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Renal Functional State in Patients with Chronic Heart Failure with Mid-Range Ejection Fraction

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Abstract: Objective: To investigate renal functional parameters in patients with chronic heart failure with mid-range ejection fraction (HFmrEF) and to evaluate the clinical significance of renal dysfunction (RD) in this population.

Methods: A total of 88 male patients with post-infarction cardiosclerosis (PICS) and HFmrEF (NYHA functional class II–III) were prospectively enrolled and divided into two groups based on the presence of renal dysfunction.

Results: Patients with concomitant RD demonstrated a significant reduction in glomerular filtration rate (GFR) by 23.0% ($P<0.01$) and an elevation in serum creatinine by 21.8% ($P<0.01$) compared with patients without RD. Microalbuminuria was detected in 86.7% of RD patients. Analysis of cardiorenal correlations revealed significant associations between GFR and left ventricular ejection fraction, diastolic function indices, and remodelling parameters.

Conclusion: Renal dysfunction aggravates the clinical course of HFmrEF and is independently associated with worsened cardiac functional state. The established cardiorenal correlations underscore the importance of systematic renal function assessment in patients with HFmrEF.

Keywords: Chronic heart failure; mid-range ejection fraction; renal dysfunction; microalbuminuria; glomerular filtration rate; cardiorenal syndrome.

Introduction: The co-existence of renal dysfunction (RD) and chronic heart failure (CHF) represents a clinically significant bidirectional interaction that has been consistently demonstrated in large-scale epidemiological studies [1, 7]. In patients with CHF, impaired cardiac output and elevated venous pressures promote haemodynamic and neurohumoral disturbances that ultimately compromise renal perfusion and tubular function. Conversely, reduced kidney function accelerates fluid retention, activates the renin-angiotensin-aldosterone system, and amplifies inflammatory pathways, thereby worsening cardiac performance [7, 10]. Among the CHF phenotypes, heart failure with mid-range ejection fraction (HFmrEF), defined as a left ventricular ejection fraction (LVEF) of 40–49%, constitutes a clinically heterogeneous group positioned between heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) [6]. The prevalence, pathophysiological mechanisms, and prognostic implications of RD in HFmrEF remain incompletely characterized, and targeted studies in this population are limited.

Post-infarction cardiosclerosis (PICS) represents one of the most common etiologies of HFmrEF in Central Asian populations. Ischemic myocardial injury promotes adverse ventricular remodeling, reduces LVEF, and creates conditions conducive to cardiorenal syndrome

(CRS) [8, 10]. Identifying the extent and correlates of renal involvement in this subgroup is therefore of considerable practical importance for optimizing treatment strategies and risk stratification.

The primary aim of the present study was to characterize renal functional parameters — serum creatinine, microalbuminuria (MAU), and glomerular filtration rate (GFR) — in HFmrEF patients with and without RD, and to assess cardiorenal relationships through correlation analysis with echocardiographic indices of systolic and diastolic function.

METHODS

This was a prospective comparative study conducted at the cardiology department of the Republican Specialized Scientific and Practical Medical Centre of Therapy and Medical Rehabilitation, Republic of Uzbekistan. A total of 88 male patients aged 18 years or older with documented PICS and HFmrEF (LVEF 40–49%) were consecutively enrolled. The interval since the index myocardial infarction ranged from 6 months to 5 years, and all patients had NYHA functional class II or III CHF [2]. Participants were stratified into two groups according to the presence of renal dysfunction: Group I (n = 45) comprised patients with HFmrEF without RD, and Group II (n = 43) comprised patients with HFmrEF and concomitant RD. All patients provided written informed consent prior to enrolment.

Exclusion criteria: Patients were excluded if they had any of the following: severe diabetes mellitus requiring insulin therapy; chronic obstructive pulmonary disease or clinically significant respiratory failure; hepatic insufficiency; pre-existing stage IV–V chronic kidney disease unrelated to CHF; a history of acute cerebrovascular accident within the preceding 12 months; high-grade cardiac arrhythmias (Lown class IV–V); resistant arterial hypertension (systolic blood pressure >180 mmHg despite triple therapy); or advanced heart failure (NYHA class IV). All patients underwent abdominal and renal ultrasonography to exclude developmental anomalies, renal masses, and nephrolithiasis prior to inclusion.

Renal functional status was evaluated by determining fasting serum creatinine concentration (µmol/L), urinary albumin excretion (microalbuminuria defined as >0.16 mg/L), and GFR calculated using the Cockcroft–Gault formula. Chronic kidney disease (CKD) staging was performed according to the KDIGO 2012 classification based on GFR and albuminuria categories. Combined cardiovascular–renal risk was further categorized as low, moderate, high, or very high based on the degree of GFR reduction and the severity of albuminuria within the context of cardiorenal syndrome.

Statistical analysis was performed using Biostat for Windows, version 4.03 (McGraw-Hill, USA). Continuous variables are expressed as mean ± standard deviation (M ± δ). Between-group comparisons of normally distributed variables were performed using the independent-samples Student t-test. Correlations between continuous variables were assessed using Pearson's correlation coefficient (r). Statistical significance was set at $P < 0.05$. The strength of correlations was interpreted as weak (r = 0.30–0.40), moderate (r = 0.41–0.60), or strong (r > 0.60).

RESULTS

Baseline renal function parameters for both groups are summarised below. In Group I patients (HFmrEF without RD), mean serum creatinine was 79.0 ± 8.49 µmol/L, and mean GFR was 99.58 ± 8.36 ml/min, indicating preserved renal function. In Group II patients (HFmrEF with RD), GFR was significantly reduced by 23.0% compared with Group I ($P < 0.01$), accompanied by a significant increase in serum creatinine of 21.8% ($P < 0.01$). Microalbuminuria was detected in 36 of 43 patients in Group II (86.7%).

CKD staging in Group II revealed Stage I CKD in 7 patients (16.3%), Stage II CKD in 21 patients (48.8%), and Stage III CKD in 15 patients (34.9%), indicating that the majority of patients with RD had mild-to-moderate kidney disease.

Risk stratification for combined CKD progression and cardiovascular complications (CVC) within the framework of cardiorenal syndrome revealed distinct profiles between the two groups. In Group I, 15 patients (33.3%) had a low combined risk, 19 patients (42.3%) had a moderate risk, and 11 patients (24.4%) had a high risk of CVC in the context of CRS.

In Group II, the distribution shifted markedly toward higher risk categories: 23 patients (53.5%) had a very high risk, 12 patients (27.9%) had a high risk, and 8 patients (18.6%) had a moderate risk. No patients in Group II were classified as low risk, reflecting the substantially greater cardiorenal burden in patients with concomitant RD.

Correlation analysis between GFR and echocardiographic parameters of cardiac structure and function is presented in Table 1. In Group I patients with HFmrEF, GFR demonstrated significant moderate inverse correlations with diastolic blood pressure (DBP; $r = -0.46$; $P < 0.01$) and LVEF ($r = -0.46$; $P < 0.01$), as well as with isovolumetric relaxation time (IVRT; $r = -0.51$; $P < 0.01$). A strong positive correlation was observed between GFR and endothelium-dependent vasodilation (ECVD; $r = 0.69$; $P < 0.001$), suggesting that endothelial dysfunction and renal impairment progress

in parallel.

In Group II patients (HFmrEF with RD), significantly stronger correlations emerged. GFR was strongly inversely correlated with LVEF ($r = -0.74$; $P < 0.001$) and inversely correlated with DBP ($r = -0.63$; $P < 0.01$). Furthermore, a moderate positive correlation was identified between GFR and the mitral inflow E/A ratio ($r = 0.55$; $P < 0.01$), as well as between GFR and the pulmonary venous E/A ratio ($r = 0.49$; $P < 0.01$), suggesting that deteriorating renal function is closely associated with worsening left ventricular diastolic performance.

Table 1.

Cardiorenal correlation coefficients between GFR and echocardiographic parameters in patients with HFmrEF

Parameter	Group I (n = 45)	Group II (n = 43)
GFR – Systolic BP (SBP)	r = 0.04	r = 0.22
GFR – Diastolic BP (DBP)	r = −0.46**	r = −0.63**
GFR – LVEF	r = −0.46**	r = −0.74***
GFR – Mitral E/A ratio	r = 0.09	r = 0.55**
GFR – IVRT	r = −0.51**	r = 0.13
GFR – Pulmonary venous E/A (PE/PA)	r = 0.09	r = 0.49**
GFR – ECVD	r = 0.69**	r = 0.17

Note: **P < 0.01; ***P < 0.001. LVEF = left ventricular ejection fraction; IVRT = isovolumetric relaxation time; ECVD = endothelium-dependent vasodilation; BP = blood pressure.

DISCUSSION

The present study confirms and extends prior observations regarding the prevalence and clinical significance of renal dysfunction in patients with HFmrEF caused by post-infarction cardiosclerosis. Our findings demonstrate that concomitant RD is associated with a substantial deterioration in both renal and cardiac functional parameters, manifesting as reduced GFR, elevated serum creatinine, high rates of microalbuminuria, and stronger inverse correlations with echocardiographic measures of ventricular performance.

The 23.0% reduction in GFR observed in Group II patients is consistent with the concept of cardiorenal syndrome type 2, in which chronic cardiac dysfunction induces progressive structural and functional renal impairment [8]. The haemodynamic mechanisms likely include chronically reduced renal perfusion pressure secondary to low cardiac output, elevated central venous pressure transmitted to the renal venous system, and compensatory activation of the sympathetic nervous system and renin-angiotensin-aldosterone axis [7]. The finding that 86.7% of patients with RD demonstrated microalbuminuria further highlights the degree of glomerular injury and suggests that urinary albumin excretion may serve as a sensitive and accessible marker of cardiorenal interaction in this population.

The CKD risk stratification results are clinically alarming: over half of Group II patients (53.5%) were classified as having a very high combined risk of CKD progression and cardiovascular complications within the CRS framework. In contrast, only 24.4% of Group I patients reached the high-risk threshold, with a third classified as low risk. These differences underscore the prognostic weight of renal dysfunction in HFmrEF and suggest that early detection and management of RD should be integrated into routine cardiological practice.

The cardiorenal correlation analysis revealed several noteworthy associations. In Group I, the moderate inverse correlation between GFR and LVEF ($r = -0.46$) and the strong positive correlation with ECVD ($r = 0.69$) suggest that even subclinical renal impairment in patients without overt RD is linked to endothelial dysfunction and beginning ventricular systolic deterioration. In Group II, the strengthening of the GFR–LVEF correlation to $r = -0.74$, along with the emergence of significant associations with diastolic function indices (E/A ratio), implies that renal dysfunction amplifies both systolic and diastolic abnormalities, contributing to a self-reinforcing cycle of cardiorenal deterioration.

Notably, in Group I patients, a significant negative correlation was identified between GFR and IVRT ($r = -0.51$), which was absent in Group II. This difference may reflect different stages of diastolic remodelling: prolonged IVRT is a marker of impaired relaxation (Stage I diastolic dysfunction), predominantly seen in earlier-stage disease, whereas pseudonormalisation and restrictive filling patterns characterise more advanced diastolic dysfunction in Group II patients, in whom the E/A ratio becomes the

dominant correlate. Several limitations of the present study merit acknowledgement. First, the study included exclusively male patients, which limits the generalisability of the findings to women. Second, the cross-sectional design precludes causal inference regarding the temporal sequence of cardiorenal deterioration. Third, GFR was estimated using the Cockcroft–Gault formula rather than measured directly or calculated by CKD-EPI, which may introduce systematic bias. Fourth, the exclusion of patients with severe comorbidities may have resulted in a relatively healthy study sample, potentially underestimating the true prevalence and severity of RD in an unselected HFmrEF population.

CONCLUSION

Renal dysfunction is highly prevalent among patients with HFmrEF caused by post-infarction cardiosclerosis and is independently associated with deteriorated cardiac functional state, as evidenced by lower LVEF, impaired diastolic filling, and more advanced ventricular remodelling. The strong cardiorenal correlations identified, particularly between GFR and LVEF, E/A ratio, and ECVD, confirm that renal and cardiac dysfunction are closely intertwined in this patient group and should be evaluated in parallel.

These findings support the implementation of systematic renal function screening — including GFR estimation and urinary albumin measurement — as part of standard cardiological assessment in patients with HFmrEF. Future prospective studies with larger, mixed-sex cohorts and longitudinal follow-up are warranted to establish causal pathways and evaluate the impact of targeted cardiorenal interventions on clinical outcomes.

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