Clinical and Prognostic Significance of Hyperuricemia in Patients with Chronic Heart Failure and Cardiorenal Syndrome

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Abstract

Background: Chronic heart failure is often accompanied by renal dysfunction and cardiorenal syndrome. Hyperuricemia is increasingly recognized not only as a metabolic disorder but also as a marker of oxidative stress, inflammation, endothelial dysfunction, impaired renal perfusion, and poor prognosis. Its interaction with heart and kidney dysfunction may contribute to disease progression and increased cardiovascular risk. Objective: To evaluate the clinical and prognostic significance of hyperuricemia in patients with chronic heart failure and cardiorenal syndrome. Methods: This observational study included 142 patients with NYHA class II–IV heart failure and renal dysfunction. Clinical parameters, serum uric acid, renal function markers, inflammatory indicators, ECG, and echocardiography were assessed. Patients were divided into hyperuricemia and normouricemia groups (defined as >420 μmol/L in men and >360 μmol/L in women). Clinical severity, renal function, cardiac parameters, and hospitalization rates were compared. Results: Hyperuricemia was present in 45.1% of patients. These patients showed more advanced heart failure, lower ejection fraction, worse renal function, higher inflammatory markers, and more frequent congestion. Rehospitalization rates were higher in the hyperuricemia group. The combination of hyperuricemia, reduced eGFR, and albuminuria identified a subgroup at particularly high risk. Conclusion: Hyperuricemia has important clinical and prognostic value in chronic heart failure with cardiorenal syndrome. It may serve as a useful biomarker for risk stratification, especially when combined with renal and inflammatory markers, supporting improved monitoring and management.

Keywords: *chronic heart failure, hyperuricemia, serum uric acid, cardiorenal syndrome, renal dysfunction, estimated glomerular filtration rate, albuminuria, prognosis.*

Introduction

Chronic heart failure is one of the most important clinical problems in modern cardiology and internal medicine. It is associated with high morbidity, repeated hospitalization, reduced quality of life and increased mortality. The disease develops as a result of structural or functional cardiac abnormalities that impair the ability of the heart to maintain adequate tissue perfusion. The clinical manifestations include

dyspnea, fatigue, reduced exercise tolerance, peripheral edema, congestion and progressive limitation of physical activity.

Renal dysfunction is one of the most frequent and clinically important comorbid conditions in patients with chronic heart failure. The coexistence of heart failure and kidney impairment is commonly described as cardiorenal syndrome. This syndrome reflects a bidirectional pathological interaction in which cardiac dysfunction contributes to renal injury, while renal impairment aggravates heart failure through fluid retention, electrolyte imbalance, neurohormonal activation and systemic inflammation.

In chronic heart failure, renal dysfunction may develop due to reduced cardiac output, increased central venous pressure, renal venous congestion, impaired renal perfusion, activation of the renin-angiotensin-aldosterone system, sympathetic nervous system stimulation and chronic inflammatory mechanisms. The 2023 focused update of the European Society of Cardiology heart failure guidelines reflects ongoing changes in evidence-based management of heart failure, particularly in relation to therapies that influence cardiovascular and renal outcomes.

Hyperuricemia is defined as an elevated serum uric acid concentration. Uric acid is the final product of purine metabolism and is mainly excreted by the kidneys. Traditionally, hyperuricemia has been associated with gout and urate nephrolithiasis. However, in recent decades, elevated serum uric acid has also been studied as a potential marker of cardiovascular disease, renal dysfunction, arterial hypertension, metabolic syndrome and chronic heart failure. ESC educational materials note that elevated uric acid is associated with hypertension, chronic kidney disease, type 2 diabetes and metabolic syndrome.

The relationship between hyperuricemia and chronic heart failure is biologically plausible. In heart failure, tissue hypoxia and increased xanthine oxidase activity may enhance uric acid production. At the same time, reduced renal blood flow and impaired glomerular filtration decrease uric acid excretion. Elevated uric acid may further contribute to oxidative stress, endothelial dysfunction, microvascular injury and inflammation. Recent research in cardiorenal syndrome has reported that hyperuricemia is associated with adverse outcomes, including increased mortality risk.

Kidney function assessment is essential in patients with chronic heart failure and suspected cardiorenal syndrome. KDIGO emphasizes the importance of estimated glomerular filtration rate and albuminuria categories for chronic kidney disease prognosis and risk stratification. Therefore, serum uric acid should not be interpreted in isolation, but together with creatinine, estimated glomerular filtration rate, albuminuria, congestion status and cardiovascular risk factors.

Despite growing interest, the role of hyperuricemia in chronic heart failure remains controversial. It is still debated whether elevated serum uric acid is an independent causal factor, a marker of disease severity or both. Nevertheless, its association with renal dysfunction, inflammation and adverse clinical outcomes suggests that it may

have practical value in risk stratification of patients with heart failure and cardiorenal syndrome.

Objective

The objective of this study was to evaluate the clinical and prognostic significance of hyperuricemia in patients with chronic heart failure and cardiorenal syndrome and to determine its association with heart failure severity, renal dysfunction, albuminuria, inflammatory activity, echocardiographic parameters and hospitalization frequency.

Materials and Methods

Study design

This was an observational clinical-prognostic study aimed at assessing the relationship between serum uric acid level and clinical outcomes in patients with chronic heart failure complicated by renal dysfunction.

Study population

The study included 142 patients diagnosed with chronic heart failure and signs of cardiorenal syndrome. Patients were recruited from cardiology and internal medicine clinical settings. All patients had chronic heart failure of New York Heart Association functional classes II–IV.

The diagnosis of chronic heart failure was based on clinical symptoms, medical history, physical examination, electrocardiography, echocardiography and laboratory findings. Cardiorenal syndrome was considered when chronic heart failure was accompanied by reduced estimated glomerular filtration rate, increased creatinine, albuminuria or other signs of renal dysfunction.

Inclusion criteria

Patients were included if they met the following criteria:

Chronic heart failure of NYHA functional class II–IV.

Age above 40 years.

Clinical or laboratory evidence of renal dysfunction.

Availability of serum uric acid measurement.

Availability of echocardiographic and laboratory data.

Exclusion criteria

Patients with acute myocardial infarction, acute kidney injury unrelated to heart failure, severe liver failure, active malignancy, acute infectious disease, pregnancy, active gout attack or current chemotherapy were excluded. Patients receiving urate-lowering therapy before inclusion were either analyzed separately or excluded from primary comparison depending on statistical requirements.

Clinical assessment

Clinical assessment included age, sex, duration of chronic heart failure, etiology of heart failure, functional class, dyspnea severity, exercise tolerance, peripheral edema, pulmonary congestion, nocturnal dyspnea, blood pressure, heart rate, body mass index and comorbid diseases.

The main etiological factors of heart failure included ischemic heart disease, arterial hypertension, post-infarction cardiosclerosis, dilated cardiomyopathy, diabetes mellitus and valvular heart disease.

Laboratory assessment

Laboratory examination included serum uric acid, creatinine, urea, estimated glomerular filtration rate, sodium, potassium, fasting glucose, lipid profile, C-reactive protein, complete blood count and urine analysis. Albuminuria or microalbuminuria was assessed using urinary albumin excretion or albumin-to-creatinine ratio when available.

Estimated glomerular filtration rate was calculated using standard validated clinical formulas. Hyperuricemia was defined as serum uric acid above 420 μmol/L in men and above 360 μmol/L in women.

Instrumental assessment

Electrocardiography was performed to evaluate rhythm disturbances, conduction abnormalities, signs of myocardial ischemia and left ventricular hypertrophy.

Echocardiography was used to assess left ventricular ejection fraction, left ventricular end-diastolic diameter, left atrial size, left ventricular hypertrophy, diastolic dysfunction, valvular abnormalities and estimated pulmonary artery pressure.

Grouping of patients

Patients were divided into two groups:

Group 1 included patients with chronic heart failure, cardiorenal syndrome and hyperuricemia.

Group 2 included patients with chronic heart failure, cardiorenal syndrome and normal serum uric acid concentration.

Clinical characteristics, renal parameters, inflammatory markers, echocardiographic data and hospitalization frequency were compared between groups.

Outcomes

The main evaluated outcomes were heart failure severity, NYHA functional class, reduced left ventricular ejection fraction, renal dysfunction, albuminuria, inflammatory activity, heart failure decompensation and rehospitalization.

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation. Categorical variables were presented as percentages. Differences between groups were analyzed using standard statistical methods. Correlation analysis was performed to evaluate associations between serum uric acid and estimated glomerular filtration rate, creatinine, albuminuria, C-reactive protein, left ventricular ejection fraction and hospitalization frequency. A p-value of less than 0.05 was considered statistically significant.

Results

General characteristics

Among 142 patients with chronic heart failure and cardiorenal syndrome, hyperuricemia was detected in 64 patients, representing 45.1% of the study population. The remaining 78 patients had normal serum uric acid levels.

Patients with hyperuricemia were generally older and had a longer duration of chronic heart failure. They more frequently had arterial hypertension, ischemic heart disease, diabetes mellitus, obesity and chronic kidney disease. The coexistence of multiple comorbidities was more common in the hyperuricemia group.

Heart failure severity

Patients with hyperuricemia had more severe clinical manifestations of chronic heart failure. NYHA functional classes III–IV were more frequent in the hyperuricemia group compared with the normouricemia group. These patients more often had dyspnea at low levels of physical activity, peripheral edema, pulmonary congestion and reduced exercise tolerance.

The frequency of heart failure decompensation was higher in patients with elevated serum uric acid. Rehospitalization due to worsening heart failure was more common in this group, indicating an unfavorable clinical prognosis.

Renal function

Renal dysfunction was more pronounced in patients with hyperuricemia. Serum creatinine and urea levels were higher in the hyperuricemia group, while estimated glomerular filtration rate was significantly lower.

A negative correlation was observed between serum uric acid and estimated glomerular filtration rate. As uric acid levels increased, renal filtration capacity decreased. This relationship supports the association between hyperuricemia and impaired kidney function in cardiorenal syndrome.

Albuminuria and microalbuminuria were more frequently detected in patients with hyperuricemia. This suggests that elevated serum uric acid is associated not only with reduced filtration, but also with glomerular and endothelial injury.

Inflammatory activity and metabolic parameters

C-reactive protein levels were higher among patients with hyperuricemia. This indicates that elevated uric acid may be associated with low-grade systemic inflammation. Inflammatory activity was more pronounced in patients with advanced heart failure and reduced renal function.

Patients with hyperuricemia also had more frequent dyslipidemia, higher triglyceride levels and increased body mass index. Type 2 diabetes mellitus and impaired glucose metabolism were more common in this group, supporting the association between hyperuricemia and cardiometabolic risk.

Echocardiographic findings

Echocardiographic assessment showed that patients with hyperuricemia had lower left ventricular ejection fraction compared with patients with normal uric acid levels. Left ventricular hypertrophy, left atrial enlargement and diastolic dysfunction were more common in the hyperuricemia group.

The presence of reduced ejection fraction together with elevated uric acid and reduced estimated glomerular filtration rate identified patients with a particularly severe cardiorenal phenotype.

Correlation analysis

Correlation analysis revealed a positive relationship between serum uric acid and creatinine, urea, C-reactive protein and NYHA functional class. A negative correlation was found between serum uric acid and estimated glomerular filtration rate, left ventricular ejection fraction and exercise tolerance.

The strongest adverse clinical profile was observed in patients with combined hyperuricemia, albuminuria and reduced estimated glomerular filtration rate. This subgroup had the highest frequency of heart failure decompensation and rehospitalization.

Discussion

The findings of this study demonstrate that hyperuricemia is clinically and prognostically significant in patients with chronic heart failure and cardiorenal syndrome. Elevated serum uric acid was associated with more severe heart failure, worse renal function, albuminuria, inflammation, impaired left ventricular function and increased hospitalization frequency.

The relationship between hyperuricemia and heart failure severity may be explained by several mechanisms. Chronic heart failure is associated with tissue hypoxia and impaired energy metabolism. Under hypoxic conditions, purine degradation increases and xanthine oxidase activity rises, leading to increased uric acid production. Xanthine oxidase activation is also accompanied by generation of reactive oxygen species, which may worsen oxidative stress and myocardial injury.

Renal dysfunction is another major contributor to hyperuricemia. Since uric acid is mainly excreted through the kidneys, reduced glomerular filtration and impaired tubular handling lead to uric acid accumulation. In patients with cardiorenal syndrome, venous congestion and reduced renal perfusion further aggravate this process.

At the same time, hyperuricemia may contribute to renal injury. Elevated uric acid may impair endothelial nitric oxide availability, promote renal microvascular dysfunction, increase oxidative stress and activate inflammatory pathways. These mechanisms may contribute to progressive decline in estimated glomerular filtration rate. KDIGO classifies chronic kidney disease prognosis using both GFR and albuminuria categories, which supports the clinical relevance of combining uric acid assessment with these renal markers.

Albuminuria was more common among patients with hyperuricemia. This is clinically important because albuminuria reflects glomerular damage and systemic endothelial dysfunction. The combination of hyperuricemia and albuminuria may therefore identify patients with advanced cardiorenal injury and higher risk of adverse outcomes.

Inflammation also plays an important role. Higher C-reactive protein levels in the hyperuricemia group suggest that uric acid may be associated with inflammatory

activity. Modern reviews describe hyperuricemia as a contributor to oxidative stress, inflammation and microvascular dysfunction, which may promote cardiovascular and renal disease progression.

The association between hyperuricemia and reduced left ventricular ejection fraction may reflect more advanced myocardial damage. Patients with elevated uric acid had more frequent left ventricular hypertrophy, diastolic dysfunction and lower systolic function. These findings suggest that serum uric acid may help identify a severe phenotype of chronic heart failure.

The prognostic significance of hyperuricemia is supported by recent evidence in cardiorenal syndrome populations. A 2025 study reported that hyperuricemia increased mortality risk in patients with cardiorenal syndrome and that the relationship between uric acid and adverse outcomes remained clinically relevant.

However, it is important to interpret hyperuricemia carefully. Elevated uric acid may be both a marker and a mediator of disease progression. It may reflect reduced kidney function, diuretic use, tissue hypoxia and metabolic dysfunction. At the same time, it may directly contribute to oxidative stress, endothelial injury and renal microvascular damage. Therefore, uric acid should not be evaluated as an isolated parameter, but as part of an integrated cardiorenal risk profile.

Therapeutic implications remain complex. The routine use of urate-lowering therapy in asymptomatic hyperuricemia solely for cardiovascular prevention remains debated. However, identification of hyperuricemia should prompt more careful evaluation of renal function, congestion status, blood pressure, metabolic profile and treatment regimen. In patients with gout, urate nephrolithiasis or symptomatic hyperuricemia, urate-lowering therapy should be considered according to standard clinical indications.

The management of patients with chronic heart failure and cardiorenal syndrome should be comprehensive. It should include optimization of heart failure therapy, control of congestion, preservation of renal function, correction of metabolic abnormalities, monitoring of electrolytes and careful use of diuretics. The ESC heart failure focused update reflects the importance of evidence-based therapies that improve outcomes in heart failure and cardiorenal populations.

Thus, hyperuricemia may be a useful additional biomarker for identifying high-risk patients with chronic heart failure and cardiorenal syndrome.

Conclusion

Hyperuricemia is frequent in patients with chronic heart failure and cardiorenal syndrome and is associated with a more severe clinical course. Patients with elevated serum uric acid more often have advanced NYHA functional class, congestion, reduced exercise tolerance, lower left ventricular ejection fraction and repeated hospitalization.

Elevated serum uric acid is closely associated with renal dysfunction. Patients with hyperuricemia have higher creatinine and urea levels, lower estimated glomerular filtration rate and more frequent albuminuria. The combination of hyperuricemia,

reduced estimated glomerular filtration rate and albuminuria identifies a subgroup with particularly high cardiorenal risk.

Hyperuricemia may reflect oxidative stress, endothelial dysfunction, inflammation, reduced renal excretion and neurohormonal activation. Therefore, it should be considered not only a metabolic abnormality, but also an additional clinical-prognostic marker in chronic heart failure complicated by renal dysfunction.

Serum uric acid should be interpreted together with estimated glomerular filtration rate, albuminuria, creatinine, inflammatory markers, congestion status and echocardiographic parameters. Such an integrated approach may improve early risk stratification and help optimize treatment strategy.

Further prospective studies are required to determine whether targeted correction of hyperuricemia can improve hard cardiovascular and renal outcomes in patients with chronic heart failure and cardiorenal syndrome.

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