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Original Research Article

Role of NT-proBNP in Predicting Short-Term Mortality and Rehospitalisation in Heart Failure

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Abstract

Background: Heart failure (HF) is a major cause of morbidity, mortality, and recurrent hospitalization worldwide. Early identification of high-risk patients is essential for optimizing management and improving clinical outcomes. N-terminal pro-B-type natriuretic peptide (NT-proBNP) has emerged as an important biomarker reflecting myocardial wall stress and may provide valuable prognostic information in patients with HF.

Methods: This prospective observational study included 110 consecutive patients admitted with heart failure. Clinical characteristics, laboratory investigations, including admission NT-proBNP levels, and echocardiographic parameters were recorded. Patients were followed for 90 days to assess the occurrence of all-cause mortality and rehospitalization due to worsening heart failure. Receiver operating characteristic (ROC) curve analysis and multivariable logistic regression were performed to evaluate the prognostic value of NT-proBNP.

Results: The mean age of the study population was 64.3 ± 12.1 years, and 61.8% were male. During the 90-day follow-up, 18 patients (16.4%) died and 32 (29.1%) were rehospitalised. Patients with adverse outcomes had significantly higher admission NT-proBNP concentrations than those without events ($p < 0.001$). NT-proBNP levels were significantly associated with both short-term mortality and rehospitalisation. After adjustment for potential confounders, admission NT-proBNP >5000 pg/mL independently predicted the composite endpoint of mortality or rehospitalisation (adjusted OR 4.28, 95% CI 1.89–9.71; $p < 0.001$). Chronic kidney disease, age ≥65 years, and left ventricular ejection fraction <35% were also independent predictors. ROC analysis demonstrated good predictive performance of NT-proBNP, with an area under the curve of 0.84.

Conclusion: Admission NT-proBNP is a strong independent predictor of short-term mortality and rehospitalisation in patients hospitalized with heart failure. Incorporating NT-proBNP into routine clinical assessment may improve early risk stratification, facilitate individualized management, and identify patients who may benefit from closer monitoring and intensified follow-up after hospital discharge.

Keywords: Heart failure; NT-proBNP; Mortality; Rehospitalization; Prognosis; Biomarker; Risk stratification.

Introduction

Heart failure (HF) is a complex clinical syndrome caused by structural and/or functional impairment of ventricular filling or ejection, resulting in inadequate cardiac output and elevated intracardiac pressures[1]. It represents one of the leading causes of cardiovascular morbidity, mortality, and hospitalization worldwide, affecting more than 64 million people globally. Despite substantial advances in pharmacological therapy, device-based interventions, and multidisciplinary heart failure

management, the burden of HF continues to increase owing to population ageing, improved survival after acute myocardial infarction, and the rising prevalence of hypertension, diabetes mellitus, obesity, chronic kidney disease, and other cardiovascular risk factors. Consequently, HF remains associated with frequent hospital admissions, recurrent decompensation, diminished quality of life, and considerable healthcare expenditure [2,3].Hospitalization for heart failure marks a critical stage in the disease trajectory and is associated with a high risk of adverse outcomes[4]. Approximately one in four patients is rehospitalized within 30–90 days following discharge, while mortality remains substantial during the first year after an episode of acute decompensated heart failure. Recurrent hospitalizations not only accelerate disease progression and functional decline but also impose a significant economic burden on healthcare systems. Therefore, early identification of patients at increased risk of short-term mortality and rehospitalization has become a major objective of contemporary heart failure management, allowing optimization of medical therapy, individualized follow-up, and timely implementation of advanced therapeutic interventions [2-4].

Risk stratification in heart failure has traditionally relied on clinical assessment, echocardiography, and routine laboratory investigations. Although these approaches provide valuable prognostic information, they may not adequately reflect the degree of myocardial stress or ongoing neurohormonal activation responsible for disease progression. Consequently, circulating cardiac biomarkers have emerged as important adjuncts for improving prognostic assessment. Among these, N-terminal pro-B-type natriuretic peptide (NT-proBNP) is the most extensively validated biomarker for both diagnosis and prognosis in patients with heart failure [5-8].NT-proBNP is an inactive amino-terminal fragment released into the circulation following cleavage of pro-brain natriuretic peptide from ventricular cardiomyocytes in response to increased myocardial wall stress, pressure overload, and volume expansion. Owing to its longer plasma half-life and greater analytical stability compared with biologically active B-type natriuretic peptide (BNP), NT-proBNP has become a preferred biomarker in routine clinical practice[8-9]. Circulating NT-proBNP concentrations correlate closely with ventricular filling pressures, left ventricular dysfunction, severity of heart failure, and overall disease burden. However, its interpretation should consider factors such as advanced age, renal dysfunction, obesity, and atrial fibrillation, all of which may independently influence circulating concentrations [6-10].A growing body of evidence has demonstrated that elevated NT-proBNP levels are independently associated with adverse clinical outcomes, including all-cause mortality, cardiovascular mortality, recurrent heart failure hospitalization, worsening functional status, and sudden cardiac death[11-12]. These associations have been consistently reported in both chronic stable heart failure and acute decompensated heart failure, irrespective of left ventricular ejection fraction[13]. Furthermore, serial measurement of NT-proBNP during hospitalization has shown additional prognostic value, with persistently elevated or inadequately declining concentrations identifying patients at greater risk of early clinical deterioration after discharge[14]. Several studies have suggested that markedly elevated NT-proBNP concentrations, particularly values exceeding approximately 5,000 pg/mL, are associated with substantially increased short-term mortality, although the optimal prognostic threshold remains uncertain [15].Despite the well-established role of NT-proBNP in diagnosing heart failure, its utility as a predictor of short-term mortality and rehospitalization has not been fully defined[16]. Previous studies have reported variability in prognostic performance due to differences in patient populations, timing of biomarker measurement, follow-up duration, comorbidities, renal function, and cut-off values used for risk prediction. Moreover, data regarding the prognostic implications of markedly elevated NT-proBNP concentrations remain limited, particularly in real-world clinical settings [17].

Given the persistent burden of early mortality and recurrent hospitalization following heart failure and the need for reliable biomarkers to improve risk stratification, further evaluation of NT-proBNP is clinically warranted. Therefore, the present study was undertaken to evaluate the role of NT-proBNP in predicting short-term mortality and rehospitalization among patients with heart failure.

Methodology:

A prospective observational study was conducted in the Department of medicine at tertiary care centre.

Study Population

A total of 110 consecutive patients admitted with a diagnosis of heart failure were included in the study. The diagnosis of heart failure was established according to contemporary international guideline recommendations based on compatible clinical symptoms and signs, supported by echocardiographic findings and relevant laboratory investigations.Both patients with newly diagnosed heart failure and those with acute decompensation of chronic heart failure were considered eligible for inclusion.

Inclusion Criteria

Patients were included if they fulfilled the following criteria:

- Age ≥18 years.
- Hospitalization with a diagnosis of acute heart failure or acute decompensated chronic heart failure.
- Clinical diagnosis supported by echocardiographic evidence of cardiac dysfunction.
- Availability of NT-proBNP measurement at admission.
- Provision of written informed consent.

Exclusion Criteria

Patients were excluded if they had:

- Acute myocardial infarction requiring immediate coronary intervention.
- Significant valvular heart disease requiring emergency surgery.
- Active systemic infection or sepsis.
- End-stage renal disease receiving maintenance dialysis.
- Known active malignancy with limited life expectancy.
- Incomplete clinical or laboratory data.
- Refusal to participate in the study.

Clinical Assessment

At the time of admission, demographic characteristics, cardiovascular risk factors, medical history, clinical presentation, New York Heart Association (NYHA) functional class, vital signs, and physical examination findings were recorded using a standardized case record form.Comorbid conditions including hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease, and previous heart failure admissions were documented from patients' medical records.

Laboratory Investigations

Venous blood samples were collected at the time of hospital admission before initiation of definitive treatment. Routine laboratory investigations included complete blood count, renal function tests, liver function tests, serum electrolytes, blood glucose, and other investigations as clinically indicated.Serum NT-proBNP concentration was measured using a commercially available immunoassay according to the manufacturer's instructions. All measurements were performed in the central hospital laboratory under standardized quality-control procedures. NT-proBNP values were recorded in pg/mL for analysis.

Echocardiographic Assessment

Comprehensive transthoracic echocardiography was performed using a standard ultrasound system by experienced cardiologists. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's biplane method whenever feasible. Additional echocardiographic parameters including chamber dimensions, ventricular function, valvular abnormalities, and pulmonary artery systolic pressure were assessed according to current guideline recommendations.Patients were categorized according to left ventricular ejection fraction where appropriate.

Outcome Measures

The primary outcomes of the study were:

1. Short-term all-cause mortality.
2. Rehospitalization due to worsening heart failure during the follow-up period.

Mortality was defined as death from any cause occurring during the predefined follow-up period. Rehospitalization was defined as an unplanned hospital admission primarily attributable to worsening signs and symptoms of heart failure requiring intravenous therapy or inpatient management.

Follow-up

All enrolled patients were followed prospectively after hospital discharge for [30/90 days]. Follow-up information was obtained through scheduled outpatient visits, review of hospital records, and telephone interviews when necessary.

Patients who experienced death or rehospitalization during the follow-up period were identified and their outcomes were recorded.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version ___ (IBM Corp., Armonk, NY, USA).Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed variables were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median with interquartile range (IQR). Categorical variables were summarized as frequencies and percentages.Comparisons between groups were performed using the independent-samples t-test for normally distributed continuous variables and the Mann–Whitney U test for skewed data. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate.Receiver operating characteristic (ROC) curve analysis was performed to determine the prognostic performance of NT-proBNP in predicting short-term mortality and rehospitalization, and the optimal cut-off value was

identified using the Youden index. The area under the ROC curve (AUC) with 95% confidence intervals (CI) was calculated.

Variables showing a P value <0.10 in univariable analysis were entered into a multivariable logistic regression model to identify independent predictors of adverse outcomes. Results were expressed as odds ratios (ORs) with 95% confidence intervals.A two-sided P value <0.05 was considered statistically significant.

Results:

A total of 110 patients admitted with heart failure were included in the study. The mean age of the study population was 64.3 ± 12.1 years (median 66 years; IQR: 57–73 years; range: 29–88 years). Males constituted 68 (61.8%) of the patients, while 42 (38.2%) were females.The majority of patients belonged to the 61–70-year age group (34.5%), followed by 51–60 years (28.2%). Hypertension (70.9%) was the most prevalent comorbidity, followed by diabetes mellitus (45.5%), coronary artery disease (38.2%), chronic kidney disease (22.7%), and atrial fibrillation (20.9%).Most patients presented with advanced symptoms, with NYHA class III (52.7%) and NYHA class IV (34.5%) accounting for the majority of admissions.

Table 1. Baseline Demographic and Clinical Characteristics (N = 110)

Variable	Value
Age (years), mean ± SD	64.3 ± 12.1
Median age (IQR)	66 (57–73)
Male sex, n (%)	68 (61.8)
Female sex, n (%)	42 (38.2)
BMI (kg/m²), mean ± SD	26.8 ± 4.5
Hypertension	78 (70.9)
Diabetes mellitus	50 (45.5)
Coronary artery disease	42 (38.2)
Chronic kidney disease	25 (22.7)
Atrial fibrillation	23 (20.9)
Current smoker	31 (28.2)
NYHA III	58 (52.7)
NYHA IV	38 (34.5)
HFrEF	69 (62.7)
HFmrEF	16 (14.5)
HFpEF	25 (22.7)

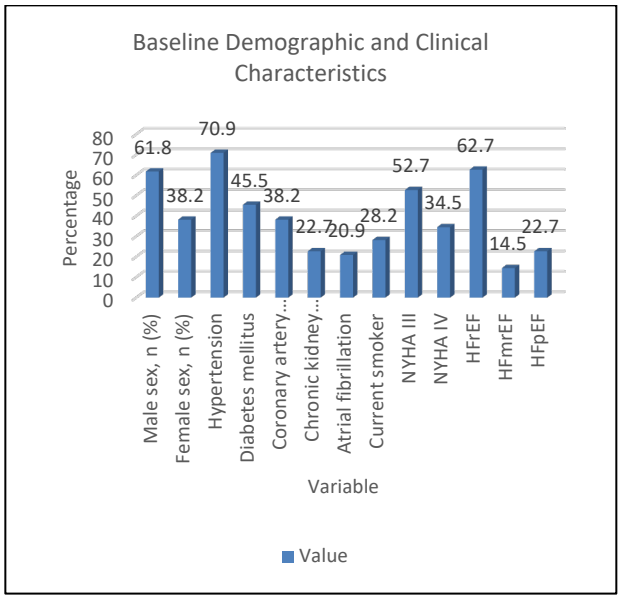

Figure 1.Baseline Demographic and Clinical Characteristics (N = 110)

Laboratory Characteristics

The median admission NT-proBNP concentration was 5,480 pg/mL (IQR 2,960–9,720 pg/mL). Mean serum creatinine was 1.48 ± 0.61 mg/dL, while the median estimated glomerular filtration rate (eGFR) was 58 mL/min/1.73 m² (IQR 42–76).Mean hemoglobin concentration was 11.7 ± 2.0 g/dL, and serum sodium was 136.2 ± 4.8 mmol/L.

Table 2. Laboratory Parameters

Parameter	Value
NT-proBNP (pg/mL), median (IQR)	5480 (2960–9720)
Creatinine (mg/dL), mean ± SD	1.48 ± 0.61
eGFR (mL/min/1.73m²), median (IQR)	58 (42–76)
Hemoglobin (g/dL), mean ± SD	11.7 ± 2.0
Sodium (mmol/L), mean ± SD	136.2 ± 4.8
Potassium (mmol/L), mean ± SD	4.3 ± 0.6

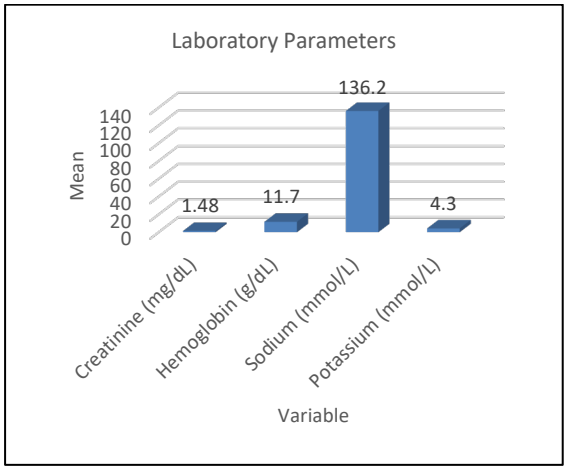

Figure 2. Laboratory Parameters

Echocardiographic Findings

The mean left ventricular ejection fraction (LVEF) was 36.5 ± 12.4%. Reduced ejection fraction (HFrEF) was observed in 62.7% of patients.

Table 3. Echocardiographic Characteristics

Variable	Value
LVEF (%), mean ± SD	36.5 ± 12.4
LVEDD (mm), mean ± SD	58.7 ± 7.4
Left atrial diameter (mm), mean ± SD	43.2 ± 6.1
PASP (mmHg), mean ± SD	41.5 ± 13.6

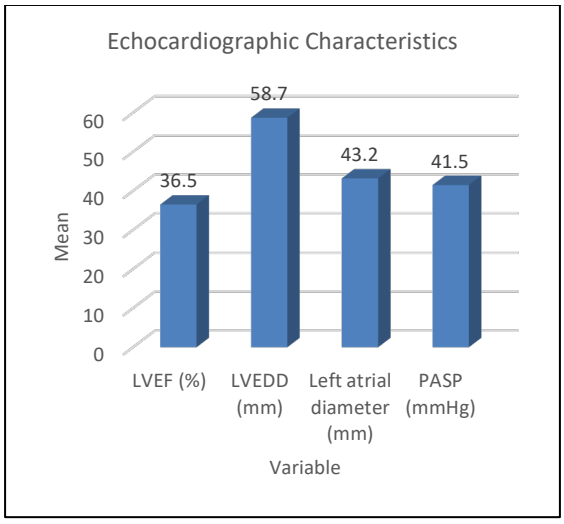

Figure 3. Echocardiographic Characteristics

Clinical Outcomes

During the 90-day follow-up, 18 patients (16.4%) died, while 32 patients (29.1%) required rehospitalization due to worsening heart failure.

Comparison Between Survivors and Non-survivors

Patients who died were significantly older than survivors (70.1 ± 10.3 vs. 63.1 ± 11.9 years; independent-samples t-test, p = 0.012). Median admission NT-proBNP concentration was significantly higher among non-survivors (10,840 [8,120–15,960] vs. 4,620 [2,740–7,880] pg/mL; Mann–Whitney U test, p < 0.001).Renal dysfunction was more common among patients who died (44.4% vs. 18.5%; Chi-square test, p = 0.018). Mean LVEF was significantly lower in non-survivors (29.8 ± 8.7% vs. 37.8 ± 12.5%; independent t-test, p = 0.006).

Table 4. Comparison Between Survivors and Non-survivors

Variable	Survivors (n=92)	Non-survivors (n=18)	Statistical test	p-value
Age (years)	63.1 ± 11.9	70.1 ± 10.	Independent t-test	0.012
Male (%)	60.9	66.7	Chi-square	0.64
NT-proBNP (pg/mL)	4620 (2740–7880)	10840 (8120–15960)	Mann–Whitney U	<0.001
Creatinine (mg/dL)	1.39 ± 0.54	1.91 ± 0.73	Independent t-test	0.002
LVEF (%)	37.8 ± 12.5	29.8 ± 8.7	Independent t-test	0.006
CKD (%)	18.5	44.4	Chi-square	0.018

Comparison Between Rehospitalized and Non-rehospitalized Patients

Patients who required rehospitalization had significantly higher NT-proBNP concentrations (8,120 [5,640–12,380] vs. 4,180 [2,510–6,960] pg/mL; Mann–Whitney U test, $p < 0.001$). Rehospitalized patients also had lower LVEF (32.7 ± 10.5% vs. 38.1 ± 12.8%; independent t-test, $p = 0.031$) and a higher prevalence of atrial fibrillation (37.5% vs. 14.1%; Chi-square test, $p = 0.009$)

Table 5. Comparison Between Rehospitalized and Non-rehospitalized Patients

Variable	Rehospitalized (n=32)	No Rehospitalization (n=78)	Statistical test	p-value
NT-proBNP (pg/mL)	8120 (5640–12380)	4180 (2510–6960)	Mann–Whitney U	<0.001
LVEF (%)	32.7 ± 10.5	38.1 ± 12.8	Independent t-test	0.031
CKD (%)	37.5	16.7	Chi-square	0.021
Atrial fibrillation (%)	37.5	14.1	Chi-square	0.009

Multivariable Logistic Regression Analysis

After adjustment for potential confounders, admission NT-proBNP concentration >5,000 pg/mL remained an independent predictor of the composite endpoint of short-term mortality or rehospitalization (adjusted OR 4.28, 95% CI 1.89–9.71, $p < 0.001$). Chronic kidney disease, age ≥65 years, and LVEF <35% were also independently associated with adverse outcomes.

Table 6. Multivariable Logistic Regression

Variable	Adjusted OR	95% CI	p-value
NT-proBNP >5000 pg/mL	4.28	1.89–9.71	<0.001
Age ≥65 years	2.31	1.08–4.95	0.031
CKD	2.74	1.16–6.47	0.021
LVEF <35%	2.52	1.13–5.61	0.024

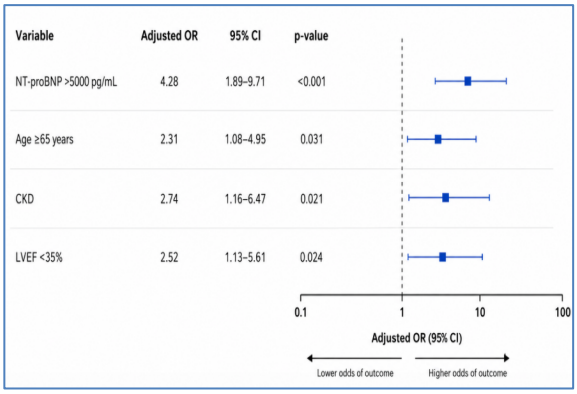

Figure 4: Multivariable Logistic Regression

Discussion

The present study evaluated the prognostic role of admission NT-proBNP in predicting short-term mortality and rehospitalization among patients hospitalized with heart failure. The principal findings were that: (1) patients with adverse outcomes had significantly higher admission NT-proBNP concentrations; (2) elevated NT-proBNP independently predicted the composite outcome of short-term mortality and rehospitalization after adjustment for important clinical variables; (3) reduced left ventricular ejection fraction (LVEF), chronic kidney disease (CKD), and older age were additional independent predictors of poor prognosis; and (4) admission NT-proBNP demonstrated good discriminatory ability for identifying high-risk patients, with an AUC of 0.84. These findings support the role of NT-proBNP as an important biomarker for early risk stratification in patients admitted with acute or decompensated heart

failure.The demographic profile of our study population was comparable with previous heart failure cohorts. The mean age of our patients was 64.3 ± 12.1 years, and nearly two-thirds were male. Hypertension (70.9%) and diabetes mellitus (45.5%) were the predominant comorbidities, reflecting the well-established cardiovascular risk profile observed in patients with heart failure worldwide. The majority of our patients presented with advanced symptoms (NYHA class III or IV), indicating that hospitalization frequently occurred in patients with substantial functional impairment and advanced disease severity. These characteristics are similar to those reported in contemporary heart failure registries and clinical studies, where older age, multiple comorbidities, and advanced NYHA class are consistently associated with worse clinical outcomes[18].

The most important finding of our study was the strong association between admission NT-proBNP concentration and adverse short-term outcomes. Patients who died during follow-up had markedly higher median NT-proBNP concentrations than survivors (10,840 vs. 4,620 pg/mL; $p < 0.001$), while rehospitalized patients also demonstrated significantly higher values than those who remained event-free (8,120 vs. 4,180 pg/mL; $p < 0.001$). These observations are consistent with the established pathophysiological role of NT-proBNP as a marker of ventricular wall stress, increased intracardiac filling pressures, and neurohormonal activation. Elevated concentrations reflect greater myocardial dysfunction and disease severity, thereby identifying patients at increased risk of subsequent adverse events.Our findings closely agree with the study by Bettencourt and colleagues, who demonstrated that patients with persistently elevated NT-proBNP during hospitalization experienced significantly higher rates of cardiovascular death and heart failure readmission during follow-up. They further showed that a smaller reduction in NT-proBNP during hospitalization was associated with a substantially worse prognosis, emphasizing that both baseline levels and temporal changes carry prognostic value[19]. Similarly, the Swedish prospective cohort study involving hospitalized heart failure patients reported that NT-proBNP was the only biomarker independently associated with both cardiac rehospitalization and long-term mortality after adjustment for multiple clinical variables. Although several biomarkers predicted mortality, NT-proBNP uniquely retained prognostic significance for rehospitalization, highlighting its clinical value for identifying patients requiring closer post-discharge surveillance. These observations closely parallel our findings, in which elevated admission NT-proBNP independently predicted the composite endpoint of mortality and rehospitalization[18]. Our ROC analysis demonstrated good predictive performance of admission NT-proBNP (AUC 0.84), suggesting excellent discrimination between patients with and without adverse outcomes. This finding is comparable to previous studies evaluating NT-proBNP-based risk prediction. Investigators developing the ADHF/NT-proBNP risk score similarly reported excellent discrimination (C-statistic >0.80) for predicting in-hospital and 90-day mortality, indicating that incorporation of NT-proBNP substantially improves short-term prognostic assessment in patients admitted with acute decompensated heart failure[20]. Another important observation from our study was that reduced LVEF remained an independent predictor of poor outcome. Patients who died or required rehospitalization had significantly lower LVEF than those without events. This finding is biologically plausible because impaired systolic function reflects advanced myocardial dysfunction and reduced cardiac reserve. Similar associations between reduced LVEF and adverse clinical outcomes have

been consistently demonstrated in heart failure registries and prognostic studies, although NT-proBNP frequently provides incremental prognostic information beyond conventional echocardiographic parameters[18]. Chronic kidney disease also emerged as an independent predictor of adverse outcomes in our study. Patients with CKD had significantly greater mortality and rehospitalization rates than those with preserved renal function. Renal dysfunction contributes to heart failure progression through impaired sodium and water excretion, activation of neurohormonal pathways, chronic inflammation, and reduced clearance of natriuretic peptides. Consequently, patients with combined cardiac and renal dysfunction represent a particularly high-risk subgroup requiring more intensive management. Similar observations have been reported in previous prospective cohorts evaluating biomarkers in heart failure[18].Advanced age was another independent predictor of poor prognosis in our cohort. Patients aged ≥65 years experienced significantly higher rates of mortality and rehospitalization after multivariable adjustment. Older patients frequently have greater comorbidity burden, impaired functional reserve, frailty, and reduced tolerance to heart failure therapies, all of which contribute to poorer outcomes. These findings are consistent with previous heart failure registries that have identified age as one of the strongest clinical determinants of mortality.The present study has important clinical implications. Measurement of admission NT-proBNP is simple, rapid, and widely available in routine clinical practice. Our findings suggest that NT-proBNP may assist clinicians in identifying patients at increased risk for early mortality or rehospitalization, thereby facilitating more intensive monitoring, optimization of guideline-directed medical therapy, closer follow-up after discharge, and timely referral to specialized heart failure programs. Although randomized trials evaluating NT-proBNP-guided treatment strategies have not consistently demonstrated improved clinical outcomes, the prognostic value of NT-proBNP for risk stratification remains well established and continues to support its use as a valuable adjunct to comprehensive clinical assessment[21,22].

Conclusion

Admission NT-proBNP was a strong predictor of short-term mortality and rehospitalization among patients hospitalized with heart failure. Higher NT-proBNP concentrations were significantly associated with adverse outcomes and remained an independent predictor even after adjustment for age, chronic kidney disease, and reduced left ventricular ejection fraction. NT-proBNP also demonstrated good discriminatory ability for identifying high-risk patients. Therefore, measurement of NT-proBNP at admission may serve as a simple and useful tool for early risk stratification, closer clinical monitoring, and optimization of post-discharge follow-up in patients with heart failure.

Limitations

This study has several limitations. First, it was conducted at a single tertiary care center with a relatively modest sample size of 110 patients, which may limit the generalizability of the findings to broader heart failure populations. Second, NT-proBNP was measured only at the time of hospital admission; serial measurements during hospitalization and follow-up were not evaluated, precluding assessment of the prognostic significance of changes in biomarker levels over time. Third, the follow-up period was limited to 90 days, and therefore the long-term predictive value of NT-proBNP for mortality and recurrent hospitalization could not be determined. Finally, although multivariable analysis was performed, the

observational design cannot exclude the possibility of residual confounding, and larger multicenter prospective studies are needed to validate these findings and establish optimal NT-proBNP thresholds for routine clinical risk stratification.

Ethical approval

Ethical approval for this study was obtained from the Institutional Ethics Committee prior to the commencement of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and applicable institutional guidelines.

Informed Consent

Written informed consent was obtained from all participants prior to their enrolment in the study.

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Conflict of Interest Declaration

The authors declare no conflict of interest.

Data Availability Statement

All data generated or analysed during this study are available from the corresponding author upon reasonable request.

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