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RESEARCH ARTICLE

Assessing hs-Troponin T and NT-proBNP in acute heart failure and cardiorenal syndrome: Diagnostic, prognostic, and functional interrelationships

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Background: Acute heart failure (AHF) is frequently complicated by renal dysfunction, leading to cardiorenal syndrome (CRS), and poses significant management challenges.

Objective: This study aimed to elucidate the interrelationships between cardiac function, renal impairment and key biomarkers: high-sensitivity troponin T (hs-Troponin T) and N-terminal pro-brain natriuretic peptide (NT-proBNP), in patients with AHF with and without CRS.

Methods: In this prospective observational study, 60 adult patients admitted with AHF were stratified into two groups based on renal function. Baseline clinical data, laboratory measurements, and echocardiographic assessments were performed within 48 h of admission.

Results: Patients with CRS exhibited a significantly lower left ventricular ejection fraction (34.73 ± 2.49% vs. 41.70 ± 5.08%, $p<0.001$), elevated serum creatinine levels, and a more deranged lipid profile than patients with AHF alone. Both hs-Troponin T and NT-proBNP levels were markedly higher in the CRS group, with significant inverse correlations between these biomarkers and the ejection fraction. Multivariate analysis revealed that elevated NT-proBNP levels (OR 9.465, $p<0.01$) were strong predictors of prolonged hospitalization.

Conclusion: These findings highlight the complex interplay between cardiac and renal dysfunction in patients with AHF. Elevated levels of hs-troponin T and NT-proBNP, particularly NT-proBNP, underscore their potential as valuable diagnostic and prognostic tools for early risk stratification and management in high-risk patients.

Keywords: CRS, AHF, left ventricular dysfunction, hs-TnT, NT-proBNP

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Introduction

Acute heart failure (AHF) is a complex clinical syndrome in which myocardial stress, injury, and neurohormonal activation converge to impair the cardiac performance [1,2]. In recent years, substantial research has focused on the mechanistic underpinnings of circulating biomarkers in AHF and cardiorenal syndrome (CRS), with particular emphasis on high-sensitivity troponin T (hs-TnT) and N-terminal pro–brain natriuretic peptide (NT-proBNP) [3,4].

NT-proBNP is derived from the cleavage of the prohormone proBNP, which is synthesized and released predominantly by ventricular myocytes in response to increased wall stress and volume overload [5]. The stimulus for this release is the mechanical stretching of cardiac fibers, and levels of NT-proBNP correlate with the severity of ventricular dysfunction [6]. Moreover, because NT-proBNP is primarily cleared by the kidneys, renal impairment, as seen in CRS, can result in elevated circulating levels not only by increased production, but also by decreased clearance [7]. Previous studies have demonstrated that NT-proBNP levels are robust predictors of heart failure severity and prognosis, although their interpretation can be complicated in patients with concomitant renal dysfunction [6,8}.

High-sensitivity troponin T (hs-TnT), on the other hand, serves as a sensitive marker of myocardial injury [9]. Traditionally associated with acute myocardial infarction, troponin release is now recognized as a continuum that reflects even subtle cardiomyocyte damage due to chronic wall stress, neurohormonal toxicity, or inflammation [10]. In AHF, elevated hs-TnT levels have been linked to worse outcomes, even in the absence of overt ischemia, because they capture ongoing cellular injury that may result from the hemodynamic and metabolic derangements of heart failure [11]. The kinetics of troponin release, along with the improved analytical sensitivity of modern assays, allow for the detection of even minor degrees of myocardial damage, thereby enhancing risk stratification [12].

In CRS settings, the interplay between cardiac and renal dysfunction becomes particularly critical. The impaired renal function characteristic of CRS contributes to the accumulation of NT-proBNP owing to reduced clearance, while the same renal dysfunction may exacerbate myocardial injury through volume overload and neurohormonal activation [7,13]. This bidirectional relationship has been well documented in mechanistic studies and clinical investigations, which underscores that biomarkers such as NT-proBNP and hsTnT not only serve as indicators of primary cardiac pathology but also reflect secondary renal contribution to disease progression [14,15].

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Previous studies have provided critical insights into the mechanisms underlying these biomarkers. For example, Zhang, *et al.* [16] demonstrated that rapid measurement of BNP-related peptides can reliably aid in the diagnosis of AHF, with levels correlating to the degree of myocardial stretch and dysfunction. Similarly, a study by Roos, *et al.* [17] showed that serial changes in hs-TnT can predict outcomes in patients with decompensated heart failure, supporting the view that ongoing cardiomyocyte injury-even when subclinical-carries significant prognostic value.

Moreover, research has highlighted that the predictive power of NT-proBNP level may be modified by renal function [18]. As noted in CRS studies, every decrease in estimated glomerular filtration rate (eGFR) is associated with a proportional increase in NT-proBNP level, thereby complicating the interpretation of this biomarker in patients with combined heart and kidney dysfunction [19]. Such findings have led to a more nuanced approach where clinicians must integrate both cardiac and renal assessments to accurately stratify the risk in AHF patients [20].

Given these complex interrelationships, our study was designed to clarify how declining left ventricular ejection fraction (LVEF) interacts with renal dysfunction to modulate circulating hs-TnT and NT-proBNP levels. In doing so, we aimed to evaluate the combined prognostic utility of these biomarkers in predicting prolonged hospitalization in patients with AHF and CRS. By integrating insights from previous mechanistic studies and recent clinical evidence, we sought to refine risk stratification strategies and ultimately guide more personalized therapeutic interventions.

Materials and Methods

Study Design and Participants

This prospective observational study included 60 patients at the Al-Sadr Teaching Hospital in Najaf, Iraq, between January 2024 and December 2024. Adult patients (aged ≥18 years) with a primary diagnosis of AHF were consecutively enrolled. Patients were stratified into two groups based on renal function at admission: those with AHF alone and those with acute cardiorenal syndrome (ACRS) [21]. ACRS was defined as the presence of renal impairment, operationalized as a serum creatinine >1.5 mg/dL or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², in conjunction with clinical symptoms of heart failure [22,23]. These thresholds were selected in accordance with established guidelines and previous studies [24,25]. Patients with acute myocardial infarction, severe valvular heart disease, chronic liver disease, or other systemic illnesses that might confound biomarker interpretation were excluded. Written informed consent was obtained from all participants, and the study protocol was approved by the Institutional Ethics Committee (Approval No.34328) in accordance with the Declaration of Helsinki [26].

Clinical and Laboratory Data Collection

Baseline demographic and clinical characteristics, including age, sex, body mass index (BMI), New York Heart Association (NYHA) class, and duration of hospitalization, were recorded upon admission. Venous blood samples were drawn within 24 h of admission for comprehensive laboratory evaluation. All assays were performed on the same sample to ensure consistency and repeated measurements were not performed. The following laboratory parameters were assessed.

Renal Function

Serum creatinine levels were measured using an enzymatic method, and eGFR was calculated using the CKD-EPI Formula [27]:

$$eGFRcr = 142 \times \min(Scr/\kappa, 1)\alpha \times \max(Scr/\kappa, 1)\text{-}$$
$$1.200 \times 0.9938Age \times 1.012 \text{ [if female]}.$$

Liver Function

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin levels were determined using standard automated clinical chemistry assays.

Lipid Profile

Levels of low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides were measured using enzymatic colorimetric methods.

Cardiac Biomarkers

High-sensitivity Troponin T (hs-Troponin T): Quantification was performed using the Elecsys® Troponin T high-sensitivity assay (Roche Diagnostics) with a 99th percentile upper reference limit of 13.5 ng/l [28]. The calibration and standardization procedures were performed according to the manufacturer's recommendations.

N-terminal pro-brain natriuretic peptide (NT-proBNP) levels were measured using the Roche Elecsys pro-BNP assay in accordance with established diagnostic thresholds for heart failure [29].

Echocardiographic Assessment

Transthoracic echocardiography was performed within 48 hours of admission by experienced cardiologists using a Vivid E9 system (GE Healthcare). Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson biplane method following the recommendations of the American Society of Echocardiography [30]. In addition, the images were independently reviewed by two blinded cardiologists to ensure consistency in the LVEF assessment. (Additional echocardiographic parameters, such as diastolic or right ventricular function, were recorded if deemed to be clinically relevant.)

Statistical Analysis

GraphPad Prism 9 software was used to ascertain the impact of disparate groups (patients versus controls) on the

study parameters. A T-test was used to conduct a significant comparison of means. The Chi-square test was implemented to perform a significant comparison of percentages at the 0.05 and 0.01 probability levels. Estimations of correlation coefficients and multiple linear regression analyses were conducted for the variables. The sensitivity and specificity of the parameters were evaluated in both the patient and control groups. Cutoff values for the biomarkers were established using Receiver Operating Characteristic (ROC) curve analysis to optimize both sensitivity and specificity. The Youden Index was used to determine the optimal threshold for each parameter [31].

Results

As shown in Table 1, the age, sex distribution, and BMI were not significantly different between the AHF and CRS groups (p>0.05). In contrast, the ejection fraction was significantly lower in the CRS (34.73 ± 2.49) than in the AHF (41.70 ± 5.08; p<0.001). Patients with CRS more frequently presented with an advanced NYHA class (70% in class IV vs. none in AHF, p<0.001) and required longer hospitalizations (100% vs. 36.7% beyond one week, p<0.001).

Serum creatinine was markedly higher in CRS (2.64 ± 0.53 vs. 1.14 ± 0.07 mg/dL), reflecting lower eGFR (55.04 ± 9.66 vs. 69.35 ± 10.37 mL/min/1.73 m²), both p<0.001. Liver enzyme (AST and ALT) and total bilirubin levels were also elevated in CRS patients (all p<0.001). Among the lipid parameters, LDL and triglycerides were significantly higher and HDL was significantly lower in CRS patients (all p<0.05). Lastly, hs-troponin T (832.50 ± 83.30 vs. 605.27 ± 101.82 pg/mL) and NT-proBNP (7.08 ± 1.52 vs. 5.34 ± 1.33 ng/mL) were significantly elevated in CRS (p<0.001), indicating greater cardiac strain (Table 1).

The correlations among cardiac function parameters and biomarkers are presented in Figure 1. Ejection fraction demonstrated significant inverse correlations with creatinine (r = –0.563, p<0.0001), hs-troponin T; r = –0.546, p<0.0001, and NT-proBNP; r = –0.459, p<0.0001). Conversely, creatinine exhibited strong positive correlations with hs-troponin T (r = 0.711, p<0.0001) and NT-proBNP (r = 0.667, p<0.0001). A similarly robust positive association was observed between hs-troponin T and NT-proBNP (r = 0.627, p<0.0001).

Table 2, in the ACRS group, both hs-Troponin T (B = 0.020, p = 0.027) and NT-proBNP (B = 1.915, p = 0.004) significantly predicted ejection fraction. Their standardized beta coefficients (0.388 for hs-Troponin T and 0.395 for NT-proBNP) indicated moderate effect sizes, suggesting that elevated levels of these biomarkers are closely associated with changes in left ventricular function among ACRS patients.

As shown in Table 3, higher hs-troponin T values were associated with a modest but significant increase in the odds of hospitalization beyond one week (OR range: 1.006–1.010, p<0.01). In contrast, NT-proBNP demonstrated a stronger predictive effect (odds ratio [OR] up to 9.465, p<0.01), indicating that elevated biomarker levels substantially increased the likelihood of extended inpatient care.

Hs-troponin t demonstrated diagnostic accuracy for AKI secondary to AHF, with an area under the ROC curve AUC of 0.958 (p < 0.0001). At a cut-off value of ≤720.08, Hs-TnT achieved 80.00% sensitivity and 100.00% speci-

Table 1. Baseline Clinical and Laboratory Characteristics of the Studied Groupsa

Characteristic	AHF (n = 30)	Acute CRS (n = 30)	p
Age, years (mean ±SD)	62.97 ± 5.60	64.60 ± 7.09	0.587 I NS
Sex			
Male , n (%)	19 (63.3%)	13(43.3%)	0.098 F NS
Female ,n (%)	11 (36.7%)	17 (56.7%)	
BMI, kg/m² (mean ±SD)	28.46 ± 1.44	28.85 ± 1.75	0.620 I NS
Ejection fraction, % (mean ±SD)	41.70 ± 5.08	34.73 ± 2.49	<0.001 I***
NYHH			
Class II , n (%)	8 (26.7%)	0 (0.0%)	<0.001 F***
Class III , n (%)	22 (73.3%)	9 (30.0%)	
Class IV , n (%)	0 (0.0%)	21 (70.0%)	
Hospitalization			
Week ≤ one	19 (63.3%)	0 (0.0%)	<0.001 F***
Week >one	11(36.7%)	30 (100%)	
Creatinine, mg/dl (mean ±SD)	1.14 ± 0.07	2.64 ±0.53	<0.001 I***
eGFR (MDRD) (mean ±SD)	69.35 ± 10.37	55.04 ± 9.66	<0.001 I***
AST, U/L (mean ±SD)	26.24 ± 4.02	41.77 ± 5.18	<0.001 I***
ALT, U/L (mean ±SD)	30.07 ± 6.87	39.58 ± 7.11	<0.001 I***
Total Bilirubin, mg/dl (mean ±SD)	0.86 ±0.14	1.24 ± 0.19	<0.001 I***
Total CHO, mg/dl, (mean ±SD)	171.67 ±5.51	164.69 ± 1.52	<0.001 I***
TG, mg/dl (mean ±SD)	127.25±5.77	137.33 ±16.45	0.009 I**
LDL CHO, mg/dl (mean ±SD)	83.77 ±1.38	76.25 ±8.46	<0.001 I***
HDL, mg/dl (mean ±SD)	49.45 ±1.94	43.04 ± 1.65	<0.001 I***
Hs-Troponin T, pg/mL (mean ±SD)	605.27 ±101.82	832.50 ±83.30	<0.001 I***
NT-proBNP, ng/mL (mean ±SD)	5.34 ±1.33	7.08 ± 1.52	<0.001 I***

n: number of cases; SD: standard deviation; Fisher's exact test; I: independent samples t-test; NS: not significant (P ≥ 0.05).

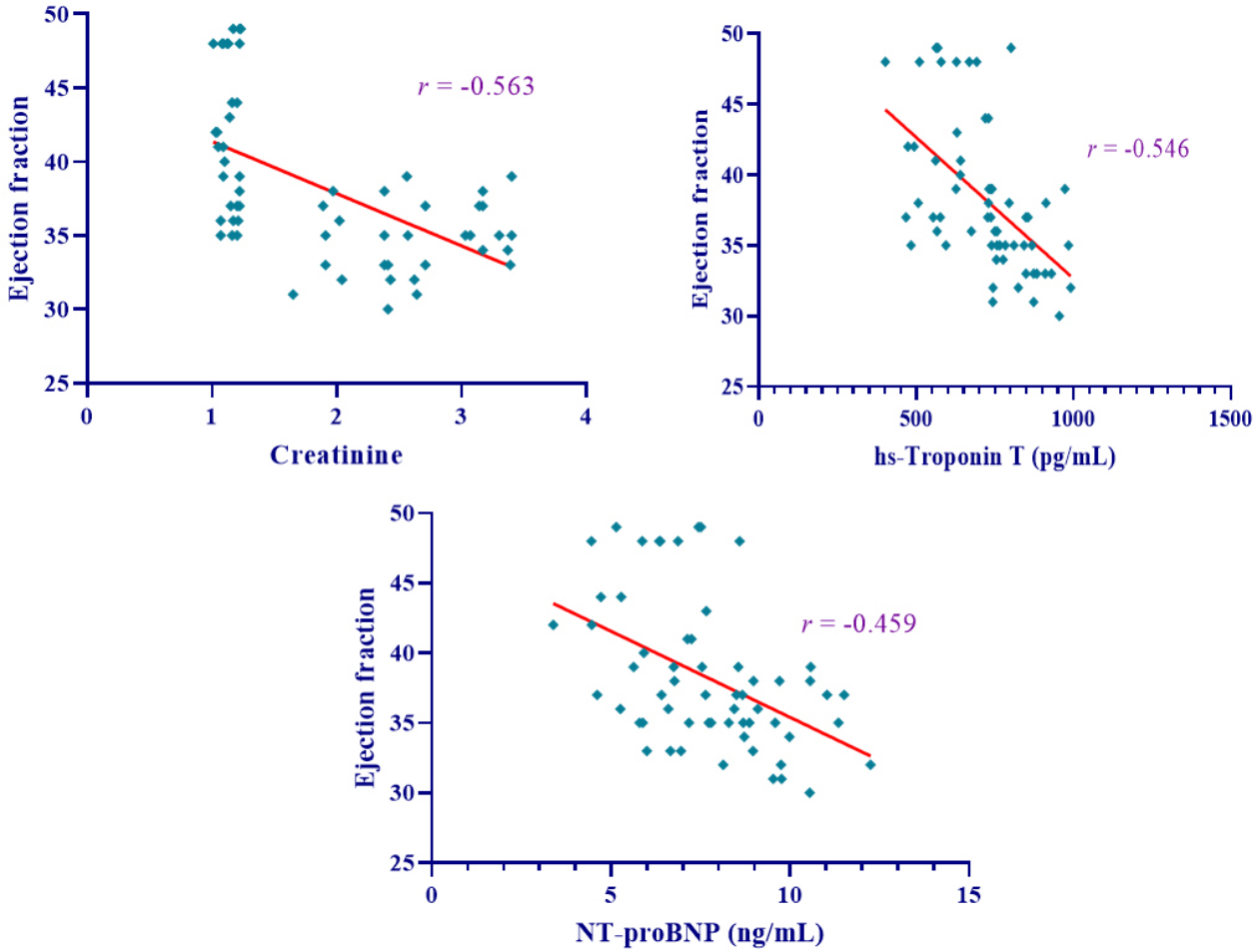


Fig. 1. graphical charts of these correlations of theses biomarkers

Table 2. Linear Regression Analysis of Ejection Fraction on Cardiac Biomarkers

Coefficients [a,b]								
Groups	Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
AHF +ACRS	hs-Troponin T (pg/mL)	0.020	0.009	0.388	2.273	0.027	0.002	0.038
	NT-proBNP (ng/mL)	1.915	0.628	0.395	3.048	0.004	0.656	3.174

a. Dependent Variable: Ejection fraction

b. Linear Regression through the Origin

Table 3. Multivariate Logistic Regression of Cardiac Biomarkers Predicting Hospitalization Duration

	Hospitalization	B	SIG.	OR	95% confidence interval for (or)	
Predictors of biomarkers					Lower Bound	Upper Bound
Hs-troponin T (pg/ml)	Week ≤ one [a]	0.006	0.032	1.006	1.001	1.011
	Week >one [a]	0.007	0.008	1.007	1.002	1.013
	Week >one [b]	0.010	0.0001*	1.010	1.004	1.015
NT-proBNP (ng/ml)	Week ≤ one [a]	1.281	0.0001*	3.599	1.897	6.831
	Week >one [a]	2.248	0.001*	9.465	9.465	9.465
	Week >one [b]	0.967	0.003*	2.630	1.386	4.991

A. The reference category is: healthy control

B. The reference category is: week ≤ one.

ficity. Comparatively, NT-proBNP exhibited a robust diagnostic performance, with an AUC of 0.91 ($p < 0.0001$). At its optimal threshold (≤7.66), NT-proBNP yielded 90.00% sensitivity and 83.00% specificity. Both biomarkers displayed statistically significant discriminative capacities ($p< 0.0001$), though Hs-TnT demonstrated superior specificity (100.00% vs. 83.00%) while NT-proBNP showed higher sensitivity (90.00% vs. 80.00%) at their respective cut-offs.

Discussion

In this study, we examined the interrelationships between left ventricular function, renal impairment, and key cardiac hs-Troponin T and NT-proBNP, in patients with

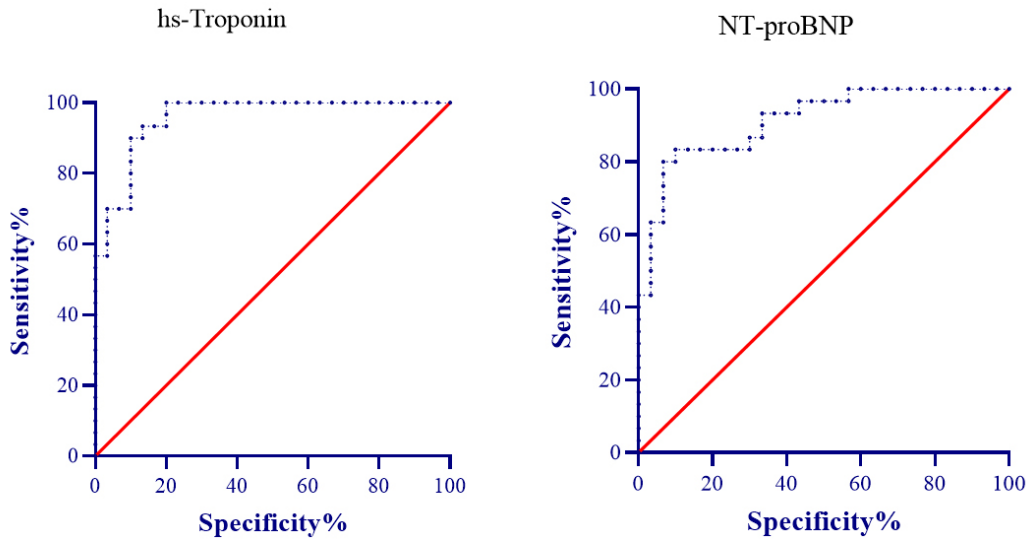


Fig. 2. ROC Curves: Diagnostic Accuracy of hs-TnT and NT-proBNP

AHF, both with and without concomitant renal dysfunction CRS. Our findings revealed that CRS patients exhibit significantly lower left ventricular ejection fraction (LVEF), elevated serum creatinine, and a more atherogenic lipid profile than patients with AHF alone. Moreover, both hs-troponin T and NT-proBNP levels were substantially higher in the CRS group, exhibiting strong inverse correlations with LVEF and strong positive correlations with serum creatinine levels. These findings reinforce the concept that declining myocardial function and worsening renal performance occur in parallel and are reflected in these biomarkers [32].

A key observation was that while demographic characteristics such as age, sex, and BMI were similar between the groups, CRS patients were markedly more symptomatic, with 70% presenting with NYHA class IV, and experienced significantly prolonged hospitalizations. The lower LVEF in CRS patients underscores the compounded impact of renal dysfunction on myocardial performance, a finding consistent with previous reports [33,34]. Our correlation analyses revealed that LVEF was inversely related to serum creatinine, hs-Troponin T, and NT-proBNP levels. These relationships suggest that as cardiac function deteriorates, renal impairment worsens and biomarker levels increase. In parallel, the strong positive correlations between serum creatinine and cardiac biomarkers (hs-Troponin T; NT-proBNP) highlight the bidirectional nature of the cardiorenal interaction. This interplay, whereby reduced cardiac output diminishes renal perfusion and exacerbates myocardial injury, has been well-documented [7,35].

Linear regression analysis revealed that in the CRS group, elevated hs-troponin T and NT-proBNP levels were significant predictors of reduced LVEF, indicating that ongoing myocardial injury and neurohormonal activation directly contribute to left ventricular dysfunction. These findings indicate that ongoing myocardial injury and neurohormonal activation, as reflected by these biomarkers, directly contribute to left ventricular dysfunction [36]. Notably, hs-troponin T appears to directly mirror myocardial injury, which may be accentuated in the presence of renal dysfunction owing to both reduced clearance and increased cardiac stress [37]. In contrast, Hs-TnT and NT-proBNP demonstrate strong diagnostic utility for AKI in AHF, with Hs-TnT prioritizing specificity and NT-proBNP favoring sensitivity, both showing significant discriminative capacity despite differing performance profiles.

Beyond these observations, the interplay between left ventricular dysfunction and renal impairment involves a complex network of neurohormonal, inflammatory, and oxidative stress pathways [38]. Reduced cardiac output in heart failure precipitates renal hypoperfusion, triggering activation of the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system, which not only contributes to further myocardial remodeling but also exacerbates renal injury [39]. At the molecular level, the dynamics of these biomarkers offer deeper insights into their underlying pathophysiologies. High-sensitivity troponin T is released following cardiomyocyte injury and apoptosis, and its kinetics are influenced by both the extent of injury and the renal clearance efficiency [40]. NT-proBNP synthesis is driven by increased myocardial wall stress, and its plasma levels reflect a balance between production and renal clearance [41].

The inflammatory and oxidative stress mechanisms further complicate this relationship. Cytokine-mediated inflammation leads to endothelial dysfunction, which is characterized by reduced NO bioavailability and increased vascular stiffness, thereby impairing myocardial perfusion and accelerating renal injury [42]. Oxidative stress, which promotes apoptotic signaling in cardiomyocytes, may amplify troponin release and accelerate myocardial damage [43].

Recent advances in biomarker kinetics have highlighted the emerging mediators that link cardiac and renal pathologies. For example, fibroblast growth factor-23 (FGF-23) and soluble klotho have been associated with early fibrotic

and inflammatory changes in both myocardium and kidneys [44,45]. Additionally, transforming growth factor-beta (TGF-β) signaling has been implicated in fibrosis in both tissues, suggesting shared molecular pathways in cardiac and renal remodeling [46,47].

These observations have several implications. First, the combined measurement of hs-troponin T and NT-proBNP can facilitate the early identification of high-risk patients who are prone to more severe cardiac dysfunction and prolonged hospital stays. Such early risk stratification could allow clinicians to adopt more aggressive management strategies, potentially reducing morbidity and optimizing resource allocation. Second, given its superior discriminative ability, hs-troponin T may be particularly useful as a rapid triage marker to distinguish AHF patients with underlying renal impairment in emergency settings. Finally, the clear association between these biomarkers and left ventricular dysfunction supports their integration into clinical decision-making algorithms to tailor therapeutic interventions more precisely.

Strength and Limitations

Despite these promising findings, several limitations should be acknowledged. An observational single-center design may limit the generalizability of our results, and the cross-sectional nature of our analysis precludes definitive conclusions regarding causality. Future longitudinal and multicenter studies are needed to confirm these observations and to determine whether biomarker-guided management strategies can translate into improved patient outcomes. Additionally, further research should explore the molecular mechanisms-such as neurohormonal activation, oxidative stress, and inflammatory pathways-that underlie the interplay between cardiac and renal dysfunction.

Conclusion

Our study demonstrated that concomitant renal dysfunction is associated with significantly impaired cardiac function and elevated troponin T and NT-proBNP levels in patients with AHF. The strong interrelationships between these parameters offer mechanistic insights into the pathophysiology of cardiorenal syndrome and underscore the potential of these biomarkers for diagnostic and prognostic applications. Notably, hs-Troponin T showed superior diagnostic accuracy, suggesting its utility in early risk stratification and in guiding more targeted therapeutic interventions in this high-risk patient population.

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Authors' contribution

The authors contributed equally to the conceptualization of the research, collected data, and participated in data analysis and writing, editing, and review.

Conflict of interest

None to declare.

Ethical aproval

The study protocol was approved by the Institutional Ethics Committee (Approval No.34328) in accordance with the Declaration of Helsinki.

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Availability of data and material

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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