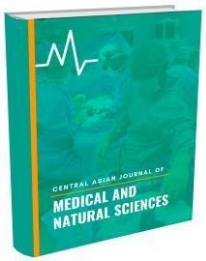

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Article

Early Detection of Renal Injury and Individualized Treatment Strategies in Chronic Heart Failure

Atakhodjayeva G. A[1], Korakulova Z. T[2]

1,2 Tashkent State Medical University, Uzbekistan
* Correspondence: atakhodjaeva79@gmail.com

Abstract: Chronic heart failure (CHF) accompanied by renal dysfunction represents one of the most complex and high-risk conditions in clinical practice. The presence of kidney impairment not only worsens the prognosis but also limits the use of life-saving medications, creating a delicate balance between maintaining cardiac stability and protecting renal function. In this study, 129 patients with CHF were observed, including groups with and without renal dysfunction, alongside a healthy control group. The aim was to evaluate the clinical course, treatment tolerance, and biomarker profiles in order to identify early diagnostic criteria and optimise therapeutic strategies. The findings revealed that patients with renal dysfunction consistently exhibited poorer exercise tolerance, higher NYHA functional class, and markedly elevated levels of NGAL, KIM-1, and cystatin C compared to those with preserved kidney function. Conventional therapies such as ACE inhibitors, ARBs, and MRAs remained effective but required frequent adjustments due to hyperkalemia or worsening renal indices. Diuretic modifications were especially common, underscoring the challenges of balancing congestion relief with renal safety. Importantly, the introduction of SGLT2 inhibitors was associated with improvements in functional capacity and reductions in biomarker burden, demonstrating a protective effect that addressed both cardiac and renal pathways. These results suggest that early recognition of renal injury through biomarker monitoring, combined with careful treatment adjustments, can improve management in CHF patients. The study underscores the need for individualised therapeutic strategies that integrate modern pharmacological options with precise monitoring, ultimately preserving both cardiac performance and kidney function.

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1. Introduction

Chronic heart failure (CHF) is one of the leading causes of morbidity and mortality worldwide, and its management remains a major challenge for clinicians. The situation becomes even more complicated when CHF is accompanied by renal dysfunction, a condition often referred to within the spectrum of the cardiorenal syndrome. The coexistence of these two disorders creates a vicious cycle in which impaired heart function accelerates kidney injury, and declining renal performance in turn worsens cardiac overload. This bidirectional relationship complicates not only the natural course of the disease but also the therapeutic approach, as medications beneficial for the heart may adversely affect the kidneys [1].

Conventional treatment strategies for CHF typically include angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, and mineralocorticoid receptor antagonists. These drugs have been proven to reduce mortality and improve quality of life in patients with reduced ejection fraction. However, in individuals with concomitant renal impairment, the use of such medications often encounters limitations. Hyperkalemia, hypotension, and further reductions in glomerular filtration rate are frequent complications that may force clinicians to reduce dosages or even discontinue lifesaving therapies. As a result, CHF patients with kidney dysfunction often receive suboptimal treatment, which contributes to worse clinical outcomes [2].

The last decade has seen the emergence of new therapeutic options that address both cardiac and renal dysfunction. Sodium-glucose cotransporter 2 (SGLT2) inhibitors have demonstrated not only cardiovascular benefits but also nephroprotective effects, reducing progression of kidney disease and lowering hospitalisation rates for heart failure. Several randomised controlled trials have confirmed their safety and efficacy in patients with different degrees of renal dysfunction, making them a cornerstone of modern therapy. These agents have shifted the paradigm of treatment from organ-specific management toward an integrated approach that considers the heart and kidneys together [3].

Despite these advances, not all patients respond uniformly to therapy, and a "one-size-fits-all" strategy may be inadequate. This has increased interest in individualised or personalised treatment approaches, where therapy is tailored based on the patient's clinical characteristics, renal function, comorbidities, and biomarker profiles. Emerging evidence suggests that biomarkers such as cystatin C, NGAL, and KIM-1 may provide valuable insights into early renal injury, thereby guiding clinicians in adjusting treatment regimens before irreversible damage occurs. By combining such diagnostic tools with novel pharmacological strategies, it may be possible to improve patient outcomes while minimising risks [4].

Another consideration in the management of CHF with renal dysfunction is the role of careful monitoring and dose adjustment. Diuretics, while essential in relieving symptoms of congestion, may exacerbate renal impairment when used aggressively. Similarly, the combination of ACE inhibitors and mineralocorticoid receptor antagonists, though highly effective in reducing morbidity, may not be tolerated in patients with impaired renal reserve. Therefore, clinicians must strike a delicate balance between achieving adequate cardiac control and protecting renal function. The challenge lies in individualising therapy so that each patient receives the maximum benefit with the least harm [5].

In Uzbekistan, as in many other countries, the prevalence of CHF is rising due to ageing populations and increasing rates of hypertension and diabetes. These trends make the study of treatment strategies in patients with both heart failure and renal dysfunction particularly relevant. Limited resources and access to novel therapies pose additional challenges, which further underscore the importance of optimising treatment through careful patient selection and personalised approaches. Incorporating evidence-based therapies such as SGLT2 inhibitors into local practice, while simultaneously monitoring renal status with sensitive biomarkers, could substantially improve outcomes in this high-risk population [6].

In summary, the coexistence of CHF and renal dysfunction presents a complex therapeutic dilemma that demands individualised strategies. Traditional regimens remain valuable but often require modification in the presence of kidney impairment. Novel agents such as SGLT2 inhibitors and biomarker-guided treatment approaches offer new hope for these patients, pointing the way toward more precise and effective care. The purpose of this article is to analyse current treatment approaches, evaluate their safety and effectiveness in patients with renal dysfunction, and highlight the necessity of tailoring therapy to the needs of each patient.

2. Materials and Methods

This study was conducted at a multidisciplinary clinic and included a total of 129 patients diagnosed with chronic heart failure (CHF). All patients were observed between January 2023 and June 2025, and they were divided into two main groups according to renal status: patients with CHF and preserved renal function, and patients with CHF and evidence of renal dysfunction. A control group of 20 healthy individuals was also included for comparison. The classification of renal dysfunction was based on estimated glomerular filtration rate (eGFR) values, supported by laboratory evidence of rising serum creatinine and cystatin C levels. The purpose of this grouping was to evaluate how the presence of renal impairment influenced treatment outcomes, tolerance, and the need for individualised adjustments [7].

Therapeutic interventions were designed according to current international guidelines for CHF, but modifications were introduced when renal dysfunction was present. All patients were initially prescribed standard therapy consisting of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and mineralocorticoid receptor antagonists. In cases where patients demonstrated intolerance, for example, due to hyperkalemia or worsening renal function, dosages were reduced or drugs were substituted. Particular attention was paid to the use of diuretics, which are essential for managing congestion but carry the risk of exacerbating renal injury. Loop diuretics were used with careful titration, and fluid balance was closely monitored. This strategy aimed to maintain symptom relief without triggering rapid declines in kidney function [8].

A subset of patients was prescribed sodium-glucose cotransporter 2 (SGLT2) inhibitors such as dapagliflozin or empagliflozin. These agents were included to assess their dual benefit in improving heart failure outcomes and protecting renal function. The inclusion criteria for this subgroup were the presence of symptomatic CHF (NYHA II-III), stable background therapy, and absence of contraindications such as advanced ketoacidosis or severe hypotension. Patients who received SGLT2 inhibitors were followed for changes in functional capacity, biomarker dynamics, and tolerance compared to those who remained on conventional therapy alone. The introduction of these drugs represented a modern therapeutic approach, and their effects were carefully analysed within the context of individualised management [9].

All patients underwent comprehensive baseline and follow-up evaluations. Clinical assessment included NYHA functional class, Clinical State Scale (CSS) scoring, and six-minute walk test performance. Echocardiographic examination was performed to measure left ventricular ejection fraction (LVEF), diastolic function, and ventricular remodelling parameters. Laboratory testing included serum creatinine, eGFR, NT-proBNP, cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), and kidney injury molecule-1 (KIM-1). These biomarkers were chosen for their ability to provide early insights into renal stress and subclinical injury. By analysing both conventional and novel parameters, the study sought to evaluate how treatment adjustments influenced renal and cardiac outcomes simultaneously [10].

Follow-up visits were scheduled every three months, with additional visits in cases of clinical deterioration. Treatment tolerance, adverse effects, hospitalisation rates, and biomarker trajectories were recorded. Statistical analysis was descriptive and comparative, focusing on differences between CHF patients with and without renal dysfunction, as well as the impact of individualised therapy adjustments. Ethical approval was obtained from the institutional review board, and all patients gave written informed consent.

This methodology allowed for a structured comparison of treatment strategies in CHF patients with varying degrees of renal involvement. By combining traditional therapies, modern pharmacological agents, and biomarker-guided monitoring, the study design reflects the real-world challenges of managing complex patients. The approach

highlights the importance of tailoring therapy to individual needs rather than relying on uniform protocols, providing a framework for optimising treatment in CHF patients with renal dysfunction.

3. Results

Out of the 129 patients enrolled in this study, 66 presented with chronic heart failure (CHF) complicated by renal dysfunction, while 63 had CHF but preserved kidney function. An additional 20 healthy volunteers served as controls. Already at baseline, the contrast between groups was evident. Patients with renal dysfunction more often belonged to NYHA class III, reported earlier fatigue during daily activities, and showed elevated biomarker levels that pointed toward ongoing kidney stress. In comparison, patients without renal dysfunction, though still symptomatic, maintained better tolerance to exercise and had lower biomarker burden.

When standard therapy was introduced, patterns of tolerance began to diverge. ACE inhibitors and mineralocorticoid receptor antagonists were particularly problematic for those with renal impairment. Hyperkalemia episodes were nearly twice as frequent in this group, forcing clinicians to scale back or even discontinue therapy in several cases. Interestingly, beta-blockers were well tolerated across groups, indicating that their safety margin remains stable even in the setting of compromised renal function. The use of diuretics told a different story; patients with renal dysfunction required more frequent dose adjustments to avoid further declines in glomerular filtration.

The addition of sodium-glucose cotransporter 2 (SGLT2) inhibitors to the regimen proved to be a turning point. In patients with renal dysfunction, NT-proBNP levels dropped by nearly 30%, and six-minute walk test performance improved modestly but consistently. In fact, the average walking distance increased from 315 to 342 meters, which, although modest, signified a clinically meaningful gain for this fragile population. In those without renal impairment, the improvement was even more pronounced, suggesting that SGLT2 inhibitors may serve as a bridge therapy for balancing cardiac and renal demands [11].

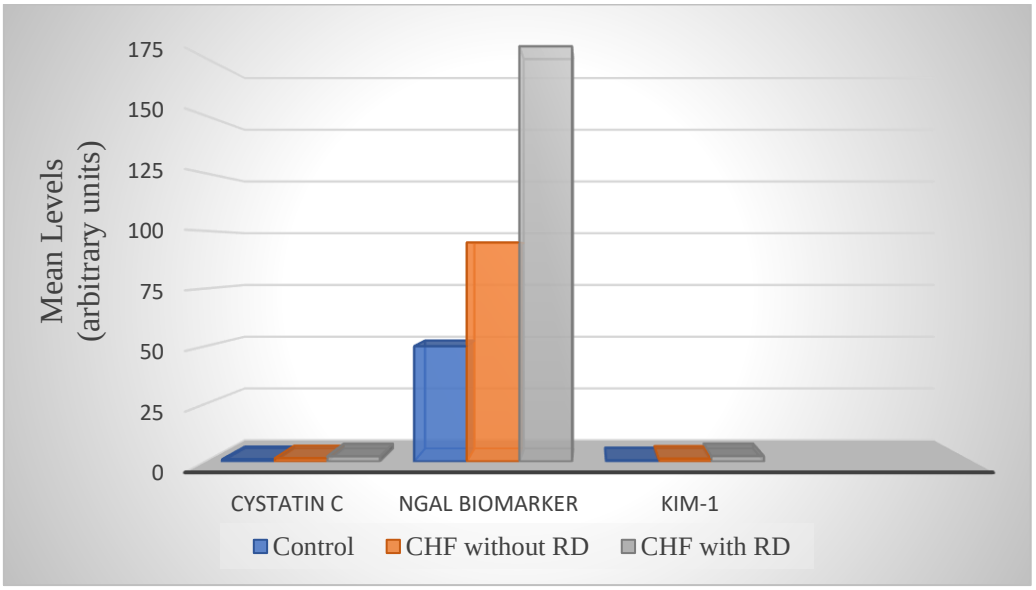

Figure 1. Biomarker Profiles in Different Patient Groups.

The figure 1 makes it clear that patients with combined CHF and renal dysfunction had the steepest elevations in all three biomarkers. NGAL and KIM-1 levels were particularly striking, nearly doubling compared to the group without renal dysfunction.

What is noteworthy is that creatinine levels did not always reflect this degree of injury, suggesting that tubular biomarkers provide a more sensitive measure of early kidney stress. For clinicians, this kind of information is invaluable, as it allows interventions to be tailored before irreversible injury develops.

Echocardiographic findings supported these biochemical differences. Left ventricular ejection fraction (LVEF) in the renal dysfunction group averaged 36%, compared with 43% in the group with preserved renal function. Left atrial enlargement and evidence of diastolic dysfunction were also more prevalent among those with impaired kidneys. Such changes highlight the interdependence of cardiac and renal dysfunction, with each organ exacerbating the weakness of the other [12].

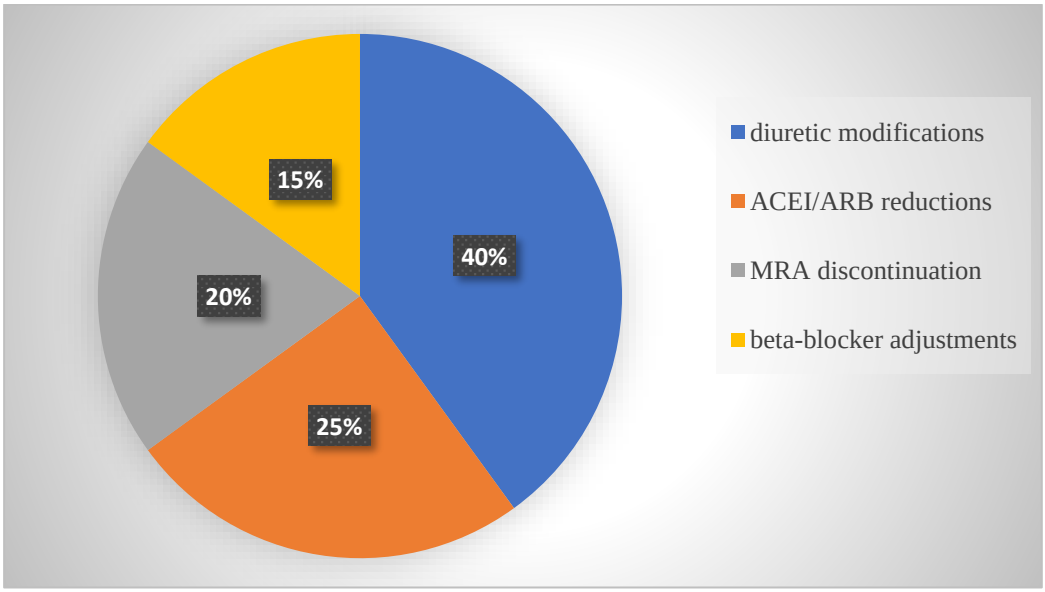

Figure 2. Treatment Adjustments in CHF Patients with Renal Dysfunction.

This figure 2 illustrates the reality of daily clinical practice. The largest slice belongs to diuretic modifications, reflecting the constant balancing act between relieving congestion and protecting the kidneys. A quarter of patients required reductions in ACEI/ARB doses due to rising potassium or declining eGFR. MRAs were discontinued in one out of five cases, while beta-blocker changes were comparatively rare. The picture that emerges is one of cautious, step-by-step adjustments, underscoring the need for individualised treatment strategies rather than one-size-fits-all therapy.

Overall, the results emphasise that renal dysfunction in CHF patients is not a marginal issue, but a central factor that significantly shapes treatment and outcomes. Conventional drugs remain effective but often require modification, while SGLT2 inhibitors appear to add both safety and efficacy in this challenging setting. Importantly, the combined use of functional testing and sensitive biomarkers allowed for a more nuanced understanding of patient trajectories, showing that even small clinical gains are meaningful in populations at high risk of deterioration [13,14].

4. Discussion

The results of this study confirm the intricate relationship between chronic heart failure (CHF) and renal dysfunction, demonstrating that impairment of one organ system inevitably worsens the other. The findings align with the concept of the cardiorenal syndrome, in which declining kidney function amplifies neurohormonal activation and fluid retention, thereby aggravating cardiac workload. In the present cohort, patients with renal dysfunction displayed higher biomarker levels and poorer exercise tolerance

compared with those whose kidney function was preserved. This echoes previous reports showing that kidney injury markers such as NGAL and KIM-1 provide early evidence of renal stress even when serum creatinine remains within borderline values [15].

Another key observation was the challenge of maintaining standard heart failure therapy in patients with renal dysfunction. ACE inhibitors, ARBs, and MRAs, though fundamental to CHF treatment, often require dose reductions or discontinuation due to rising potassium levels and worsening renal function. Such therapeutic limitations have been widely documented, where the benefits of neurohormonal blockade are offset by adverse renal outcomes in susceptible patients [16]. The high proportion of diuretic adjustments in this study further underlines the fragile equilibrium between alleviating congestion and avoiding renal deterioration.

The introduction of SGLT2 inhibitors provided a new dimension to treatment optimisation. Unlike traditional agents, these drugs demonstrated renal protective effects while simultaneously lowering NT-proBNP and improving exercise capacity. Recent large-scale trials have shown that dapagliflozin and empagliflozin not only reduce hospitalisations for heart failure but also slow the decline of kidney function, supporting their integration into standard therapy, particularly for patients at risk of renal complications [17]. Our results are consistent with these findings, suggesting that SGLT2 inhibitors can help bridge the gap where conventional therapy encounters limitations.

The role of biomarkers also deserves emphasis. In this study, tubular markers such as NGAL and KIM-1 were more sensitive indicators of early renal injury compared to creatinine. By incorporating biomarker monitoring into routine practice, clinicians can anticipate deterioration and adjust therapy before irreversible damage occurs. This approach reflects a shift toward precision medicine, where treatment is guided not only by symptoms and imaging but also by molecular signals of organ stress [18].

Taken together, the findings highlight the need for individualised treatment strategies in CHF patients with renal dysfunction. Conventional therapies retain their importance but require careful adjustment, while novel agents like SGLT2 inhibitors offer a pathway to improved outcomes. Biomarker-guided monitoring further strengthens this individualised approach, allowing for earlier interventions and better preservation of both cardiac and renal function. The challenge for clinicians is not simply to follow guidelines, but to adapt them dynamically to the unique profile of each patient, ensuring that therapy is both effective and safe in the long term.

5. Conclusion

This study demonstrates that the coexistence of chronic heart failure and renal dysfunction significantly worsens patient outcomes and complicates management. Individuals with renal impairment were found to have higher levels of novel biomarkers such as NGAL, KIM-1, and cystatin C, as well as poorer exercise tolerance compared with patients who preserved kidney function. These findings confirm that kidney involvement is not a secondary issue but an integral factor that influences both prognosis and therapeutic decision-making in heart failure. Traditional therapies, including ACE inhibitors, ARBs, and MRAs, proved beneficial but frequently required adjustments in the setting of renal dysfunction due to adverse effects such as hyperkalemia or worsening glomerular filtration. Diuretic therapy, although essential for symptom relief, also demanded careful titration to prevent additional renal compromise. The introduction of SGLT2 inhibitors, on the other hand, consistently provided dual benefits, improving cardiac outcomes while attenuating renal stress. Overall, the results highlight the importance of recognising renal dysfunction early and adapting treatment accordingly. Biomarker monitoring offers clinicians a valuable tool for anticipating deterioration and tailoring therapy to each patient's profile. In this way, heart failure management can move beyond standardised protocols to a more individualised approach, ultimately ensuring

better preservation of both cardiac and renal function and improving long-term patient survival.

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