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A retrospective study of the association between serum uric acid and risk of coronary heart disease complicated with different types of chronic heart failure

Lei Yu[1,2*], Jianbin Sun[1] and Xinguang Liu[2*]

Abstract

Heart failure (HF) is a terminal stage of cardiovascular diseases, classified based on ejection fraction. Serum uric acid (SUA) has been implicated in the pathogenesis and progression of coronary artery disease (CAD) with HF, yet its predictive value remains unclear. This study aimed to evaluate the predictive role of SUA in the progression of HF in CAD patients and its potential to differentiate HF types. A retrospective analysis was conducted on 342 CAD patients, including 29 with CAD alone and 313 with CAD complicated by varied HF types. Biochemical parameters and HF severity were assessed, and logistic regression analyses were performed to identify independent predictors of HF progression. Significant differences were observed in biochemical parameters, including glutamic–pyruvic transaminase (ALT), glutamic oxalacetic transaminase (AST), alkaline phosphatase (ALP), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), creatine kinase–MB (CK–MB), SUA, lactate dehydrogenase (LDH), myoglobin (MTO), between groups. SUA levels were significantly higher in CAD patients with HF, particularly in those with reduced ejection fraction. Univariate and multivariate logistic regression analyses identified history of hypertension, AST, and SUA as independent predictors of HF progression, with SUA showing the highest odds ratio. In addition, SUA levels were positively correlated with Gensini scores, indicating its association with CAD severity. SUA is a strong predictor of HF progression in CAD patients, especially for patients with HFrEF, which can serve as a diagnostic and prognostic marker for HF progression in CAD patients.

Keywords Coronary artery disease, Ejection fraction, Gensini score, Heart failure, Logistic regression analysis, Serum uric acid

Introduction

Coronary artery disease (CAD), the most common cardiovascular disorder worldwide, is the leading cause of death in western countries in both men and women. Until 2020, more than 1.97 billion CAD patients had been diagnosed, which casts great burden to the public health system and caregivers in both developed and developing countries [1]. Based on the Framingham Heart Study in 1961, more than 200 conventional risk factors associated with CAD have been identified [2–5]. Based on these previous reports, non-conventional risk

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factors of CAD have also been defined, including but are not limited to metabolic syndrome, sleep apnea, depression, anxiety, insufficiency of trace elements, hyperhomocysteinemia, and hyperuricemia [5, 6]. Heart failure (HF) is caused by impaired ventricular filling and/or ejection function, which is characterized by pulmonary and/or systemic congestion and insufficient blood perfusion to organs and tissues [7], and there are nearly 60 million HF patients worldwide. As the terminal stage of various cardiovascular diseases including CAD, HF has become a significant public health burden worldwide. In 2016, HF was classified based on ejection fraction into three groups: the type with preserved ejection fraction (HFpEF) group (LVEF ≥ 50%), the type with mid-range ejection fraction (HFmrEF) group (LVEF 40–49%), and the type with reduced ejection fraction (HFrEF) group (LVEF < 40%) [8].

Of the aforementioned non-conventional risk factors, serum uric acid (SUA) is the ultimate product of purine metabolism, and the dynamic disturbance between the synthesis and elimination of UA will contribute to the elevation of SUA level [9]. Over the last 10 years, there has been a significant global increase in the incidence of hyperuricemia (HUA) due to changing dietary and lifestyle choices. [10]. Numerous additional metabolic variables, including abnormalities of lipid and glucose metabolism, interact with the disturbed metabolism of UA [11, 12]. SUA functions as an antioxidant in plasma and has oxidative and antioxidant effects at normal levels. However, once the SUA level rises above a particular point, it causes a variety of conditions such hypertension, vascular disease, and atherosclerosis [13, 14]. Acute coronary syndrome, chronic coronary syndrome, stroke, and all-cause and CV mortality are only a few of the numerous outcomes in the cardiovascular sector for which SUA is thought to play a significant role in cardiac function [15, 16]. Moreover, a causable relationship between SUA and adverse cardiovascular outcomes was observed via clinical imaging: the higher SUA level contributes positively to Gensini score and CAD severity [17]. Furthermore, greater mortality, the onset of atrial fibrillation, and the development of chronic heart failure (HF) are all linked to the SUA level [18–20]. Though it has been suggested that SUA plays a significant role in the formation of CAD, there is ongoing discussion about whether SUA serves as a risk factor, a diagnostic marker, or an active player in the pathophysiology of CAD with HF. Based on the previous findings, it seemed that SUA has a relatively clear relationships with the occurrence and development of CAD and development of HF. However, in current clinical studies, a direct correlation between SUA and progression of HF in CAD patients is still lacking. Whether SUA can be employed as a diagnostic criterion of HF types in CAD patients also remains uncertain. Given the increased incidence of CAD complicate with HF, a comprehensive analysis of the anticipating potential of SUA for the development of CAD complicated with HF is needed.

In the current study, we hypothesized that SUA could not only serve as a marker representing the development of chronic HF in CAD patients, but could also be employed as a diagnostic criterion for different types of HF in CAD patients. Thus, a retrospectively epidemiological investigation was performed to explore the relationship between the SUA level and the development of CAD complicated with different chronic HF types in our hospital from Dec 2022 to Oct 2023, which aimed to investigate the potential of SUA as an indicator for the anticipation and diagnosis of HF in CAD patients.

Methods

Patients

The current analysis enrolled 342 CAD patients from Dec 2022 to Oct 2023 in Wuhan City No.3 Hospital (Fig. 1). The included CAD patients should meet the following criteria: (1) coronary angiography indicating stenosis of ≥ 50% in one or multiple coronary arteries diagnosed by two experienced clinicians using the GE2100 medical angiography X-ray machine (GE, USA) following the standard protocol of Judkins method; and (2) A history of myocardial infarction. The HF of CAD patients were then diagnosed based on the criteria: (1) presence of typical symptoms and signs of HF; (2) evidence of structural heart disease (e.g., left ventricular hypertrophy, left atrial enlargement) and/or diastolic dysfunction; and (3) echocardiographic examination excluding valvular heart disease, pericardial diseases, hypertrophic cardiomyopathy, and restrictive (infiltrative) cardiomyopathies. The exclusive criteria were as followings: (1) patients with in-stent restenosis, coronary muscle bridge, coronary artery bypass grafting or peripheral atherosclerosis; (2) patients with acute heart failure, severe liver and kidney insufficiency or with long-term diuretics; (3) patients with other structural heart diseases other than CAD; (4) patients with acute and chronic inflammatory diseases, such as hepatitis, enteritis, gastritis, etc.; (5) patients with connective tissue diseases and autoimmune diseases; (6) patients with recent infection, surgery (≤ 6 months), stroke, trauma, etc.; (7) patients with parasitic infection; (8) patients without complete clinicopathological data; (9) patients with malignant tumors and blood diseases; (10) patients with a history of gout or taking uric acid-lowering drugs; and (11) patients with long-term use of liver-protecting drugs and hypolipidemic drugs. All the included patients signed informed consent and possessed complete clinicopathological data. Based on the

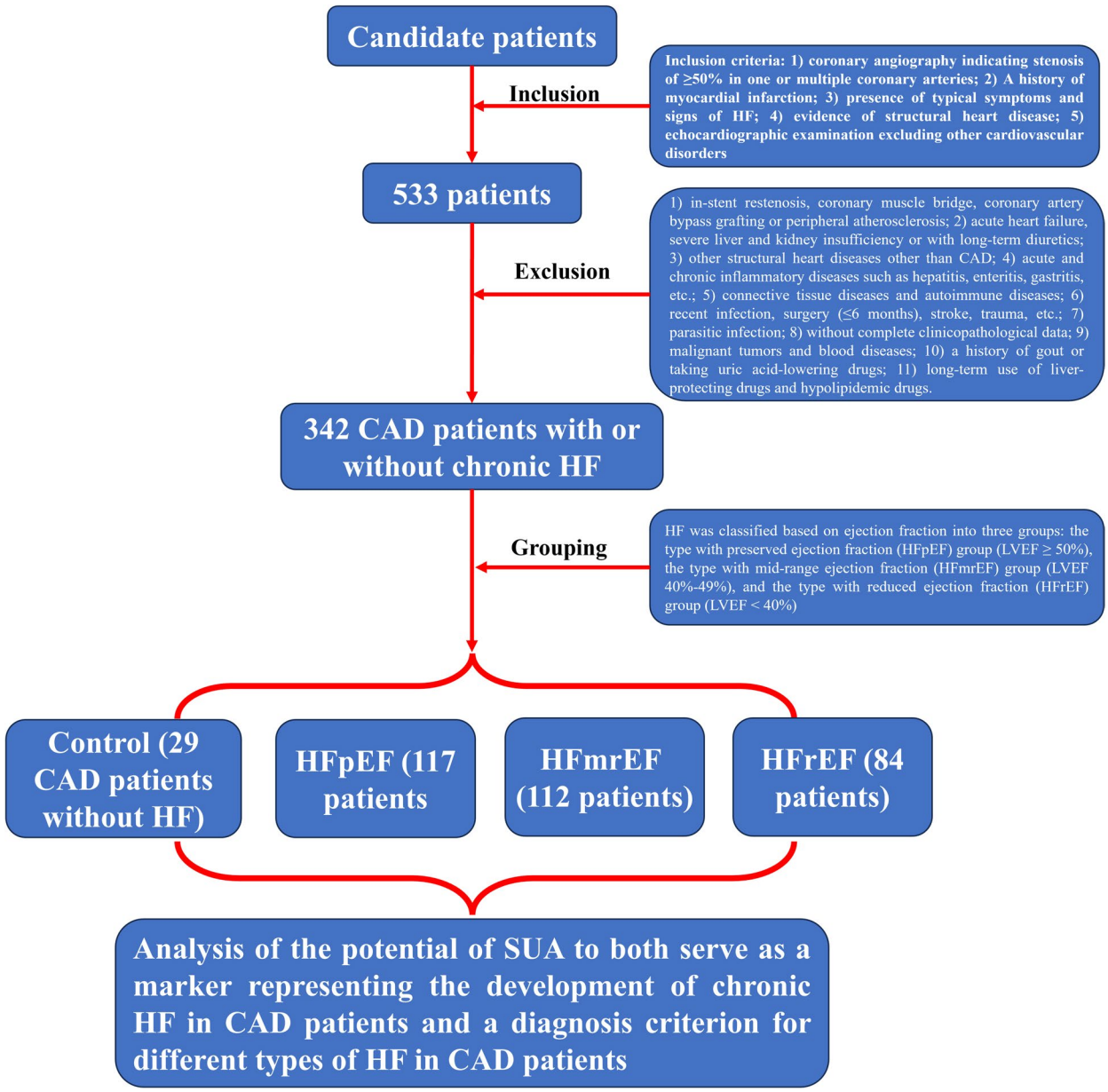

Fig. 1 Flowchart elucidating the inclusion, exclusion, and grouping processes of the current study

aforementioned criteria, the patients were divided into the HFpEF group (117 patients), HFmrEF group (112 patients), HFrEF group (84 patients), and control group (29 CAD patients without HF). All the investigation of the current study was performed under the approval of the ethic committee of REDACTED as well as the Declaration of Helsinki.

Detection of biochemical parameters

The kidney function parameters including SUA, total CO_2 (t-CO_2), creatine (Cr), liver function parameters including glutamic–pyruvic transaminase (ALT), glutamic oxalacetic transaminase (AST), alkaline phosphatase (ALP), and cholinesterase (ChE), blood lipid parameters including total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), and myocardial enzyme including cardiac troponin T (cTnT), creatine kinase–MB (CK–MB), lactate dehydrogenase (LDH), and myoglobin (MTO) were measured using upon the admission of patients in our hospital and deposited for analysis.

Detection of left ventricular ejection fraction (LVEF)

In this study, all echocardiographic examinations were performed by a dedicated specialist with extensive experience in cardiac ultrasound imaging diagnosis. The equipment used for the ultrasonographic evaluations was a Philips IE33 color Doppler ultrasound system (Philips, USA) with a probe frequency range of 2–4 MHz. Cardiac motion, including the movement of valves and ventricular walls, was observed through various probe planes. Patients with severe valvular disease or significant arrhythmias were excluded from the study. For each patient, response indicators were measured over a minimum of three cardiac cycles. After image acquisition and freezing, left ventricular ejection fraction (LVEF) was measured using the Simpson method, with measurements taken between end-diastole and end-systole. The results were then recorded for further analysis. HF was then classified based on LVEF value: the type with preserved ejection fraction (HFpEF) group (LVEF ≥ 50%), the type with mid-range ejection fraction (HFmrEF) group (LVEF 40–49%), and the type with reduced ejection fraction (HFrEF) group (LVEF < 40%).

Gensini score

The classification of CAD was performed following American Heart Association, as shown in Table S1. The CAD patients were then further divided into different groups based on the criteria: mild group, Gensini socre ≤ 9; medium group, 9 < Gensini socre ≤ 49.75; and severe group, Gensini socre > 49.75.

Statistical analysis

Normally distributed continuous data were expressed as mean and standard deviation (mean ± SD), and two independent samples *t* test were used for comparison between the two groups. One-way ANOVA was used for comparison between groups. For continuous data that did not conform to be normal distribution, data were expressed as median (quartile), and rank sum test of two independent samples was used for comparison between two groups, and rank-sum test group for multiple groups was used for comparison between multiple groups. Chi-square tests were used for comparison between groups of categoric data (n, %). The influence factors of CAD with HF were first analyzed using univariate logistic regression analysis, and factors with significant *P* value were then integrated into multivariate logistic regression to further confirm the contributing factors to the progression of HF in CAD patients. Pearson correlation analyses were used for distribution data correlation analysis, and spearman correlation analyses were used for non-normal data correlation analysis. Statistical significance was accepted once the *P* value is smaller than 0.05 after the analysis using GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, California USA, www.graphpad.com).

Results

Clinicopathological information

In the current study, 342 cases were enrolled, which were divided into HFpEF group (117 patients), HFmrEF group (112 patients), HFrEF group (84 patients), and control group (29 patients without HF). Then the clinicopathological information of patients in the four groups were compared, and there were statistical no differences regarding male proportion (59.7% in HFpEF group, 53.6% in HFmrEF group, 51.3% in HFrEF group, and 52.1% in in Control group) ($P > 0.05$), smoking proportion (52.3% in HFpEF group, 47.6% in HFmrEF group, 49.2% in HFrEF group, and 58.6% in in Control group) ($P > 0.05$), history of hypertension (71.6% in HFpEF group, 67.4% in HFmrEF group, 69.2% in HFrEF group, and 68.7% in in Control group) ($P > 0.05$), and history of diabetes mellitus (26.8% in HFpEF group, 27.2% in HFmrEF group, 19.4% in HFrEF group, and 21.7% in in Control group) ($P > 0.05$) among the four groups. The detail information of other clinicopathological information is shown in Table 1, and no significant difference was detected among the groups.

Biochemical parameters

The detection results of biochemical parameters are shown in Table 2. The data showed that the three parameters regarding liver function, including ALT (23.1 ± 3.8 in HFpEF group, 33.2 ± 7.8 in HFmrEF group, 21.5 ± 4.9 in HFrEF group, 21.5 ± 2.9 in Control group), AST (27.7 ± 6.7 in HFpEF group, 32.7 ± 4.3 in HFmrEF group, 29.6 ± 5.9 in HFrEF group, 18.6 ± 3.2 in Control group), and ALP (83.9 ± 13.1 in HFpEF group, 82.8 ± 14.3 in HFmrEF group, 99.6 ± 25.9 in HFrEF group, 80.4 ± 14.7 in Control group), were significantly higher in HFmrEF group ($P < 0.0001$) (Table 2). However, there was no significant difference in ChE between the four groups ($P = 0.23$). The analysis of the blood lipids and blood glucose groups showed that statistical differences were detected regarding TG and HDL-C ($P < 0.0001$) (Table 2), but there was no significant difference regarding parameters, such as TC ($P = 0.34$), LDL-C ($P = 0.48$), and FBG ($P = 0.30$) (Table 2). The analysis results of renal function showed that there was significant difference regarding SUA (379.9 ± 34.5 in HFpEF group, 457.2 ± 44.3 in HFmrEF group, 529.6 ± 65.9 in HFrEF group, 323.6 ± 35.9 in Control group) between the four groups ($P < 0.0001$) and patients in HFrEF had the highest level of SUA. However, there was no significant difference regarding Cr ($P = 0.27$), BUN ($P = 0.33$), and t-CO_2 ($P = 0.86$) (Table 2). In the case of myocardial enzyme spectrum, all the

Table 1 Clinicopathological information

	Control ($n=29$)	HFpEF ($n=117$)	HFmrEF ($n=112$)	HFrEF ($n=84$)	*P* value
Age [median (quantile)]	52.5 (48.6, 56.1)	52.3 (48.4, 58.4)	55.3 (47.4, 59.3)	55.7 (48.4, 58.1)	0.11
Male [*n* (%)]	15 (51.7%)	60 (51.3%)	61 (54.5%)	43 (51.2%)	0.96
Disease history					
Smoking [*n* (%)]	17 (58.6%)	61 (52.1%)	53 (47.3%)	41 (48.8%)	0.70
Drinking [*n* (%)]	5 (17.3%)	23 (19.7%)	24 (21.4%)	17 (20.2%)	0.96
Hypertension [*n* (%)]	20 (68.9%)	84 (71.8%)	75 (66.9%)	58 (69.0%)	0.88
Diabetes mellitus [n (%)]	6 (20.7%)	31 (26.5%)	30 (26.8%)	16 (19.0%)	0.54
COPD [*n* (%)]	5 (17.2%)	16 (13.7%)	16 (14.8%)	11 (13.1%)	0.99
Drug use history					
β-receptor blockers [*n* (%)]	9 (31.0%)	41 (35.1%)	31 (27.6%)	24 (28.5%)	0.63
Hydragogue [*n* (%)]	14 (48.2%)	54 (46.1%)	38 (33.9%)	40 (47.6%)	0.16
Ca^{2+} channel blocker [*n* (%)]	15 (51.7%)	63 (53.8%)	55 (49.1%)	40 (47.6%)	0.82
ACEI or ARBs [*n* (%)]	6 (20.7%)	25 (21.3%)	17 (15.2%)	20 (23.8%)	0.47
Nitrate esters [*n* (%)]	25 (86.2%)	86 (73.5%)	91 (81.3%)	66 (78.5%)	0.99

COPD, chronic obstructive pulmonary disease

Table 2 Difference regarding clinical indicators between two groups

Parameters	Control ($n=29$)	HFpEF ($n=117$)	HFmrEF ($n=112$)	HFrEF ($n=84$)	*P* value
SUA (μmol/L)	306.6 ± 38.8	379.9 ± 34.5	457.2 ± 44.3	529.6 ± 65.9	**< 0.0001**
t-CO_2 (mmol/L)	24.6 ± 3.6	25.6 ± 4.1	23.1 ± 4.5	25.1 ± 3.7	0.86
Cr (μmol/L)	64.7 ± 7.4	66.0 ± 9.5	65.3 ± 11.3	62.1 ± 10.7	0.27
ALT (U/L)	21.5 ± 2.9	23.1 ± 3.8	33.2 ± 7.8	21.5 ± 4.9	**< 0.0001**
AST (U/L)	18.6 ± 3.2	27.7 ± 6.7	32.7 ± 4.3	29.6 ± 5.9	**< 0.0001**
ALP (U/L)	80.4 ± 14.7	83.9 ± 13.1	82.8 ± 14.3	99.6 ± 25.9	**0.0043**
ChE (U/L)	8821 ± 586	8761 ± 668	8681 ± 738	8514 ± 537	0.23
TC (μmol/L)	5.8 ± 1.1	5.9 ± 2.8	4.9 ± 3.3	5.5 ± 3.2	0.34
TG (mmol/L)	1.4 ± 0.6	1.9 ± 0.5	2.9 ± 0.7	2.5 ± 0.4	**< 0.0001**
LDL-C (mmol/L)	2.9 ± 0.4	3.0 ± 0.6	3.3 ± 1.2	3.1 ± 1.5	0.48
HDL-C (mmol/L)	1.2 ± 0.3	1.5 ± 0.2	1.8 ± 0.2	2.1 ± 0.2	**0.0031**
FBG (mmol/L)	5.5 ± 1.3	5.7 ± 1.6	5.4 ± 1.7	5.2 ± 1.8	0.30
cTNT (ng/ml)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	NA
CK–MB (ng/ml)	1.7 ± 0.3	1.9 ± 0.2	2.3 ± 0.1	2.2 ± 0.3	**< 0.0001**
LDH (U/L)	168.9 ± 12.1	186.4 ± 15.5	246.4 ± 24.5	213.2 ± 19.5	**< 0.0001**
MTO (mg/ml)	21.5 ± 3.5	26.5 ± 2.9	33.5 ± 3.7	31.4 ± 2.8	**< 0.0001**

Bold represents statistically significant

parameters, including LDH, CK–MB scores, and MTO showed significant difference between the two groups (Table 2) ($P<0.0001$). The biochemical parameters overall demonstrate that the types of HF in CAD patients were associated with abnormal production of serum indicators.

Risk factor analysis of HF

The results of univariate logistic regression analysis showed factors including, SUA [2.98 (1.93–4.03)], ALT level [0.87 (0.82–0.93)], AST level [0.86 (0.81–0.90)], ALP [0.97 (0.95–0.99)], TG level [0.17 (0.11–0.28)], HDL-C level [0.63 (0.52–0.88)], CK-MB level [0.00 (0.00–0.01)], LDH level [0.92 (0.90–0.94)], and MTO level [0.62 (0.56–0.69)] all contributed to the progression of different HF types (Table 3). Further multivariate logistic regression analysis based on the results of univariate logistic regression analysis identified history of hypertension SUA level [4.84 (3.75–5.95)], AST [0.60 (0.37–0.98)], TG [0.02 (0.00–0.49)], CK–MB [0.00 (0.00–0.04)], LDH [0.81 (0.68–0.97)], and MTO [0.39 (0.21–0.71)] as the independent predictive factor for the progression of

Table 3 Risk factors influencing the onset of EOCAD analyzed by univariate logistic regression analysis

Parameter	OR (95% CI)	*P* value
Age	0.99 (0.96–1.02)	0.51
Smoking	0.78 (0.78–1.33)	0.35
Hypertension	0.49 (0.44–0.62)	0.62
Diabetes mellitus	0.56 (0.42–0.60)	0.81
SUA	1.98 (1.93–2.03)	**< 0.00001**
tCO_2	0.93 (0.91–0.94)	0.45
ALT	0.87 (0.82–0.93)	**< 0.00001**
AST	0.86 (0.81–0.90)	**< 0.00001**
ALP	0.97 (0.95–0.99)	**< 0.00001**
TG	0.17 (0.11–0.28)	**< 0.00001**
HDL-C	0.63 (0.52–0.88)	**0.0004**
CK–MB	0.00 (0.00–0.01)	**< 0.00001**
LDH	0.92 (0.90–0.94)	**< 0.00001**
MTO	0.62 (0.56–0.69)	**< 0.00001**

Bold represents statistically significant

different HF types (Table 4). For patients with hypertension, higher serum level of SUA, AST, TG, CK–MB, LDH, and MTO, the odd to develop HF is higher. Of the different serum parameters, the odd value of SUA was the highest and the *P* value was the lowest (Table 4).

Association between Gensini score and SUA

Spearman correlation analysis of Gensini score showed that the score was in positive relation with SUA (rs = 0.371, *P* = 0.02) (Table 5), but had no obvious relation with AST (rs = 0.011, *P* = 0.88), TG (rs = − 0.131, *P* = 0.09), CK–MB (rs = − 0.045, *P* = 0.55), LDH (rs = − 0.153, *P* = 0.46), and MTO (rs = − 0.082, *P* = 0.29) levels (Table 5), suggesting that SUA could serve as a predictor for the severity of coronary artery lesions in CAD patients.

Table 4 Risk factors influencing the onset of EOCAD analyzed by multivariate logistic regression analysis

Parameter	OR (95% CI)	*P* value
SUA	2.84 (2.75–2.95)	**0.0004**
ALT	0.74 (0.46–1.18)	0.20
AST	0.60 (0.37–0.98)	**0.041**
ALP	1.18 (1.00–1.39)	0.05
TG	0.02 (0.00–0.49)	**0.016**
HDL-C	4.22 (4.05–5.35)	0.17
CK–MB	0.00 (0.00–0.04)	**0.011**
LDH	0.81 (0.68–0.97)	**0.020**
MTO	0.39 (0.21–0.71)	**0.002**

Bold represents statistically significant

Table 5 Correlation analysis regarding serum parameters and Gensini score using Pearson's correlation analysis

Parameter	r	*P* value
SUA	0.377	**0.02**
AST	0.011	0.88
TG	− 0.131	0.09
CK–MB	− 0.045	0.55
LDH	− 0.153	0.46
MTO	0.082	0.29

Bold represents statistically significant

Discussion

The current study explored the relation between SUA and progression of different types of CAD complicated with HF. The data showed that SUA, AST, TG, CK–MB, LDH, and MTO could be potential predictive factors for the progression of HF, and of the different parameters, the odd value of SUA is the highest, suggesting that SUA might provide more valuable information for the severity of CAD with HF. However, the current excluded patients with severe chronic heart failure, severe liver and kidney insufficiency or with long-term diuretics, and thus the close relation of SUA seems to be more likely applied to CAD patients complicated with chronic HF, which is independent of renal function and negatively correlated with ejection fraction.

HF refers to a condition where the heart's systolic function and/or diastolic function is impaired, leading to an inability to adequately pump the venous return from the heart. This results in blood congestion in the venous system and insufficient perfusion in the arterial system, causing a syndrome of circulatory dysfunction. The main manifestations of this syndrome include pulmonary congestion and venous congestion. Almost all cardiovascular diseases eventually lead to the development of heart failure, including CAD, cardiomyopathy, hemodynamic overload, and myocardial damage caused by various physical and chemical factors [21]. According to relevant data, approximately 65% of HF cases are caused by CAD [22]. The primary reason CAD leads to chronic HF is that myocardial ischemia results in myocardial cell death, which subsequently triggers myocardial remodeling. Due to the prolonged state of ischemia, the myocardial tissue cannot receive sufficient oxygen supply, leading to nutritional disorders and atrophy. Eventually, this results in the proliferation of myocardial fibrous tissue and a decrease in myocardial compliance.

The traditional diagnosis "gold standard" for CAD is coronary angiography, but various complications, such as allergic reaction, acute heart failure and shock,

contrast-induced nephropathy etc., are associated with the operation due to its invasiveness [23], which all contributes to great physical and psychological issues affecting the life quality for patients. Therefore, it is necessary to establish a novel diagnostic criterion that is both non-invasive and inexpensive with low risk. Smoking, gender, dyslipidemia, diabetes, and hypertension are well-characterized risk factors for traditional CAD [19]. For instance, serum bilirubin levels were associated with troponin positivity in patients with non-ST-segment elevation acute coronary syndrome [24]. However, whether these factors also contribute to the progression of HF is not fully assessed. Currently, various biochemical parameters have been shown to be related to the severity of different CAD including those complicated with HF, such as concentrations of NT-proBNP, glycated hemoglobin, Hcy, Cys C, SUA, etc. [23]. Similar results were also come up with in the current study, the retrospective analysis of 342 patients with CAD showed that higher serum level of AST and SUA have higher odd to develop HF in CAD patients. In addition, of the different parameters, the contribution to the progression of HF by SUA seems to outweight others.

Regarding the association between SUA and chronic HF, it is reported that patients with chronic HF are often associated with hyperuricemia, and 56% of patients with HF caused by ischemic cardiomyopathy, dilated cardiomyopathy, hypertensive heart disease, and valvular heart disease have a SUA level > 416.5 μmol/L [25]. For every 59.5 μmol/L increase in SUA, the mortality rate of HF increases by 13% [20], which is negatively correlated with LVEF as well. Moreover, SUA levels are also related to the ejection fraction in HF patients: higher uric acid levels may serve as an independent risk factor for heart failure and are a strong independent predictor of poor prognosis in moderate to severe chronic HF patients [26–28]. A linear relationship between SUA levels and mortality in patients with moderate to severe heart failure, indicating that SUA levels may help predict the prognosis of these patients [29]. More recent research indicates a close association between HUA and CAD with chronic HF: elevated uric acid levels are strongly correlated with the worsening symptoms, reduced exercise tolerance, and increased mortality in CAD with chronic HF patients [30, 31]. Based on these findings, SUA has a relatively clear negative impact on the occurrence and development of CAD. However, in current clinical studies, there is still insufficient in-depth research on whether there is a direct correlation between SUA and progression of HF. To verify the conclusion of these previous studies, the current study performed a retrospective analysis with the information collected from 324 CAD patients, and the data showed that SUA level was significantly higher in CAD patients with HF than patients without HF, especially for patients of HFrEF type. Moreover, both univariate and multivariate logistic regression analyses has identified SUA as the independent risk factor for CAD with HF, conforming that SUA could serve as a predictor for the onset of HF in CAD patients.

Uric acid (UA) is the end product of purine metabolism in the human body, which is produced by the xanthine oxidase (XO), an enzyme that is ubiquitous produced in cardiovascular system and is present in various organ [32, 33]. XO in myocardium is mostly localized in capillary endothelial cells, which can activate mitochondrial reactive oxygen species (ROS) by granulocytes and activate mitochondrial reactive oxygen species (ROS) activity in the event of cardiac reperfusion injury. Thus, the process of the production of SUA by XO enzymes contributes to the onset of CAD: SUA acts as a pro-oxidant that promotes lipoprotein oxidation by inducing lipids peroxidation, which promotes platelet aggregation and the formation of SUA crystals, causing the formation of coronary thrombosis and damages to the arterial intima [16]. SUA has also been implicated in endothelial dysfunction by reducing nitric oxide (NO) bioavailability, which is essential for vascular relaxation and protection against atherosclerosis [34]. In addition, both free UA and urate crystals can induce inflammation by activating macrophages [35], while soluble uric acid activates the NLRP3 inflammasome, thereby promoting inflammation [36]. Elevated SUA promotes monocyte chemoattractant protein-1 (MCP-1) synthesis and nuclear factor-kappa B (NF-κB) activation in vascular smooth muscle cells, which in turn triggers an inflammatory response in the intima [37]. These inflammatory responses can cause endothelial cells to synthesize and release endothelin, plasminogen activator inhibitor, and other coagulation factors, further increasing platelet activity, activating the coagulation system, and promoting platelet adhesion and aggregation on the vessel walls. Apart from causing endothelial dysfunction, oxidative stress, and inflammatory responses, SUA can contribute to vascular smooth muscle cell proliferation, an essential process in the development of intimal thickening and atherosclerotic plaques [34]. These mechanisms collectively underlie the involvement of SUA in the pathogenesis of CAD and HF, and together with our findings, the high SUA can also serve as a promising predictor for the progression of CAD with different types of chronic HF, which forms a supplement to the future clinical application of SUA in the diagnosis of cardiovascular disorders. Nevertheless, the value of SUA in predicting HF progression in CAD patients lacks clinical verification and its predictive value appears to be less robust than that of NT-proBNP.

Compared with SUA, NT-proBNP is a well-established biomarker for diagnosing and prognosticating HF and has demonstrated superior predictive accuracy for HF outcomes. For instance, a study found that while SUA improved HF prediction beyond conventional risk factors, it did not add significant prognostic value when NT-proBNP was already considered [38]. Regarding inflammatory markers, such as high-sensitivity C-reactive protein (hs-CRP), these markers indicate systemic inflammation, which plays a role in the pathophysiology of HF. However, just like SUA, the predictive value of hs-CRP is generally inferior to that of NT-proBNP [39]. In clinical practice, NT-proBNP remains the benchmark biomarker for HF diagnosis and prognosis, with SUA and inflammatory markers serving as supplementary indicators that may provide additional context in specific scenarios [39–41]. Thus, the application of SUA in clinical practice might serve as a non-invasive supplement to the measurement of NT-proBNP or a quick screening strategy in the diagnosis of HF in CAD patients.

Collectively, the current analysis provided additional information for assessing the predictive potential of SUA for the onset and progression of HF in CAD patients: the results showed of various factors, SUA seems to have a closer relation to the pathogenesis of HF and could be employed as a potential predictor for the clinical diagnosis of HF in CAD patients. The results will facilitate the nursing of the CAD patients with HF by accurately determining the stage of the disorder. However, the study cohort in the current study relatively small and only contained patients from one center. In addition, the cohort in the current study excluded patients with acute heart failure, and thus might be only applied to CAD patients with chronic HF symptoms. To address those issues, future comprehensive studies with larger sample size is still needed to verify the role of SUA in the prediction and treatment of CAD with HF as well as other CADs.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-025-02403-y.

Additional file 1.

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Lei Yu performed conceptualization, data curation, formal analysis, and writing—original draft, review & editing; Jianbin Sun and Xinguang Liu performed data curation.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
All the investigation of the current study was performed under the approval of the ethic committee of Wuhan City No.3 Hospital as well as the Declaration of Helsinki.

Competing interests
The authors declare no competing interests.

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