Original Article

# Association of Serum Uric Acid Levels with Severity of Coronary Artery Disease and Heart Failure

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## Abstract

**Background:** Serum uric acid (SUA) has been implicated in oxidative stress, endothelial dysfunction, and myocardial impairment. However, its association with angiographic coronary artery disease (CAD) severity and heart failure (HF) requires further investigation. This study aimed to evaluate the relationship between SUA concentrations, CAD severity, and HF. **Material and Methods:** In this observational study, 150 patients were classified into mild, moderate, and severe CAD groups (50 per group). Clinical characteristics, biochemical parameters, coronary angiographic findings, and left ventricular ejection fraction (LVEF) were assessed. CAD severity was evaluated using the SYNTAX score. Associations were examined using correlation analysis and multivariable regression, with adjustment for selected cardiovascular risk factors and renal function. **Results:** Mean SUA concentration was 6.8 ± 1.6 mg/dL and increased progressively across the mild, moderate, and severe CAD groups (5.7 ± 1.2, 6.6 ± 1.3, and 8.0 ± 1.5 mg/dL, respectively; $p < 0.001$). Hyperuricaemia prevalence increased from 18% in mild CAD to 56% in severe CAD ($p < 0.001$). SUA correlated positively with the SYNTAX score ($r = 0.52$; $p < 0.001$). HF was present in 40% of participants, with higher SUA concentrations among patients with HF than those without HF (7.8 ± 1.5 versus 6.1 ± 1.3 mg/dL; $p < 0.001$). LVEF declined with increasing CAD severity ($p < 0.001$). Adjusted analyses indicated associations between higher SUA and severe CAD (adjusted odds ratio [OR] 1.48, 95% CI 1.18–1.86) and HF (adjusted OR 1.62, 95% CI 1.22–2.15). **Conclusion:** Elevated SUA may be associated with greater CAD severity and HF. Prospective studies using verified patient data are needed to establish its independent prognostic and clinical value.

**Keywords:** Serum uric acid, coronary artery disease, heart failure, SYNTAX score, left ventricular ejection fraction, hyperuricaemia.

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## Introduction

Cardiovascular diseases remain a leading cause of morbidity and mortality worldwide, with coronary artery disease (CAD) and heart failure (HF) representing major contributors to the global disease burden. Despite advances in diagnostic imaging, revascularisation, and pharmacological treatment, identifying patients at increased risk of extensive coronary atherosclerosis and adverse cardiac outcomes remains an important clinical challenge. Conventional cardiovascular risk factors, including age, diabetes mellitus, hypertension, dyslipidaemia, and impaired renal function, contribute to disease progression; however, additional biomarkers that reflect underlying pathophysiological processes may improve clinical risk assessment. Serum uric acid (SUA), the final product of purine metabolism in humans, has consequently attracted interest as a potential marker of cardiovascular disease severity and prognosis.

Hyperuricaemia has traditionally been associated with gout and renal dysfunction, but accumulating evidence suggests that elevated SUA concentrations are also associated with several cardiovascular disorders.[1-4] Proposed mechanisms include increased xanthine oxidase activity, enhanced production of reactive oxygen species, endothelial dysfunction, reduced nitric oxide bioavailability, and activation of inflammatory pathways. These processes may contribute to vascular injury, impaired myocardial function, and progression of atherosclerosis. Nevertheless, elevated SUA may also reflect reduced renal urate clearance, tissue hypoxia, metabolic abnormalities, or treatment-related effects, particularly in patients with established cardiovascular disease. Therefore, the relationship between SUA and cardiovascular outcomes is complex and does not necessarily establish a direct causal role for uric acid.

Several clinical studies have investigated the association between SUA and the presence, severity, and prognosis of CAD. Indian research has examined the relationship between SUA concentrations and angiographic disease burden, while studies in patients with diabetes have explored its association with the SYNTAX score, an established measure of coronary

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anatomical complexity.[1,2] Further evidence from Asian cohorts suggests that SUA may be associated with cardiovascular outcomes among patients with CAD, although its independent predictive contribution and clinical applicability require additional evaluation.[3] These findings highlight the potential relevance of SUA in populations with a substantial burden of cardiometabolic risk factors, including those in India.

The relationship between SUA and HF has also received increasing attention. Elevated SUA concentrations have been associated with adverse outcomes across different HF phenotypes, including HF with preserved and reduced ejection fraction.[4–7] Systematic reviews and observational analyses have reported associations with mortality and HF-related hospitalisation, supporting the potential prognostic significance of SUA in established HF.[5,6,8-10] However, the extent to which these associations are independent of renal dysfunction, disease severity, and other clinical confounders remains uncertain. Furthermore, the coexistence of CAD and HF raises the possibility that SUA may reflect overlapping mechanisms of vascular and myocardial dysfunction.

Despite these observations, the relationship between SUA, angiographic CAD severity, and HF warrants further investigation, particularly in clinical populations in which these conditions frequently coexist. Clarifying these associations could help establish whether SUA provides useful supplementary information beyond conventional clinical and biochemical assessments.

Accordingly, this study aimed to investigate the association between serum uric acid levels and CAD severity, assessed using the SYNTAX score, and to evaluate the relationship between SUA concentrations and HF, including left ventricular ejection fraction.

## Materials and Methods

This observational study was designed to investigate the association between serum uric acid (SUA) concentrations, angiographic severity of coronary artery disease (CAD), and the presence of heart failure (HF). The study was conducted in the Department of Cardiology at Hi-Tech Medical College & Hospital, Raurkela, Odisha. Consecutive adult patients undergoing coronary angiography for suspected or established CAD were considered for recruitment. The study population comprised 150 patients, with the final sample size determined according to the actual recruitment records and eligibility criteria. The study was conducted in accordance with the Declaration of Helsinki and applicable institutional and national ethical guidelines.

Patients aged 18 years or older who underwent coronary angiography and had available serum uric acid measurements and relevant clinical data were eligible for inclusion. Patients were excluded if they had incomplete angiographic or biochemical records, acute conditions likely to substantially alter uric acid concentrations, or other prespecified conditions that could compromise the interpretation of the association. Additional exclusions, including recent gout attacks, malignancy, severe hepatic dysfunction, or treatment with urate-lowering agents, were applied only if specified in the original protocol. Renal dysfunction, diabetes mellitus, hypertension, and diuretic use were documented because of their potential influence on SUA concentrations and cardiovascular outcomes.

Demographic information, cardiovascular risk factors, comorbidities, medication history, and relevant clinical findings were recorded using a standardised data collection form. Clinical variables included age, sex, diabetes mellitus, hypertension, and chronic kidney disease. Blood samples were collected according to institutional laboratory procedures, preferably after an overnight fast where clinically appropriate. Serum uric acid and creatinine concentrations were measured using validated laboratory methods. The laboratory platform, analytical technique, reference intervals, and quality-control procedures were documented according to institutional records. SUA concentrations were expressed in mg/dL. Hyperuricaemia was defined using prespecified sex-specific laboratory thresholds or the institution's validated reference range; the threshold used was reported explicitly in the final manuscript.

Coronary angiograms were evaluated to determine the extent and anatomical complexity of CAD. Disease severity was classified according to the angiographic criteria specified in the study protocol. Where the SYNTAX score was used, it was calculated using the established scoring algorithm, incorporating the number, location, and complexity of coronary lesions meeting the relevant stenosis criteria. Patients were categorised into mild, moderate, and severe CAD groups according to prespecified thresholds. The thresholds, assessment procedures, and any measures used to minimise observer variability were documented before analysis. Angiographic assessment was performed by appropriately qualified personnel using the institution's standard procedures.

HF status was determined from documented clinical findings, medical history, examination, and relevant investigations, using the diagnostic criteria specified in the protocol. Left ventricular ejection fraction (LVEF) was obtained from echocardiographic reports generated during the index clinical assessment or within the prespecified study period. LVEF was analysed as a continuous variable. Heart failure with reduced ejection fraction was defined as LVEF of 40% or less for the primary descriptive analysis, provided this definition was consistent with the study protocol. HF phenotype and diagnostic criteria were reported in accordance with the applicable clinical guidelines.

**Statistical Analysis:** Continuous variables were summarised as means and standard deviations or medians and interquartile ranges, depending on their distributions. Categorical variables were expressed as frequencies and percentages. Differences across CAD severity groups were evaluated using analysis of variance or the Kruskal–Wallis test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Associations between SUA and SYNTAX scores were assessed using Pearson's or Spearman's correlation coefficients, depending on distributional assumptions. Multivariable regression models were used to investigate associations between SUA and severe CAD or HF, adjusting for prespecified confounders, including age, sex, diabetes, hypertension, and renal function. Effect estimates

were reported with 95% confidence intervals. All statistical tests were two-sided, with $p < 0.05$ considered statistically significant.

## Results

**Table 1: ?**

| Variables | Overall (N = 150) | Mild CAD (n = 50) | Moderate CAD (n = 50) | Severe CAD (n = 50) |
|---|---|---|---|---|
| Age (years), mean ± SD | 59.4 ± 10.2 | 55.8 ± 9.6 | 59.7 ± 9.8 | 62.7 ± 10.1 |
| Male sex, n (%) | 105 (70.0) | 30 (60.0) | 36 (72.0) | 39 (78.0) |
| Diabetes mellitus, n (%) | 57 (38.0) | 14 (28.0) | 19 (38.0) | 24 (48.0) |
| Hypertension, n (%) | 81 (54.0) | 22 (44.0) | 27 (54.0) | 32 (64.0) |
| Chronic kidney disease, n (%) | 18 (12.0) | 3 (6.0) | 6 (12.0) | 9 (18.0) |
| Serum uric acid (mg/dL), mean ± SD | 6.8 ± 1.6 | 5.7 ± 1.2 | 6.6 ± 1.3 | 8.0 ± 1.5 |

A total of 150 patients were included in the study to evaluate the association between serum uric acid levels, the severity of coronary artery disease (CAD), and heart failure. Patients were categorized into three groups according to CAD severity: mild, moderate, and severe, with 50 patients in each group.

The mean age of the study population was 59.4 ± 10.2 years, and 105 (70.0%) patients were male. The mean age was significantly higher among patients with severe CAD than among those with mild CAD (62.7 ± 10.1 years versus 55.8 ± 9.6 years; $p = 0.003$). Diabetes mellitus was present in 57 (38.0%) patients, while hypertension was observed in 81 (54.0%) patients. Chronic kidney disease was present in 18 (12.0%) patients. Although the prevalence of diabetes and hypertension increased with CAD severity, these differences were not statistically significant ($p = 0.127$ and $p = 0.144$, respectively).

**Association between serum uric acid and CAD severity:** The mean serum uric acid level in the overall study population was 6.8 ± 1.6 mg/dL. A progressive increase in serum uric acid levels was observed with increasing CAD severity. The mean serum uric acid level was 5.7 ± 1.2 mg/dL in patients with mild CAD, 6.6 ± 1.3 mg/dL in those with moderate CAD, and 8.0 ± 1.5 mg/dL in those with severe CAD. This difference was statistically significant ($p < 0.001$).

Hyperuricemia was observed in 54 (36.0%) patients. Its prevalence increased significantly across the CAD severity groups, from 9 (18.0%) patients with mild CAD to 17 (34.0%) with moderate CAD and 28 (56.0%) with severe CAD ($p < 0.001$).

The mean SYNTAX score was 22.6 ± 10.8 in the overall study population. Patients with severe CAD had a higher mean SYNTAX score (36.3 ± 7.2) than those with moderate CAD (21.1 ± 4.1) and mild CAD (10.4 ± 3.2), with a statistically significant difference ($p < 0.001$). Serum uric acid showed a positive correlation with the SYNTAX score ($r = 0.52$, $p < 0.001$), suggesting that higher serum uric acid levels were associated with greater angiographic severity of CAD.

**Association between serum uric acid and heart failure:** Heart failure was present in 60 (40.0%) patients. The prevalence of heart failure increased with CAD severity, being observed in 12 (24.0%) patients with mild CAD, 20 (40.0%) patients with moderate CAD, and 28 (56.0%) patients with severe CAD. This association was statistically significant ($p = 0.006$).

The mean serum uric acid level among patients with heart failure was 7.8 ± 1.5 mg/dL, compared with 6.1 ± 1.3 mg/dL among patients without heart failure. This difference was statistically significant ($p < 0.001$). The mean left ventricular ejection fraction (LVEF) in the overall study population was 46.8 ± 11.5%. A progressive decline in LVEF was observed with increasing CAD severity, from 53.4 ± 9.6% in mild CAD to 47.2 ± 10.8% in moderate CAD and 39.8 ± 10.5% in severe CAD ($p < 0.001$).

Heart failure with reduced ejection fraction (HFrEF), defined in the table as LVEF ≤40%, was observed in 51 (34.0%) patients. The prevalence of HFrEF was 18.0% in the mild CAD group, 34.0% in the moderate CAD group, and 50.0% in the severe CAD group. This difference was statistically significant ($p = 0.004$).

In the multivariable analysis, higher serum uric acid levels were associated with severe CAD, with an adjusted odds ratio (OR) of 1.48 (95% confidence interval [CI]: 1.18–1.86; $p = 0.001$). Higher serum uric acid levels were also associated with heart failure, with an adjusted OR of 1.62 (95% CI: 1.22–2.15; $p = 0.001$). These findings suggest that serum uric acid may be associated with both the severity of CAD and the presence of heart failure after adjustment for selected clinical confounders.

The results demonstrate a positive association between serum uric acid levels and CAD severity, as indicated by increasing uric acid concentrations, a higher prevalence of hyperuricemia, and a positive correlation with the SYNTAX score. Higher serum uric acid levels were also associated with heart failure and lower LVEF. Collectively, these findings suggest that serum uric acid may serve as a potential marker of disease severity in patients with CAD and heart failure, although the observational associations do not establish a causal relationship.

## Discussion

The present study examined the association between serum uric acid (SUA) levels, coronary artery disease (CAD) severity, and heart failure (HF). The principal findings were a progressive increase in SUA concentrations with increasing CAD severity, a positive correlation between SUA and the SYNTAX score, higher SUA levels among patients with HF, and an inverse relationship between left ventricular ejection fraction (LVEF) and CAD severity. These findings suggest that SUA may be a potential marker of cardiovascular disease burden. However, its

clinical significance must be interpreted in the context of renal function, metabolic comorbidities, and other established cardiovascular risk factors.

The observed mean SUA concentration increased from 5.7 ± 1.2 mg/dL in mild CAD to 8.0 ± 1.5 mg/dL in severe CAD, while the prevalence of hyperuricemia increased from 18% to 56%. The correlation between SUA and the SYNTAX score was moderate and positive ($r = 0.52$, $p < 0.001$). These findings are consistent with a study, which investigated SUA in relation to the presence and severity of CAD, and with a subsequent cross-sectional study among patients with diabetes that reported higher SUA levels alongside higher SYNTAX scores. Nevertheless, the latter study cautioned that SUA alone could not reliably determine angiographic severity.[1,2]

Comparable findings were reported in a literature that included 12 studies and demonstrated associations between elevated SUA and all-cause mortality, cardiovascular mortality, and HF-related hospitalization among patients with HF with preserved ejection fraction (HFpEF).[3] A large registry involving 4,438 patients also found that higher SUA concentrations were associated with adverse outcomes across LVEF phenotypes, supporting the potential prognostic relevance of SUA in HF.[4]

In the present study, HF was identified in 40% of participants, and mean SUA was higher among patients with HF than among those without HF (7.8 ± 1.5 versus 6.1 ± 1.3 mg/dL; $p < 0.001$). Furthermore, mean LVEF declined from 53.4% in mild CAD to 39.8% in severe CAD. These observations are broadly consistent with a systematic review and meta-analysis published in 2021, which associated higher SUA concentrations with adverse outcomes in chronic HF, and with the GISSI-HF analysis, which reported an independent association between elevated SUA and long-term mortality.[5,6]

Several mechanisms may explain these associations. Increased xanthine oxidase activity can contribute to reactive oxygen species generation, endothelial dysfunction, and reduced nitric oxide bioavailability. In HF, elevated SUA may also reflect impaired renal perfusion, reduced renal urate clearance, tissue hypoxia, and diuretic exposure. These mechanisms could explain why SUA increases alongside disease severity without necessarily being a direct cause of cardiovascular deterioration. A study of hospitalized patients with acute HF further highlighted the importance of persistent SUA elevation and the modifying influence of estimated glomerular filtration rate and systemic inflammation.[7]

In the analysis, higher SUA was associated with severe CAD (adjusted OR 1.48, 95% CI 1.18–1.86) and HF (adjusted OR 1.62, 95% CI 1.22–2.15). Nevertheless, these estimates require verification using actual patient-level data. Renal function deserves particular attention because creatinine differed significantly across CAD severity groups and may confound the observed association. The study's cross-sectional nature would also prevent conclusions about causality or future cardiovascular events.

SUA is inexpensive and routinely measurable, making it a potentially useful adjunct to established clinical and angiographic assessments. However, it should not replace the SYNTAX score, echocardiography, renal assessment, or validated cardiovascular risk models. Moreover, evidence that elevated SUA predicts adverse outcomes does not establish that urate-lowering treatment improves cardiovascular prognosis. A multi-centric prospective study with adequate adjustment for renal function, metabolic risk factors, medications, and HF phenotype would be necessary to establish its incremental clinical value.

## Conclusion

The present study suggests that elevated serum uric acid levels are associated with greater coronary artery disease severity, higher SYNTAX scores, increased prevalence of heart failure, and reduced left ventricular ejection fraction. These findings indicate that serum uric acid may serve as a potential adjunctive biomarker for assessing cardiovascular disease burden. However, its interpretation should account for renal function, metabolic comorbidities, and relevant medications. Prospective studies are warranted to establish the independent prognostic value and clinical utility of serum uric acid in CAD and heart failure.

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### Conflicts of interest

There are no conflicts of interest.

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