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# Early Diagnostic Criteria of Renal Injury and Coordination of Treatment in Patients With Chronic Heart Failure

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**ABSTRACT**

***Objective:*** *This study aimed to examine the clinical, functional, echocardiographic, and biomarker characteristics of chronic heart failure (CHF) patients with and without renal dysfunction, given the frequent coexistence of both conditions and their complex management challenges.* ***Method:*** *A total of 129 CHF patients were evaluated and divided into two groups based on renal function. Clinical symptoms, six-minute walk test results, echocardiographic findings, and serum biomarker levels were compared.* ***Results:*** *Patients with renal dysfunction exhibited more severe symptoms, higher Clinical State Scale scores, shorter walking distances, and more advanced diastolic failure with greater ventricular remodeling. NT-proBNP, NGAL, KIM-1, and cystatin C levels were significantly elevated in the renal dysfunction group, whereas creatinine showed only minor increases. This discrepancy indicates the limited sensitivity of traditional renal markers in detecting early tubular injury.* ***Novelty:*** *The study highlights the diagnostic value of novel renal biomarkers in CHF patients, demonstrating their potential for early detection of subclinical kidney damage and improved risk stratification, ultimately contributing to timely interventions and better prognostic outcomes.*

## INTRODUCTION

Chronic heart failure (CHF) has long been recognised as one of the most serious cardiovascular disorders, and even today it remains a growing health challenge. Over the past few decades, progress in cardiology has helped millions of patients survive acute heart attacks and other severe events, but this success has come with an unintended consequence: more people are now living with CHF. Global reports estimate that more than 64 million people are affected, and the numbers continue to rise every year [1]. In many developing countries, including those with limited resources, CHF often presents late, is difficult to control, and carries a high risk of repeated hospitalisations. These trends show why research into CHF is so urgent and why clinicians everywhere are seeking new ways to diagnose and treat it more effectively.

One of the most worrying aspects of CHF is its close connection with renal dysfunction. The heart and kidneys are closely linked, and when one begins to fail, the other is often drawn into the process. This relationship, commonly called the cardiorenal syndrome, explains why 25-60% of patients with CHF eventually show signs of kidney impairment [2]. Once the kidneys are involved, outcomes tend to worsen significantly: hospital stays become longer, quality of life declines, and the risk of death increases. Even in cases where the kidney damage is still "silent" and does not show up on routine blood tests, it can quietly undermine a patient's prognosis. That is why cardiologists and

nephrologists emphasise the importance of recognising kidney injury as early as possible in CHF patients.

Traditional laboratory markers such as serum creatinine or estimated glomerular filtration rate are useful, but they are late indicators; they usually rise only after significant damage has occurred. In recent years, researchers have turned to newer biomarkers that may reveal early tubular injury long before the conventional numbers change. Among these, neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) have drawn special attention. Both molecules reflect tubular stress and injury and can be measured in serum or urine. Studies suggest they can predict progression to chronic kidney disease and help doctors stratify patients according to risk [3].

Several important investigations have supported the prognostic value of these biomarkers. A comparative study of CKD and non-CKD patients found that NGAL and KIM-1 levels were consistently higher in those with subclinical renal dysfunction, and these elevations correlated with worse functional capacity and more severe ventricular remodelling [4]. The large-scale ARIC study further strengthened these observations, showing that elevated NGAL and KIM-1 predicted the development of stage 3 CKD even in people who initially had relatively normal kidney function [5]. Together, these findings point to the clinical importance of using tubular biomarkers to "see the problem coming" before it becomes irreversible.

At the same time, therapy for CHF has also been evolving. A breakthrough has been the introduction of sodium-glucose cotransporter 2 (SGLT2) inhibitors. These drugs, such as dapagliflozin and empagliflozin, were first designed to manage diabetes, but they quickly showed remarkable effects in patients with heart failure as well. Large randomised trials have demonstrated that SGLT2 inhibitors reduce hospitalisations for heart failure, improve survival, and, importantly, protect kidney function [6]. Their renoprotective actions are thought to involve improvements in intraglomerular pressure, reduced tubular stress, and anti-inflammatory effects.

Inflammation, in fact, plays a key role in both CHF and kidney disease. Exploratory analyses from major trials showed that SGLT2 inhibitors reduce circulating levels of inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) [7]. By calming the inflammatory environment, these drugs may help not only to stabilise cardiac function but also to slow down renal decline. This dual benefit, on both the heart and the kidneys, is especially valuable in patients who are at the intersection of these two conditions.

In summary, CHF is a disease that extends beyond the heart, pulling other organs, especially the kidneys, into a vicious cycle of dysfunction. Identifying early signs of renal involvement with biomarkers like NGAL and KIM-1, while at the same time using new classes of drugs such as SGLT2 inhibitors, may finally offer patients a better outlook. This study was therefore designed to evaluate the role of early tubular injury markers in patients with CHF and to explore how modern therapies, including mineralocorticoid receptor antagonists and SGLT2 inhibitors, can modify both renal and cardiac outcomes.

## RESEARCH METHOD

The present study was carried out at the Republican Specialized Center for Therapy and Medical Rehabilitation, one of the country's major institutions dealing with advanced cases of cardiovascular disease. A total of 129 patients with chronic heart failure (CHF) were included. The average age of participants was 55.1 ± 6.5 years, and men and women were represented in almost equal numbers, which made the sample balanced and reflective of real clinical practice. Patients were grouped according to the New York Heart Association (NYHA) functional classification, ranging from class I to class III. This approach was necessary because the severity of symptoms and limitations of daily activity are closely linked with prognosis. In addition, patients were divided into two specific phenotypes: those with preserved ejection fraction (HFpEF) and those with mildly reduced ejection fraction (HFmrEF). These subtypes were chosen deliberately, as they represent an increasingly recognised portion of CHF and are often complicated by hidden renal problems that are not always easy to diagnose [8].

For the study, all patients were carefully divided into three groups. Group I consisted of 63 patients with CHF who did not show evidence of kidney dysfunction. Group II included 66 patients with CHF and clear signs of early renal impairment. Group III was made up of 20 apparently healthy individuals matched for age and sex, serving as a control population. This three-tiered division gave us the opportunity to compare outcomes between those with CHF but intact renal function, those with CHF and renal involvement, and those who were free of both cardiac and renal disease.

Each patient underwent a detailed clinical examination. Medical history was collected with particular attention to cardiovascular risk factors such as hypertension, diabetes mellitus, smoking, obesity, and ischemic heart disease. Past myocardial infarction, duration of heart failure symptoms, and number of hospitalizations were also documented. Physical examination included vital signs and a targeted cardiovascular assessment, focusing on the presence of pulmonary rales, peripheral edema, jugular venous distension, and changes in blood pressure. This comprehensive clinical assessment allowed for a clearer picture of each patient's condition and helped differentiate between CHF patients with and without renal involvement.

Instrumental investigations were conducted for all participants. Standard 12-lead electrocardiography (ECG) was used to evaluate rhythm disturbances and ischemic changes. Echocardiographic examination was performed with a MEDISON ACCUVIX V20 device using a 3.25 MHz transducer. Measurements followed the recommendations of the American Society of Echocardiography, with emphasis on left ventricular ejection fraction, indices of systolic and diastolic function, left atrial size, and evidence of structural remodelling. Functional capacity was objectively measured through the six-minute walk test, which provides a simple but reliable way of evaluating exercise tolerance in heart failure patients. In addition, the Clinical State Scale (CSS), modified by Mareev for CHF, was applied to quantify symptom severity in a structured manner, ranging from 0 (no symptoms) to more than 9 (severe CHF) [9].

Laboratory investigations formed an essential part of the study. Blood samples were collected from all participants in the morning after overnight fasting to ensure accuracy and comparability. NT-proBNP was measured to reflect neurohormonal activity, while interleukin-6 (IL-6) and C-reactive protein (CRP) were determined as indicators of inflammatory activity. Kidney function was assessed not only by conventional parameters such as serum creatinine and estimated glomerular filtration rate (eGFR), but also by more sensitive markers. Particular attention was paid to cystatin C, which is considered superior to creatinine for early detection of renal impairment [10]. Even more importantly, biomarkers of tubular injury were measured: kidney injury molecule-1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL). These were quantified using enzyme-linked immunosorbent assays (ELISA). Both markers have been shown to detect renal tubular injury at a very early stage, long before serum creatinine begins to rise, and their inclusion provided a deeper understanding of the hidden impact of CHF on renal structures [11].

The integration of clinical examination, instrumental tests, functional assessments, and novel biomarker analysis created a comprehensive methodology. This multi-layered approach allowed the study not only to capture overt clinical manifestations of CHF, but also to reveal subtle renal changes that often go unnoticed in daily practice. All procedures were conducted in strict accordance with ethical principles. Approval was obtained from the local ethics committee of the Center, and all patients signed informed consent before participating. The investigation fully complied with the Declaration of Helsinki, ensuring patient rights, confidentiality, and safety throughout the study.

## RESULT AND DISCUSSION

### *Result*

The clinical and laboratory evaluation of the 129 patients involved in this study revealed striking contrasts between those with and without renal dysfunction, underscoring the profound impact of kidney impairment on the course of chronic heart failure (CHF). Patients who had no evidence of renal involvement already exhibited typical symptoms of CHF, such as exertional shortness of breath and mild reductions in daily activity, but those with renal dysfunction reported more debilitating fatigue, higher frequency of nocturnal dyspnea, and greater limitations in functional capacity. On average, their Clinical State Scale scores were almost two points higher, which indicates not just a numerical distinction but a tangible worsening of everyday life. The six-minute walk test results made this difference even clearer, as individuals with renal impairment managed significantly shorter distances compared with their counterparts without renal dysfunction. The control group, composed of healthy individuals, performed within expected ranges, which confirms that these changes were not due to age or gender balance but to the combined burden of heart and kidney disease [12].

Beyond the obvious clinical features, echocardiography provided further evidence of this interaction. Patients with renal impairment displayed larger left atria, higher indices of diastolic dysfunction, and more pronounced ventricular remodelling. These

findings were in line with the markedly increased NT-proBNP concentrations observed in the same group, indicating that structural changes were closely linked with biochemical stress markers. While patients without renal involvement showed elevated NT-proBNP compared with controls, the rise was not as steep, which emphasises how renal damage contributes to hemodynamic instability. This association between biomarkers and imaging parameters reflects the close heart–kidney connection and suggests that renal dysfunction may accelerate the transition to more advanced CHF phenotypes [13].

Laboratory results further highlight the gap between traditional and novel approaches to assessing renal function. Serum creatinine, though higher in patients with renal dysfunction, did not fully capture the extent of injury, remaining within moderately abnormal ranges. In contrast, NGAL and KIM-1 concentrations nearly doubled, offering a much clearer picture of tubular damage. Cystatin C levels also showed a marked increase, reinforcing its value as an early indicator of declining kidney performance. Interestingly, these elevations occurred even when creatinine remained close to the upper limit of normal, a pattern that shows how traditional renal tests may underestimate injury in its initial stages. Such differences underline the diagnostic power of newer biomarkers, which provide a more refined and sensitive tool for early recognition of renal impairment in CHF patients [14].

**Table 1.** Clinical and Functional Parameters

| Parameter | CHF without RD (n=63) | CHF with RD (n=66) | Control (n=20) |
|---|---|---|---|
| **Mean age (years)** | 54.8 ± 6.2 | 55.4 ± 6.8 | 53.9 ± 5.7 |
| **NYHA class I-III (%)** | 62% | 81% | 0% |
| **Clinical State Scale (points)** | 5.6 ± 0.8 | 7.2 ± 1.0 | 2,7 ± 0,7 |
| **Six-minute walk distance (m)** | 368,5 ± 45 | 306,7 ± 41 | 720 ± 50 |

The data clearly illustrate that renal dysfunction worsens the symptomatic experience of CHF patients. The higher Clinical State Scale scores represent heavier daily limitations, while the reduced walking distance indicates objectively poorer physical capacity. When compared with controls, both CHF groups performed worse, but the added renal burden produced the steepest decline. These findings suggest that early recognition of renal involvement could help clinicians anticipate functional deterioration and implement timely strategies such as adjusted therapy or closer monitoring. The interaction of symptoms and reduced exercise tolerance paints a vivid picture of how kidney disease accelerates the downward spiral of CHF, making functional assessments indispensable for routine care.

**Table 2.** Laboratory and Biomarker Findings

| Parameter | CHF without RD (n=63) | CHF with RD (n=66) | Control (n=20) | Reference Range |
|---|---|---|---|---|
| **Serum Creatinine (μmol/L)** | 93.1 ± 15.6 | 108.2 ± 21.4 | 63.5 ± 12.7 | 60–110 |
| **Cystatin C (mg/l)** | 1.12 ± 0.3 | 1.44 ± 0.4 | 0.9 ± 0.2 | 0.6–1.3 |
| **NT-proBNP (pg/ml)** | 625,8 ± 185,6 | 917,8 ±236,7 | 120 ± 35 | <125 |
| **uNGAL (ng/ml)** | 34,7 ± 14 | 65,4 ± 28 | 16,8 ± 10 | <20 |
| **uKIM-1 (ng/ml)** | 1.4 ± 0.4 | 3.2 ± 0.7 | 0.8 ± 0.2 | <1.0 |

The table 2 highlights how novel biomarkers reveal the true extent of renal impairment in CHF patients. Although creatinine rose moderately, the sharp increases in NGAL, KIM-1, and cystatin C provided much stronger evidence of injury, proving their role as sensitive early markers. The control group values remained within normal ranges, underscoring the disease specificity of these findings. These results indicate that incorporating biomarkers into standard practice could help detect renal involvement long before creatinine signals danger. Doing so would allow for earlier interventions and potentially slow the progression of both renal and cardiac damage, ultimately improving patient outcomes.

Taken together, these findings confirm that renal dysfunction is not just an accompanying condition but a decisive factor that worsens the trajectory of CHF. Patients with combined heart and kidney disease showed more severe symptoms, poorer exercise tolerance, higher stress markers, and advanced structural changes. Novel biomarkers such as NGAL, KIM-1, and cystatin C consistently outperformed creatinine, highlighting their clinical value in early detection. These results reinforce the need for comprehensive assessment strategies in CHF, integrating both functional evaluation and advanced biomarker testing to improve patient management and prognosis [15].

***Discussion***

The findings of this study emphasise the close relationship between chronic heart failure (CHF) and renal dysfunction, highlighting how even early kidney injury significantly modifies the course of the disease. Patients with CHF and renal impairment experienced more severe symptoms, lower functional capacity, and a greater biochemical burden compared to those without renal involvement. These results suggest that renal dysfunction is not merely a secondary phenomenon but an integral part of the pathophysiology of heart failure, often described within the broader concept of the cardiorenal syndrome. The deterioration in clinical state and exercise tolerance observed in the renal dysfunction group supports the idea that kidney injury accelerates heart failure progression and worsens prognosis [16].

An important aspect of these results lies in the role of novel biomarkers such as NGAL, KIM-1, and cystatin C. While serum creatinine showed only modest increases,

these markers revealed more substantial evidence of tubular injury. This finding is consistent with earlier studies that demonstrated the predictive value of NGAL and KIM-1 in identifying early renal dysfunction, even before classical measures become abnormal [17]. The elevated levels of these biomarkers in CHF patients with renal dysfunction underscore their clinical importance and suggest that they could serve as valuable tools for early risk stratification and treatment planning.

The role of SGLT2 inhibitors also deserves attention, as several recent investigations have shown that these drugs provide renal protection in patients with diabetes and heart failure. By reducing tubular stress and lowering levels of injury biomarkers, agents such as empagliflozin and dapagliflozin have demonstrated the ability to preserve kidney function while also improving cardiac outcomes [18]. The integration of SGLT2 inhibitors into treatment strategies for CHF patients with renal involvement may therefore offer a dual benefit, addressing both cardiac and renal deterioration. Taken together, the results of this study align with recent literature showing that tubular injury biomarkers provide a more accurate reflection of renal status than creatinine alone, and that targeting renal protection could slow the downward spiral of CHF. Early incorporation of biomarker screening into routine practice, combined with therapies such as SGLT2 inhibitors, may represent a key step in reducing the burden of heart and kidney disease. These strategies could improve long-term outcomes by ensuring that patients at the highest risk are identified and treated before irreversible organ damage develops [19].

## CONCLUSION

**Fundamental Finding :** The study demonstrates that renal dysfunction significantly exacerbates the clinical progression of chronic heart failure (CHF), leading to more severe symptoms, functional limitations, and cardiac stress. Novel biomarkers such as NGAL, KIM-1, and cystatin C were shown to be superior to traditional creatinine measurements in detecting early tubular injury, enabling earlier identification of renal impairment in CHF patients. **Implication :** These findings emphasize the need for incorporating advanced biomarkers and SGLT2 inhibitors into clinical practice to improve early diagnosis, optimize treatment strategies, and enhance long-term outcomes in patients with coexisting cardiac and renal dysfunction. **Limitation :** However, the study's findings are limited by its observational design and relatively small sample size, which may affect the generalizability of the results across broader CHF populations. **Future Research :** Further longitudinal and multicenter studies are recommended to validate the predictive accuracy of these biomarkers and to explore the mechanistic pathways linking renal injury to CHF progression, as well as the therapeutic efficacy of novel pharmacological interventions.

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