC	**333.62 ± 14.34**	**327.24 ± 16.38**	**13.032**	**<0.001**
ALT	**44.17 ± 41.09**	**36.36 ± 51.16**	**5.017**	**<0.001**
AST	31.17 ± 27.71	33.37 ± 45.03	−1.745	0.081
BUN	**5.15 ± 2.18**	**7.27 ± 3.68**	**−22.472**	**<0.001**
UA	**478.77 ± 130.08**	**505.26 ± 127.59**	**−6.774**	**<0.001**
CysC	**8.95 ± 1.66**	**13.47 ± 4.27**	**−44.493**	**<0.001**
TG	**2.52 ± 2.25**	**2.08 ± 1.77**	**5.740**	**<0.001**
CHOL	**4.74 ± 1.09**	**4.39 ± 1.18**	**8.045**	**<0.001**
HDLC	1.18 ± 0.34	1.16 ± 0.35	1.698	0.090
LDLC	**2.83 ± 0.89**	**2.55 ± 0.91**	**8.159**	**<0.001**
APOA	**1.26 ± 0.30**	**1.23 ± 0.30**	**2.727**	**0.006**
APOB	**0.94 ± 0.70**	**0.85 ± 0.26**	**4.226**	**<0.001**
LPA	**186.28 ± 229.82**	**242.23 ± 324.19**	**−5.175**	**<0.001**
Hcy	**15.90 ± 10.37**	**18.84 ± 9.47**	**−7.687**	**<0.001**
FT3	**5.58 ± 1.06**	**5.04 ± 1.09**	**8.43**	**<0.001**
FT4	**11.78 ± 2.09**	**12.27 ± 3.01**	**−3.30**	**0.001**
TSH	**2.18 ± 1.84**	**3.23 ± 5.52**	**−4.58**	**<0.001**

White blood cell count (WBC), red blood cell count (RBC), haemoglobin (HGB), platelet count (PLT), neutrophil percentage (NE%), lymphocyte percentage (LY%), monocyte percentage (MO%), absolute lymphocyte value (ALC), absolute neutrophil count value (ANC), monocyte count (MONO) in the group with renal dysfunction haematocrit (HCT), mean corpuscular volume (MCV), mean erythrocyte haemoglobin content (MCH), mean erythrocyte haemoglobin concentration (MCHC), alanine aminotransferase (ALT), blood urea nitrogen (BUN), blood uric acid (UA), cystatin C (CysC), triglycerides (TG), cholesterol (CHOL), low-density lipoprotein cholestasis (LDLC), apolipoprotein A (APOA), apolipoprotein B (APOB), lipoprotein A (LPA), homocysteine (Hcy), serum triiodothyronine (FT3), serum-free tetraiodothyronine (FT4), thyrotropin (TSH) in the group with abnormal renal function were significantly different from those in the group with normal renal function ($P < 0.05$; indicated with bold text). NRF: normal renal function group; ARF: abnormal renal function group.

Discussion

In recent years, the prevalence and incidence of gout have been increasing annually, and the age trend indicates that the

variable	*B*	*SE*	*Wald*	*OR(95%CI)*	*P*
constant	-9.18	0.76	145.71	0.00	< 0.001
TSH	0.08	0.04	3.87	1.08(1.00~1.17)	0.049
ALC	-0.35	0.16	4.71	0.71(0.52~0.97)	0.030
CysC	0.54	0.06	92.63	1.72(1.54~1.92)	< 0.001
Hcy	0.02	0.01	4.86	1.02(1.00~1.04)	0.028
Age	0.06	0.01	69.48	1.06(1.05~1.08)	< 0.001

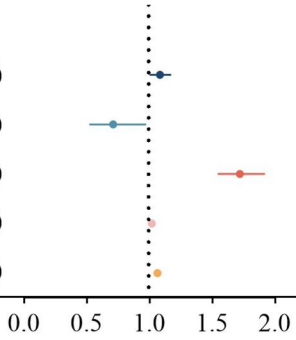

Figure 2. Logistic regression analysis of risk factors related to abnormal renal function in patients with gout. Age, cystatin C (CysC), homocysteine (Hcy), and thyroid stimulating hormone (TSH) were risk factors for gout with abnormal renal function; and absolute lymphocyte count (ALC) was a protective factor. The included variables were gender, age, haemoglobin (HGB), platelet count (PLT), neutrophil percentage (NE%), percentage lymphocytes (LY%), percentage monocytes (MO%), absolute neutrophil count (ANC), ALC, mean red cell haemoglobin content (MCH), mean cell haemoglobin concentration (MCHC), alanine aminotransferase (ALT), blood urea nitrogen (BUN), serum urate (UA), CysC, triglycerides (TG), cholesterol (CHOL), low-density lipoprotein cholesterol (LDLC), apolipoprotein A (APOA), apolipoprotein B (APOB), lipoprotein A (LPA), Hcy, serum-free triiodothyronine (FT3), serum-free tetraiodothyronine (FT4) and TSH

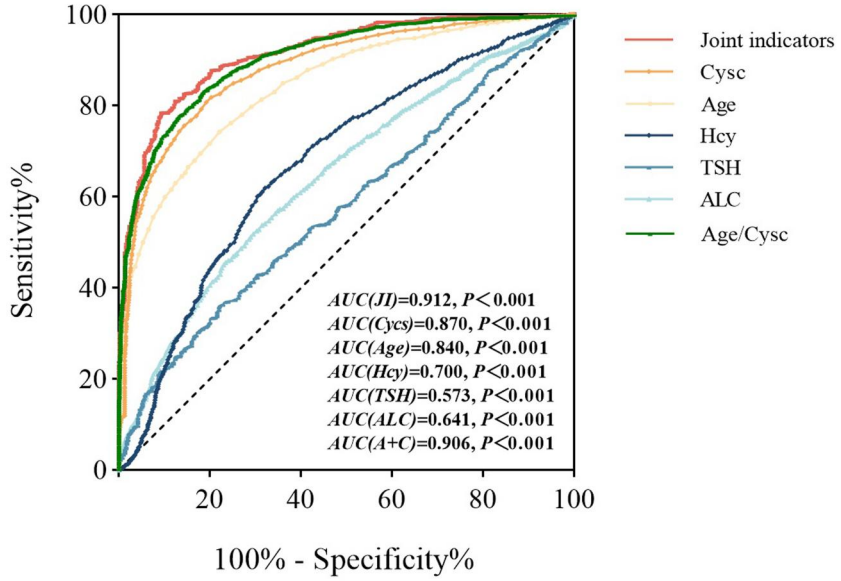

Figure 3. Receiver operating characteristic (ROC) curves predicted by age, absolute lymphocyte count (ALC), cystatin C (CysC), homocysteine (Hcy) and thyroid stimulating hormone (TSH) alone and jointly. The combined prediction of age, ALC, CysC, Hcy and TSH yielded an area under the ROC curve (AUC) of 0.912, with a sensitivity of 77.5% and specificity of 90.9%. The AUC for CysC was 0.87, for age was 0.84, for Hcy was 0.7, for TSH was 0.573 and for ALC was 0.641

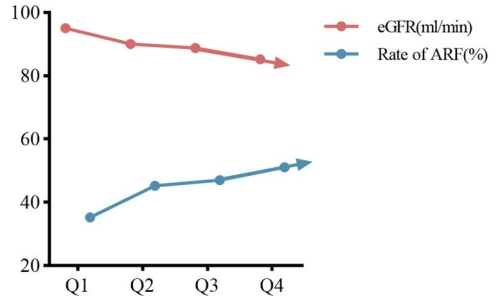

Figure 4. Proportion of abnormal renal function (ARF) at different serum urate levels and trend plot of mean eGFR level. The proportion of ARF increases with serum urate levels. Rate of ARF: proportion of abnormal renal function; eGFR: estimated glomerular filtration rate

average age of patients with gout is decreasing, which places a heavy economic burden on patients [3, 16]. Gout affects the function of joints, and abnormal UA metabolism and persistent hyperuricaemia are associated with the occurrence of multiple types of systemic damage [3]. In the pathogenesis of gout, renal damage is highly prevalent, and some studies have shown that at autopsy, almost all patients with gout exhibit some degree of renal damage, including glomerular sclerosis, arteriolar sclerosis, and interstitial fibrosis [17]. However, in the early stage of renal function impairment, patients often have no specific manifestations [8]. In this study, an eGFR <90 ml/min/1.73 m^2 was defined as abnormal renal function, which is highly important for the early prevention of CKD.

Group	Variable	*B*	*SE*	*Wold*	*OR(95%CI)*	*P*
Q1	CysC	0.51	0.13	15.38	1.67(1.30~2.16)	<0.001
	Age	0.06	0.02	8.82	1.06(1.02~1.11)	0.003
Q2	FT3	-0.42	0.19	4.76	0.66(0.46~0.96)	0.029
	CysC	0.44	0.10	19.90	1.55(1.28~1.88)	<0.001
	Age	0.09	0.02	29.59	1.09(1.06~1.12)	<0.001
Q3	Hcy	0.04	0.02	3.94	1.04(1.00~1.08)	0.047
	CysC	0.56	0.11	25.04	1.75(1.41~2.18)	<0.001
	ALC	-1.04	0.34	9.43	0.35(0.18~0.69)	0.002
	Age	0.06	0.01	18.72	1.06(1.03~1.09)	<0.001
Q4	CysC	0.58	0.13	21.17	1.79(1.40~2.30)	<0.001
	Age	0.05	0.02	8.27	1.05(1.02~1.09)	0.004

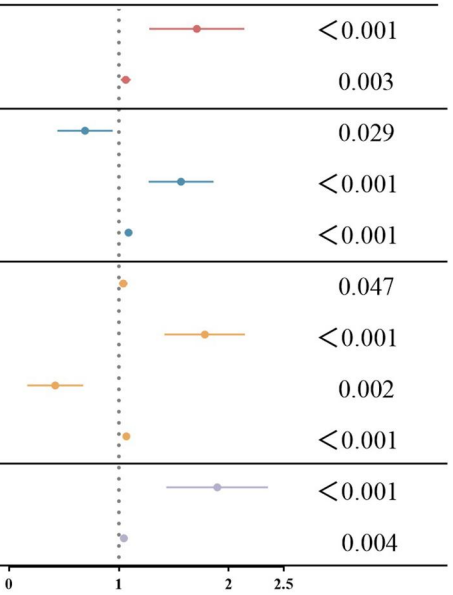

Figure 5. Logistic regression analysis of risk factors related to renal function abnormalities in patients with gout with different serum urate levels. Age and cystatin C (CysC) were risk factors for gout combined with abnormal renal function in the Q1 group. In the Q2 group, age and CysC were risk factors for gout combined with abnormal renal function, and serum-free triiodothyronine (FT3) was a protective factor. In the Q3 group, age, CysC and homocysteine (Hcy) were risk factors for gout associated with abnormal renal function, and absolute lymphocyte count (ALC) was a protective factor. In the Q4 group, age and CysC were risk factors for gout combined with abnormal renal function. Variables include: gender, age, haemoglobin (HGB), platelet count (PLT), neutrophil percentage (NE%), percentage lymphocytes (LY%), percentage monocytes (MO%), absolute neutrophil count (ANC), ALC, mean corpuscular haemoglobin content (MCH), mean corpuscular haemoglobin concentration (MCHC), alanine transaminase (ALT), blood urea nitrogen (BUN), serum urate (UA), cystatin C (CysC), triglycerides (TG), cholesterol (CHOL), low-density lipoprotein cholesterol (LDLC), apolipoprotein A (APOA), apolipoprotein B (APOB), lipoprotein A (LPA), Hcy, FT3, serum-free tetraiodothyronine (FT4) and thyroid stimulating hormone (TSH)

Studies have confirmed that the relationship between gout and the risk of developing CKD is bidirectional, and although reduced renal function can precede the development of gout, gout can also have adverse effects on renal function [18, 19]. Our results revealed that the proportion of patients with renal function abnormalities reached 45.4%, and the proportion of patients with renal function abnormalities gradually increased with age.

The causes of abnormal renal function in gout patients in the present study may be related to the following factors: (1) increased blood UA levels, UA excretion aggravating the kidney burden, or the deposition of urate crystals in the kidney, causing kidney stones, interstitial nephritis and acute and chronic renal failure; (2) kidney injury may be mediated through the activation of the renin–angiotensin–aldosterone system, which can mediate oxidative stress, cause mitochondrial dysfunction, promote vascular smooth muscle proliferation, damage endothelial cells, affect renal cell phenotypic transformation, stimulate inflammation and the immune response, and promote the occurrence and development of CKD [20]; (3) continuous hyperuricaemia promotes the development of hypertension, and hypertension further promotes kidney injury [21]. Current studies on the relationship between UA levels and renal function are not uniform, and some studies have shown a strong positive association between elevated UA levels and the risk of developing CKD [22, 23], which is a moderate independent risk factor for developing nephropathy in the general population in the USA [19]. Other studies have concluded that the opposite is true. Studies published in the New England Journal of Medicine in 2020 indicated that using allopurinol to lower UA levels does not have clinically significant benefits for kidney outcomes, including the progression of CKD [24–26]. Our study showed through univariate analysis that increased UA was associated with abnormal renal function in patients with gout, but after multivariate analysis, the UA level was no longer a risk factor for abnormal renal function in patients with gout. We further stratified the analysis of UA and showed that the proportion of patients with abnormal renal function in the Q4 group was significantly greater, whereas the proportion of patients with abnormal renal function in the Q1 group was significantly lower, suggesting that controlling UA at normal or slightly low (UA $\leq$ 360 μmol/l) levels may be more beneficial for protecting renal function.

Numerous studies have confirmed that age is a risk factor [27, 28]. Our study revealed that age was a risk factor for gout combined with abnormal renal function, which coincided with the findings of existing studies. Hcy is known to be a nonessential amino acid, an important intermediate formed by methionine metabolism, and is metabolized by remethylation and transsulfuration [29]. Clinical research indicates that increased Hcy is causally linked to renal impairment and further CKD [30–35]. Multivariate logistic regression analysis revealed that Hcy was a risk factor for abnormal renal function in gout patients. These findings suggest that damage can be indirectly predicted by analysing changes in Hcy levels during the diagnosis and treatment of gout.

CysC, a cysteine protease inhibitor in humans, is synthesized at a relatively constant rate within all nucleated cells

and is freely filtered by the glomerulus, where it is reabsorbed and catabolic in the proximal tubule [36]. CysC is a sensitive indicator for the early diagnosis of renal damage [37–42]. In this study, the serum CysC level was a risk factor for gout combined with abnormal renal function, suggesting that dynamic observation of the serum CysC level could aid in the early diagnosis of abnormal renal function.

TSH, which is secreted by the adenohypophysis and is a key glycoprotein hormone regulated by the hypothalamic–pituitary–thyroid axis, is a sensitive indicator of thyroid function [43, 44]. It has been shown that increased TSH levels are associated with a decreased GFR and the prevalence of CKD [45–47]. Our results revealed that TSH is a risk factor for abnormal renal function in patients with gout, which is consistent with the above findings and suggests that TSH can be used as an important predictor of abnormal renal function in the clinical diagnosis and treatment of gout.

Previous studies have demonstrated a correlation between lymphocyte counts and the risk of developing CKD [48–50]. According to Kim and Kim, the ALC may be related to the progression of CKD and that a lower relative lymphocyte count is independently associated with the rapid progression of CKD [50]. Our study revealed that the ALC is independently and inversely associated with renal dysfunction in gout patients, suggesting that renal function can be indirectly predicted in gout patients by evaluating the ALC.

In our current study, we further analysed the relationships between renal function and relevant clinical laboratory indicators under different UA levels. The results revealed that the proportion of patients with abnormal renal function in the Q1 group was significantly lower than that in the Q2, Q3 and Q4 groups. Multivariate binary logistic regression analysis revealed that age and CysC were risk factors for gout combined with abnormal renal function in the Q1 group. In the Q2 group, age and CysC were risk factors for gout combined with abnormal renal function, and FT3 was a protective factor. In the Q3 group, age, CysC and Hcy were risk factors for gout associated with abnormal renal function, and the ALC was a protective factor. In the Q4 group, age and CysC were risk factors for gout combined with abnormal renal function. The results of this study further suggested that the proportion of patients with abnormal renal function increased significantly with increasing UA levels and that age and CysC were always independent risk factors associated with gout at different UA levels. These results suggest that in the clinical diagnosis and treatment of gout, we should pay close attention to changes in CysC levels in gout patients, especially in elderly individuals and those with a long course of gout. Active UA-lowering and treatment standards should be used to minimize renal damage due to gout.

In conclusion, our study revealed that sex, age, HGB, PLT, NE%, ALC, MONO, EOS, MCH, MCHC, ALT, BUN, UA, CysC, TG, CHOL, LDLC, LPA, Hcy, FT3, FT4 and TSH were associated with abnormal renal function in patients with gout; age, Hcy, CysC and TSH were found to be independent risk factors for renal abnormalities in patients with gout; and the ALC was found to be an independent protective factor against renal abnormalities in patients with gout. Moreover, this study revealed that the indicators associated with abnormal renal function varied at different UA levels. This finding indicates that the UA level of gout patients fluctuates between 360 mmol/l and 600 mmol/l, which may require clinicians to pay more attention to the multisystemic laboratory examination of patients to comprehensively judge renal function, identify renal function abnormalities in a timely manner and reasonably protect renal function. However, this study has several limitations. First, this was a cross-sectional study in which all the indicators were measured only once; therefore, causality could not be verified, and the results were inevitably disturbed by experimental instruments, human factors and some confounding bias. Second, this was a single-centre study subject to selection bias. Third, the study included only age, sex and important laboratory indicators, whereas BMI, smoking status, diet structure and alcohol intake were not included. Fourth, in the stratified multivariate binary logistic regression analysis, some sample sizes were too small because of the absence of some indicators. Therefore, based on this study's findings, a more advanced prospective study can be carried out in the future, which is expected to further clarify the risk factors for abnormal renal function in patients with gout.

Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

Data availability

Data are available upon reasonable request to the corresponding author. All data relevant to this study are included in the article.

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