Original Article

Diabetes Modifies the Association between Renal Function and Left Ventricular Ejection Fraction in Heart Failure Patients: A Cross-Sectional Study

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Highlights

- Diabetes modifies the relationship between renal function and cardiac systolic performance in heart failure patients.
- Urea and creatinine showed stronger inverse associations with LVEF among patients with diabetes compared with those without diabetes.
- No significant modifying effect of diabetes was observed for hemoglobin, and the interaction with eGFR only approached significance.
- Multivariable models confirmed urea and creatinine as independent predictors of lower LVEF.

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ABSTRACT

Background: Heart failure (HF) and chronic kidney disease (CKD) frequently coexist and contribute to poor clinical outcomes, particularly in patients with diabetes mellitus. The modifying effect of diabetes on the association between renal markers and left ventricular ejection fraction (LVEF) remains poorly understood.

Objective: We sought to investigate whether diabetes modifies the relationship between renal biomarkers and LVEF in hospitalized patients with HF.

Methods: We conducted a cross-sectional analysis involving 112 patients diagnosed with HF who were admitted to a tertiary care hospital. Data were extracted from electronic medical records, including demographic characteristics, comorbidities, laboratory values, and echocardiographic assessments. The primary outcome was LVEF, as determined by transthoracic echocardiography. Renal function was evaluated using serum urea, creatinine, hemoglobin, and the estimated glomerular filtration rate (eGFR). To examine whether the association between these renal markers and LVEF differed based on diabetes status, we fitted multivariable linear regression models including interaction terms between diabetes and each renal marker. All models were adjusted for age, sex, and HF subtype (HFpEF, HFmrEF, or HFrEF).

Results: In multivariable models, both urea and creatinine remained significantly associated with LVEF (P=0.007 and P=0.005, respectively). Hemoglobin and eGFR did not show significant main effects in both unadjusted and adjusted models. In the moderation analysis, a significant interaction was found between diabetes and urea (P=0.022). Among patients with diabetes, an increase in urea was associated with a significant reduction in LVEF (P=0.022), whereas the association was attenuated in patients without diabetes. Similarly, the interaction between creatinine and diabetes was significant (β=−13.12; P=0.003). In contrast, the interaction between diabetes and eGFR approached significance (β=0.11; P=0.076). No significant interaction was found for hemoglobin and diabetes (β=−0.70; P=0.67).

Conclusion: Diabetes modifies the relationship between renal function and systolic performance in patients with HF. The stronger associations of urea and creatinine with reduced LVEF in individuals with diabetes highlight the importance of tailored risk assessment in the context of cardiorenal-metabolic disease.

Keywords: Creatinine; Ejection Fraction; Hemoglobin; Type 2 Diabetes Mellitus; Urea

RHYTHM
Research in Heart Yield and Translational Medicine

Introduction

Heart failure (HF) is a clinical syndrome in which impaired cardiac function fails to meet the body's circulatory demands. HF is a widespread and deadly condition; the global number of cases nearly doubled from 25.4 million in 1990 to 55.5 million in 2021.[1] In Asia, Indonesia has among the highest HF prevalence rates, with an age-standardized rate of approximately 900.9 cases per 100,000 population.[2]

Left ventricular ejection fraction (LVEF) is a cornerstone measure of systolic function and a well-established prognostic indicator in HF management.[3] Despite the known impact of comorbidities on HF outcomes, there is a critical gap in understanding how such factors influence LVEF specifically. There are still very few studies examining how comorbidities of HF, such as diabetes and renal dysfunction, modify LV function.[4] Addressing these uncertainties is important given the high HF burden and mortality in Indonesia and similar settings.

Renal impairment frequently accompanies HF, reflecting the bidirectional interplay between the heart and kidney. In HF, reduced cardiac output and systemic congestion lead to renal hypoperfusion and sodium retention, while uremic toxins and neurohormonal mediators (eg, activated RAAS and inflammation) further damage both organs.[5] In clinical practice, serum urea (blood urea nitrogen [BUN]), creatinine, and the estimated glomerular filtration rate (eGFR) are primary markers of renal function. These indices help stage chronic kidney disease (CKD) and guide HF management. Importantly, renal dysfunction is consistently linked to worse cardiac function and outcomes. For instance, elevated BUN strongly predicts mortality in HF; each 10 mg/dL rise in BUN was associated with a greater than 20% increase in death risk in a prior study.[6] Recent evidence confirms that increases in serum creatinine levels and decreases in eGFR independently predict an increased risk of readmission due to HF and mortality. A study reported that each decrease in eGFR stage was associated with a significant increase in HF readmission rates (HR, 1.48; 95% CI, 1.32 to 1.67) and in-hospital mortality.[7] Similarly, another study found that higher baseline creatinine levels in patients with acute decompensated HF significantly shortened the time to death or readmission,[8] underscoring the role of renal markers as important prognostic predictors.

Diabetes mellitus (DM) is prevalent in populations with HF and further worsens prognosis. In Asian HF cohorts, roughly one-third to one-half of patients have diabetes (eg, ~ 51% in Southeast Asia and ~34% in other regions).[2] In our regional context, nearly a quarter of hospitalized patients with HF had diabetes alone, and another approximately 27% had both diabetes and CKD.[9] Diabetes adversely affects the heart and kidneys through multiple mechanisms. It induces coronary microvascular endothelial dysfunction, chronic inflammation, oxidative stress, and metabolic disturbances (the hallmarks of diabetic cardiomyopathy).[10] These processes can impair myocardial contractility and exacerbate renal injury in HF. Not surprisingly, diabetes has been shown to worsen HF outcomes independently. Nonetheless, to our knowledge, no prior studies have specifically examined diabetes as an effect modifier of the relationship between renal function markers and LVEF. The literature still lacks data on whether and how diabetes alters the impact of urea, creatinine, or eGFR on cardiac systolic function.[9]

To fill this gap, we conducted a cross-sectional study in a large cohort of Indonesian inpatients with HF. Our design mirrors recent HF biomarker studies that used cross-sectional data to identify predictors of cardiac function.[11] The primary objective was to test for interactions between DM status and each renal marker (serum urea, creatinine, and eGFR) in determining LVEF across the full spectrum of HF phenotypes. We hypothesized that diabetes might amplify the deleterious effect of renal dysfunction on LVEF. By clarifying these interactions, our findings could improve risk stratification (identifying patients with HF at especially high risk due to combined diabetes–renal dysfunction) and inform integrated cardiorenal management strategies. In turn, this work may guide future research and therapeutic algorithms for patients with HF, diabetes, and kidney disease. The paper proceeds with methods detailing our patient cohort and statistical approach, followed by results on interaction analyses, and a discussion of the implications for clinical care and research.

Methods

Study Design and Ethical Consideration

The present descriptive-analytic observational study used a cross-sectional design. The study was conducted at RS Karsa Husada, a regional general hospital that serves as a referral center in East Java, Indonesia. Data were collected retrospectively and prospectively from medical records and hospital information systems from January 2024 through June 2025. This time frame was chosen to ensure an adequate number of eligible subjects and to capture the most recent trends in clinical practice and patient outcomes. Variables collected included demographic characteristics, clinical diagnoses, laboratory results, treatment modalities, and patient outcomes. All data were anonymized and coded prior to analysis to protect patient confidentiality.

As this was a retrospective and exploratory analysis, no formal a priori sample size calculation was performed. All accessible and complete patient records that met the study inclusion criteria within the defined study period were included. The final sample size of 112, representing 26.8% of the total population of 417 records, was, therefore, constrained by data availability rather than by statistical estimation. A post hoc power check indicated that this sample provides 74.8% power to detect a moderate standardized mean difference (Cohen d=0.5) at a 2-tailed significance level of α=0.05, but only 35.3% power for a smaller effect size (Cohen d=0.3). The process of record identification, screening, and inclusion is summarized in (Figure 1), which illustrates the steps from initial hospital registry retrieval to the final analyzed cohort.

The current study was reviewed and approved by the Health Research Ethics Committee of RS Karsa Husada. Ethical clearance was obtained before data collection (approval No. 60/01/EC/KEPK-FKIK/10/2024). The research protocol adhered strictly to the principles outlined in the Declaration of Helsinki and followed national guidelines for health research involving human subjects. Because the study utilized secondary data without direct patient contact, informed consent was waived by the Ethics Committee. Nevertheless, the confidentiality and privacy of all participants were maintained throughout the study. All investigators involved in this study completed institutional training on human research ethics and data protection. The collected data were stored securely in password-protected databases and were accessible only to the principal investigator and authorized research personnel. Any dissemination of results, including publication or presentation, ensured that no individual subject could be identified.

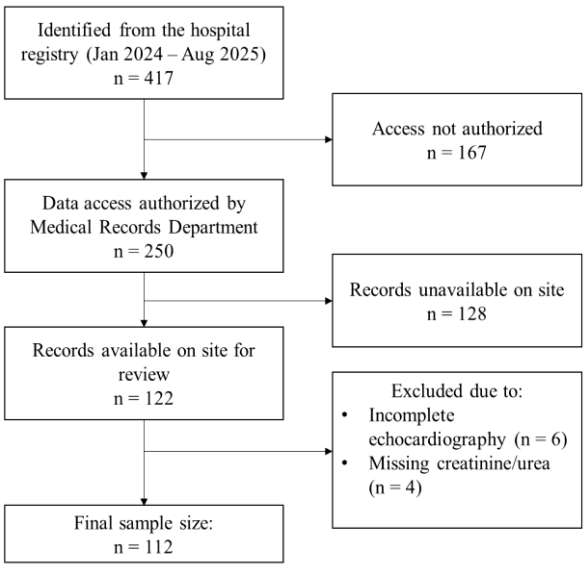

Figure 1. Flow diagram of record selection for the retrospective study on patients with heart failure.

Eligibility Criteria

Participants were selected based on predefined inclusion and exclusion criteria to ensure the relevance and validity of the data. Eligible participants were patients who received care or had medical records documented at RS Karsa Husada between January 2024 and July 2025. Inclusion criteria included adult age (≥ 18 y) and a confirmed diagnosis of HF, classified as HF with preserved ejection fraction (HFpEF), mildly reduced ejection fraction (HFmrEF), or reduced ejection fraction (HFrEF), in accordance with the 2022 American Heart Association (AHA), American College of Cardiology (ACC), and Heart Failure Society of America (HFSA) HF guidelines. Furthermore, participants were required to have complete medical records, including clinical, laboratory, and, where applicable, radiological data necessary for analysis.

Patients were excluded if they were younger than 18 years, had incomplete or missing key

clinical information, or had a diagnosis that could not be verified according to established criteria. Additional exclusion criteria included a history of congenital heart disease or significant structural heart abnormalities, cardiac surgery (eg, coronary artery bypass grafting, valve repair or replacement, or device implantation) within the past 24 months, end-stage renal disease requiring dialysis, active malignancy, severe hepatic failure, and advanced chronic obstructive pulmonary disease requiring oxygen therapy. Pregnant individuals were excluded because of differing hemodynamic parameters and disease management considerations. Patients enrolled in other interventional studies that could influence HF outcomes during the study period were also excluded, as were those who refused to consent or whose data could not be used because of confidentiality restrictions.

Data Collection and Echocardiographic Assessments

Data collection was conducted at RS Karsa Husada using both retrospective and prospective methods from January 2024 through July 2025. Clinical and demographic data were obtained from patients' medical records and included age, sex, body mass index, comorbidities (eg, hypertension, DM, and CKD), medication history, and relevant laboratory parameters, such as hemoglobin levels, serum creatinine, eGFR, and fasting blood glucose. Data entry was performed using a standardized case report form to minimize variability and ensure consistency across the dataset.

Echocardiographic assessments were conducted by certified cardiologists using standard transthoracic echocardiography in accordance with the guidelines of the American Society of Echocardiography (ASE). All echocardiographic evaluations were performed using high-resolution ultrasound machines at the hospital's cardiology unit. Parameters assessed included LVEF, left atrial diameter, LV end-diastolic dimension, LV end-systolic dimension, interventricular septal thickness, and diastolic function indices. LVEF was calculated using the modified Simpson biplane method. For patients with multiple echocardiographic records, the most recent and complete echocardiogram within the study period was utilized for analysis. Quality control was ensured through cross-validation of a random subset of echocardiographic data by a second independent cardiologist.

Study Variables

The primary variables in the present study were categorized into three main groups: demographic variables, clinical variables, and echocardiographic parameters. Demographic variables included age, sex, and year of data collection (2024 or 2025). Clinical variables included the presence or absence of DM, renal function as measured by eGFR, blood pressure status, hemoglobin level, and comorbidities, such as hypertension and ischemic heart disease. The main echocardiographic variable was LVEF. Type 2 diabetes mellitus (T2DM) status was employed as an effect modifier in analyzing the relationship between renal function and LVEF.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp, Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed data were presented as mean (SD), while nonnormally distributed data were expressed as median (IQR). Categorical variables were presented as frequencies and percentages. Comparisons of continuous variables between groups were performed using the independent *t* test or the Mann-Whitney *U* test, as appropriate. Categorical variables were compared using the χ^2 or Fisher exact test. The association between renal function (eGFR, creatinine, and urea) and LVEF was evaluated using univariable and multivariable linear regression analyses, adjusting for potential confounders, such as age, sex, hemoglobin level, and comorbidities. An interaction term between DM and renal function was included to assess whether DM modified the association between eGFR and LVEF. A *P* value of less than 0.05 was considered statistically significant.

Results

Characteristics of the Subjects

Patient characteristics stratified by DM status are summarized in (Table 1) Of the 112 patients, 24 (21.4%) had DM. The mean age was comparable between patients with DM and those without DM (62.96 vs 62.05y; P=0.719). The distribution of HF subtypes did not differ significantly across the groups (P=0.771). Patients with DM had significantly lower serum creatinine (0.84 vs 1.24 mg/dL; P=0.039), higher hemoglobin (14.34 vs 13.25 g/dL; P=0.014), and higher eGFR (104.07 vs 78.64 mL/min/1.73 m²; P=0.004). No significant difference in LVEF was observed between patients with DM and those without DM (47.17% vs 44.67%; P=0.503).

Table 1. Characteristics of the studied patients with HF divided by T2DM status

Characteristics	T2DM, n (%)		P
	No (n=88)	Yes (n=24)	
Age, mean±SD (y)	62.05±11.65	62.96±7.93	0.719
Male, n (%)	61 (69.3)	14 (58.3)	0.442
HF subtype			
HFpEF	23 (26.1)	6 (25.0)	0.771
HFmrEF	13 (14.8)	5 (20.8)	
HFrEF	52 (59.1)	13 (54.2)	
LVEF, mean±SD (%)	44.67±15.62	47.17±17.96	0.503
Urea, mean±SD (mg/dL)	45.20 (30.42)	35.76 (26.90)	0.171
Creatinine, mean±SD (mg/dL)	1.24±0.90	0.84 (0.52)	0.039
Hemoglobin, mean±SD (g/dL)	13.25±1.99	14.34±1.54	0.014
eGFR, mean±SD (mL/min/1.73 m^2)	78.64±36.13	104.07±40.92	0.004
Systolic BP, mean±SD (mmHg)	154.52±30.36	162.42±30.24	0.261
Diastolic BP, mean±SD (mmHg)	94.58±18.28	102.25±18.49	0.072
Heart rate, mean±SD (bpm)	89.09±21.22	90.67±18.53	0.741
Respiratory rate, mean±SD (/min)	23.77±7.09	25.58±11.80	0.346
Saturated oxygen, mean±SD (%)	95.06±8.18	92.33±14.91	0.238
Body temperature, mean±SD (°C)	36.31±0.49	36.39±0.40	0.458

BP: blood pressure; eGFR: estimated glomerular filtration rate; HFpEF: heart failure with preserved ejection fraction; HFmrEF: heart failure with midrange ejection fraction; HFrEF: heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction

Univariable Analysis

Univariable linear regression analyses were performed to assess the individual associations between each clinical variable and LVEF, as presented in (Table 2). Male sex was significantly associated with lower LVEF (β=−12.33; P<0.001), whereas age showed no significant relationship (β=0.14; P=0.327). Compared with patients with HFmrEF, those with HFpEF had higher LVEF (β=20.67; P<0.001), and those with HFrEF had lower LVEF (β=−7.53; P=0.010). Among renal markers, higher urea (β=−0.17; P<0.001) and creatinine (β=−4.42; P=0.014) were significantly associated with lower LVEF, whereas higher eGFR was positively associated with LVEF (β=0.14; P<0.001). Hemoglobin was not significantly associated with LVEF (β=−1.02; P=0.195). DM was not a significant predictor of LVEF in the univariable analysis (β=2.50; P=0.503).

Table 2. Univariable linear regression analysis of associations with left ventricular ejection fraction

Predictors	β Coefficient	Std. Error	P
Age (y)	0.138	0.14	0.327
Male (vs Female)	–12.329	3.028	<0.001
HFpEF (vs HFmrEF)	20.674	3.25	<0.001
HFrEF (vs HFmrEF)	–7.533	2.885	0.01
Hemoglobin	–1.021	0.782	0.195
Urea	–0.167	0.049	<0.001
Creatinine	–4.423	1.764	0.014
eGFR	0.137	0.038	<0.001
Type 2 diabetes mellitus	2.499	3.716	0.503

eGFR: estimated glomerular filtration rate; HFpEF: heart failure with preserved ejection fraction; HFmrEF: heart failure with midrange ejection fraction; HFrEF: heart failure with reduced ejection fraction

Stepwise Multivariable Analysis

We conducted stepwise multivariable linear regression to model the predictors of LVEF. In Model 1, male sex was significantly associated with lower LVEF (β=−12.09; P<0.001), whereas age and DM were not significant predictors. In Model 2, the inclusion of HF type revealed that HFpEF was associated with higher LVEF (β=19.50; P<0.001), whereas HFrEF showed a negative association (β=−6.99; P=0.015). Model 3 incorporated laboratory parameters related to the kidney and blood profile. Urea (β=−0.18; P= 0.002) and creatinine (β=4.96; P=0.019) were significantly associated with LVEF. Overall model fit improved across steps, with R^2 increasing from 0.137 in Model 1 to 0.646 in Model 3 (Table 3).

Table 3. Multivariable analysis of the association between T2DM and left ventricular ejection fraction across different models

Variables	Model 1 Estimate (SE)	P	Model 2 Estimate (SE)	P	Model 3 Estimate (SE)	P
T2DM	1.08 (3.51)	0.76	1.72 (2.46)	0.487	1.43 (2.48)	0.564
Age	0.10 (0.13)	0.431	0.10 (0.09)	0.269	0.21 (0.09)	0.022 *
Sex	-12.09 (3.07)	<0.001***	-5.16 (2.24)	0.023 *	-5.15 (2.19)	0.021 *
HFpEF	–	–	19.50 (3.23)	<0.001***	16.65 (3.17)	<0.001***
HFrEF	–	–	-6.99 (2.84)	0.015 *	-7.75 (2.79)	0.006 **
Urea	–	–	–	–	-0.18 (0.06)	0.002 **
Creatinine	–	–	–	–	4.96 (2.07)	0.019 *
Hemoglobin	–	–	–	–	-0.85 (0.52)	0.104
eGFR	–	–	–	–	0.05 (0.04)	0.167
R^2 / adj. R^2	0.137 / 0.113		0.586 / 0.566		0.646 / 0.615	
Residual SE	15.16		10.6		9.99	

T2DM: type 2 diabetes mellitus; HFpEF: heart failure preserved ejection fraction; HFrEF: heart failure reduced ejection fraction; eGFR: estimated glomerular filtration rate
Model 1: T2DM, age and sex
Model 2: T2DM, age, sex, and HF subtype
Model 3: Age, sex, HF subtype, urea, creatinine, hemoglobin, and eGFR
*Significant at P<0.05, **P<0.01, and ***P<0.001

Mediation Analysis

We explored whether urea or hemoglobin mediated the association between DM and LVEF. The average causal mediation effect for urea was 1.01 (95% CI, −0.33 to 2.43; P=0.128), whereas for hemoglobin it was −0.71 (95% CI, −2.85 to 1.04; P=0.550). In both cases, the indirect pathways were not statistically significant, and the proportion mediated was low.

Effect Modification by T2DM

We tested whether DM modified the association between renal markers and LVEF. A significant interaction was found between urea and diabetes (P=0.022), indicating a stronger inverse relationship between urea levels and LVEF in patients with DM. Similarly, the interaction between creatinine and DM was significant (P=0.003), suggesting that higher creatinine levels were associated with lower LVEF only among those with DM. No significant interaction was observed for hemoglobin and DM (P=0.673). The interaction between eGFR and DM approached significance (P=0.076), indicating a potential modifying effect that warrants further investigation. These interaction effects are conceptually illustrated in (Figure 2).

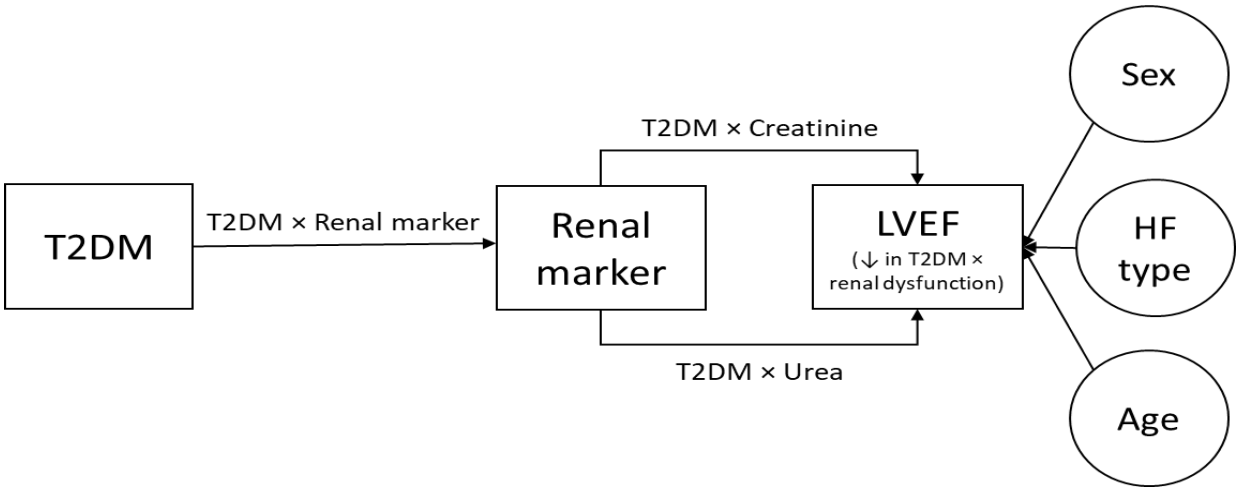

Figure 2. Conceptual framework illustrating the interaction between type 2 diabetes mellitus (T2DM) and renal dysfunction on left ventricular ejection fraction (LVEF). T2DM may contribute to reduced LVEF both directly and indirectly through renal impairment (eg, elevated urea or creatinine). An interaction between T2DM and renal dysfunction is hypothesized to exacerbate LVEF decline. The model adjusts for age, sex, and heart failure (HF) type as potential confounders.

Discussion

In the present study, we found that T2DM significantly modified the relationship between renal function markers and cardiac performance as indicated by LVEF. Specifically, elevated levels of urea and creatinine were more strongly associated with reduced LVEF in individuals with DM, highlighting the potential synergistic impact of diabetic nephropathy and cardiac dysfunction. This finding chimes with previous evidence that cardiorenal interactions are amplified in the presence of metabolic comorbidities, such as T2DM, likely because of shared mechanisms involving endothelial dysfunction, oxidative stress, and systemic inflammation.[12] Anemia exerts negative effects on LV function and LV global strain in patients with T2DM. Hemoglobin concentration is an independent factor in LV global strain.[13] These findings suggest the importance of measuring renal biomarkers in the context of diabetes when assessing cardiac function in HF management. Our findings are consistent with prior research showing that renal impairment is more detrimental to cardiac function in individuals with diabetes. Among ambulatory patients with HF and T2DM, results from a study[14] showed a steady reduction in kidney function, as indicated by declining eGFR over time. HF and kidney failure are interconnected in a bidirectional manner in patients with T2DM and cardiovascular disease.[15] Notably, our study extends these observations by formally testing interaction effects, confirming that the inverse associations between renal markers (urea and creatinine) and LVEF are significantly stronger in patients with diabetes.

While previous work has often focused on either diabetic cardiomyopathy or diabetic nephropathy in isolation, our results highlight how the interplay between these two complications may manifest more severely in terms of cardiac dysfunction. Moreover, although hemoglobin has been proposed as a link between anemia and HF progression, our findings do not support its modifying role in the diabetes–LVEF relationship, contrasting with studies that reported hemoglobin as a mediator of cardiac remodeling in populations with CKD. The observed interaction between diabetes and renal markers in predicting LVEF is biologically plausible and supported by existing evidence on the interconnected pathophysiology

of diabetic cardiomyopathy and cardiorenal syndrome. In diabetes, chronic hyperglycemia leads to microvascular damage, oxidative stress, and systemic inflammation, all of which impair both renal and myocardial function.[18] Elevated urea and creatinine levels, even within the upper-normal range, can reflect subclinical renal dysfunction that may exacerbate cardiac remodeling through neurohormonal activation and toxin accumulation. Uremic toxins such as indoxyl sulfate and *p*-cresyl sulfate have been shown to promote myocardial fibrosis and reduce cardiomyocyte contractility via proinflammatory and profibrotic pathways.[17] Additionally, reduced eGFR is associated with impaired nitric oxide bioavailability, endothelial dysfunction, and volume overload, which can aggravate LV dysfunction, particularly in the diabetic heart that is already compromised by insulin resistance and metabolic inflexibility.[16] The diabetic myocardium exhibits altered substrate utilization—favoring lipotoxicity over glucose oxidation—and mitochondrial dysfunction, making it more susceptible to further stress induced by renal impairment.[18]

In patients with HF and diabetes, the combination of renal impairment and glycemic disease portends a markedly worse prognosis. By way of example, a previous study reported that patients with HF and both diabetes and CKD had 50% to 90% higher cardiovascular mortality than those without both conditions,[19] underscoring the need for aggressive risk stratification. Clinicians should monitor renal markers (creatinine, urea, and eGFR) closely in patients with HF and diabetes and expedite therapies that benefit both heart and kidneys. Indeed, sodium-glucose transport protein 2 (SGLT2) inhibitors have shown an approximately 43% reduction in HF hospitalizations in patients with diabetes, supporting early initiation in this subgroup.[20] Similarly, renin-angiotensin-aldosterone system (RAAS) blockade (angiotensin-converting enzyme inhibitors or angiotensin receptor-neprilysin inhibitors) remains foundational in HFrEF, with proven mortality and morbidity reductions regardless of diabetes status. Integrated care models can further improve outcomes. In one Malaysian study, a nurse- and pharmacist-led multidisciplinary HF clinic achieved higher use of guideline-directed therapies, larger LVEF improvements, and far fewer HF readmissions than usual care.[21] Likewise, a recent Portuguese cardiorenal program brought cardiologists and nephrologists together to deliver comprehensive management of patients with HF and CKD.[22] Such joint cardiology–nephrology clinics and shared EMR protocols can ensure coordinated monitoring (eg, of renal markers) and optimization of SGLT2 inhibitors, RAAS inhibitors, and other HF therapies.[19,20]

Despite being based on a real-world cohort of inpatients with HF, the current study's cross-sectional design limits causal inference. Moreover, we lacked diabetes-specific data (including both onset and HbA1c) to quantify severity. This omission is important because poor glycemic control worsens HF prognosis. A study found a U-shaped relationship between HbA1c and adverse events in patients with HFrEF and diabetes (both very low and very high HbA1c levels doubled event rates).[23] As a single-center retrospective study without an a priori sample size estimation, in which the final sample (n=112) was determined by record availability, the present study may have limited generalizability. Finally, we analyzed only LVEF and did not evaluate diastolic function or strain imaging. Yet, advanced echocardiography and cardiac magnetic resonance can detect subtle myocardial dysfunction in diabetes: one study showed reduced global longitudinal strain in patients with diabetes (even with normal EF) that correlated with HbA1c. These gaps mean our findings should be viewed as hypothesis-generating.

Prospective longitudinal studies are needed to determine whether renal function markers predict subsequent LVEF decline and clinical endpoints in patients with HF, especially stratified by diabetes status. Future cohorts should collect serial eGFR, creatinine, and glycemic data to clarify temporal relationships. Subgroup analyses by HF subtype (HFrEF vs HFpEF) would also be informative because diabetes and kidney disease may impact systolic versus diastolic HF differently. Mechanistic studies could include emerging biomarkers, such as galectin-3 and soluble suppression of tumorigenicity 2, which are strong prognostic indicators in HF.[24] Advanced imaging techniques, such as strain echocardiography or cardiac magnetic resonance, may also detect early cardiac dysfunction, as previously suggested.[24]

Conclusion

Our findings indicate that elevated urea and creatinine levels were strongly associated with lower LVEF in patients with DM, suggesting a synergistic effect of metabolic and renal stress on cardiac function. These results underscore the significance of considering diabetic status when evaluating cardiorenal interactions and may inform risk stratification and early intervention strategies in HF management. Further research is warranted to explore underlying mechanisms and to assess whether integrated renal–cardiac monitoring can improve outcomes in diabetic populations.

Author Contributions

NFA and MI contributed equally to study conception, methodology design, and data analysis. SW, TRF, and KLA collected and curated clinical data. AP, AZA, and IRA provided clinical oversight and assisted in the interpretation of echocardiographic findings. DS supervised the cardiovascular aspects of the study and provided critical revisions. All authors contributed to drafting and editing the manuscript and approved the final version.

Declarations:

Ethical Approval

Ethical clearance was obtained from the Health Research Ethics Committee of RS Karsa Husada, East Java, Indonesia (approval number 60/01/EC/KEPK-FKIK/10/2024). Informed consent was waived because of the retrospective nature of the data collection and full anonymization of patient information.

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Conflict of Interest

The authors declare no competing interests.

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