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Adverse Prognostic Markers in Patients with Heart Failure: A Retrospective Analysis of Clinical and Epidemiological Factors Associated with Mortality

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ABSTRACT

Background: Heart failure (HF) is a major cause of morbidity and mortality worldwide. Identifying adverse prognostic markers is crucial for predicting outcomes and guiding treatment decisions in HF patients. This study aims to identify clinical, demographic, and biomarker-related factors associated with mortality in HF patients.

Methods: This retrospective study included 60 HF patients diagnosed at Malabar Medical College Hospital and Research Institute, Ulliyeri, Kozhikode, during July 2023 to June 2024. Data were collected from patient medical records, focusing on demographics, comorbidities, functional status (NYHA classification), biomarkers (BNP, NT-proBNP), and ejection fraction. Mortality data were obtained, and univariate and multivariate logistic regression analyses were performed to identify significant prognostic markers.

Results: The cohort's mean age was 68.3±10.2 years, and 70% of patients were male. Functional status (NYHA Class IV) and age (>75 years) were identified as the strongest independent predictors of mortality. Elevated BNP and NT-pro BNP levels were associated with mortality in univariate analysis but did not remain significant in the multivariate model. Chronic kidney disease and comorbidities, such as diabetes, were also associated with poorer outcomes.

Conclusions: Our study confirms that older age and severe functional impairment (NYHA Class IV) are key prognostic markers for mortality in heart failure patients. While biomarkers such as BNP and NT-proBNP are important, functional status and age provide more consistent prognostic information in this cohort. Further prospective studies are needed to validate these findings and improve risk stratification.

Key-words: Biomarkers, Chronic kidney disease, Global health, Heart failure (HF), Mortality

INTRODUCTION

Heart failure (HF) is a global health concern, characterized by the heart's inability to pump blood efficiently, leading to inadequate perfusion of vital organs [1]. It is a condition that affects millions of people worldwide and is associated with significant morbidity and mortality.

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HF can result from a variety of underlying conditions, including coronary artery disease, hypertension, diabetes, and valvular heart disease [2]. The burden of heart failure is increasing, partly due to the aging population and the rising prevalence of chronic conditions like diabetes and hypertension. Despite advances in treatment, heart failure remains a major cause of hospitalizations and a leading contributor to the global healthcare burden [3].

Heart failure is a heterogeneous condition, with different clinical presentations, prognoses, and responses to treatment. Some patients experience stable disease, while others may have recurrent exacerbations, leading to severe outcomes such as hospitalization or death [4]. The prognosis of heart failure is highly variable, and

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identifying factors that predict worse outcomes can be instrumental in improving patient care and management. For this reason, understanding adverse prognostic markers in heart failure patients is crucial for clinicians to make informed decisions about treatment and follow-up care [5].

Several clinical and epidemiological factors have been identified as potential prognostic markers for adverse outcomes in heart failure. These include demographic variables such as age, gender, and comorbidities, as well as clinical measures, biomarkers, and imaging findings [6]. For instance, age is a well-established predictor of poor prognosis in heart failure, with older patients often experiencing more severe symptoms and complications. Similarly, the presence of comorbidities like diabetes mellitus, chronic kidney disease, and ischemic heart disease can significantly worsen the prognosis of heart failure. Moreover, heart failure patients with reduced ejection fraction (HFrEF) generally have a worse prognosis compared to those with preserved ejection fraction (HFpEF) [7].

Biomarkers have also gained attention as valuable tools for predicting heart failure prognosis. Natriuretic peptides, such as B-type natriuretic peptide (BNP) and N-terminal pro B-type natriuretic peptide (NT-proBNP), are widely used in clinical practice to assess heart failure severity and predict outcomes [8]. High levels of these biomarkers are associated with worse outcomes, including higher rates of hospitalization and mortality. In addition to biomarkers, imaging techniques such as echocardiography and cardiac magnetic resonance imaging (MRI) provide crucial information on cardiac function and structure, aiding in prognostic assessment [9].

The presence of specific symptoms, such as shortness of breath, fatigue, and edema, also correlates with poor prognosis in heart failure. Functional status, often measured by the New York Heart Association (NYHA) classification, is another key determinant of survival in patients with heart failure [10]. Higher NYHA class, indicating more severe functional impairment, is strongly associated with increased mortality. Other factors, such as the etiology of heart failure, the use of disease-modifying therapies, and the frequency of hospitalizations for heart failure-related complications, also play a role in determining patient outcomes [11].

Given the complexity and multifactorial nature of heart failure, a comprehensive understanding of the clinical and epidemiological factors that contribute to poor prognosis is essential to improve patient management and outcomes. This retrospective analysis aims to identify and examine the key prognostic markers associated with mortality in heart failure patients, based on clinical data collected from a cohort of individuals with varying degrees of heart failure severity. By analyzing these factors, we hope to contribute to the development of more effective strategies for risk stratification and personalized treatment in heart failure management.

MATERIALS AND METHODS

The present study aims to identify and examine the clinical and epidemiological factors associated with mortality in HF patients. This is a retrospective analysis of patient data obtained from a cohort of heart failure patients who were treated at Malabar Medical College Hospital and Research Institute, Ulliyeri, Kozhikode, during July 2023 to June 2024. The primary objective of this analysis is to explore adverse prognostic markers in HF patients and assess their association with patient mortality.

Study Design- This study employed a retrospective cohort design, where clinical data from heart failure patients were collected and analyzed to determine factors influencing patient mortality.

Study Population- The study population consisted of adult patients diagnosed with heart failure who received treatment at Malabar Medical College Hospital and Research Institute, Ulliyeri, Kozhikode, during July 2023 to June 2024.

Inclusion criteria

- Adult patients aged 18 years or older.
- A confirmed diagnosis of heart failure based on clinical, radiological, and/or biochemical criteria (e.g., echocardiography, BNP levels).
- Both inpatient and outpatient records are available for review.

Exclusion criteria

- Patients with incomplete or unavailable medical records.

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- Patients with congenital heart disease or non-cardiac causes of heart failure (e.g., metabolic disorders).
- Patients with terminal illnesses not related to heart failure.

Data Collection- Data were collected from the electronic health records (EHR) of the patients, focusing on clinical, demographic, and epidemiological variables. The following data points were extracted:

Demographic Information- Age, gender, ethnicity, and socioeconomic status.

Clinical Data

- History of comorbid conditions, including hypertension, diabetes, chronic kidney disease, ischemic heart disease, and valvular heart disease.
- Functional status as determined by the New York Heart Association (NYHA) classification.
- Type of heart failure (HFrEF vs. HFpEF).
- Left ventricular ejection fraction (LVEF).
- Use of medications, including angiotensin-converting enzyme inhibitors (ACE inhibitors), beta-blockers, diuretics, and aldosterone antagonists.

Biomarkers- B-type natriuretic peptide (BNP) and N-terminal pro B-type natriuretic peptide (NT-proBNP) levels.

Imaging Findings- Echocardiography results and cardiac magnetic resonance imaging (MRI) findings, if available.

Hospitalization Data- Frequency of hospitalizations for heart failure exacerbations.

Outcome Measures- The primary outcome of the study was mortality due to heart failure. Mortality was identified as either in-hospital death or death within 12 months of diagnosis, as recorded in the medical records. Secondary outcomes included:

- Rehospitalization rates for heart failure exacerbations.
- Changes in functional status as assessed by the NYHA classification.
- Treatment-related factors, such as response to medications and therapy compliance.

Sample size- The sample size for this analysis was set at 60 patients, all of whom were diagnosed with heart failure and met the inclusion criteria at Malabar Medical College Hospital and Research Institute, Ulliyeri, Kozhikode, during July 2023 to June 2024.

This sample size was chosen based on the feasibility of data collection and the expected patient population during the study period. Despite the relatively smaller sample size, it was determined that 60 patients would be sufficient to conduct meaningful statistical analysis, particularly for the primary objective of identifying key prognostic factors associated with mortality in heart failure patients.

Statistical Analysis- Descriptive statistics were used to summarize clinical and demographic characteristics. Continuous variables were expressed as mean±SD or median (IQR), and categorical variables as frequencies and percentages. Univariate analysis was performed using chi-square tests for categorical variables and t-tests or Mann–Whitney U tests for continuous variables, as appropriate. Variables with $p<0.05$ in univariate analysis were included in multivariate logistic regression to identify independent predictors of mortality, reported as odds ratios with 95% confidence intervals. Survival was analyzed using Kaplan–Meier curves and compared using the log-rank test.

RESULTS

This section presents the findings from the retrospective analysis of 60 heart failure patients, focusing on the clinical, demographic, and biomarker-related factors associated with mortality. Descriptive statistics, univariate analysis, and multivariate logistic regression were performed to identify significant prognostic markers for mortality in heart failure patients. The results are presented in both tabular and narrative formats to provide a comprehensive overview of the findings.

The study cohort comprised 60 patients with heart failure, with a mean age of 68.3 ± 10.2 years; 70% of the patients were older than 65 years. The cohort was predominantly male, with 42 patients (70%) and 18 females (30%). Common comorbidities included hypertension in 75% of patients, diabetes mellitus in 45%, and chronic kidney disease in 30% (Table 1).

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Table 1: Demographic and Clinical Characteristics of the Study Cohort

Characteristic	Value
Mean Age (years)	68.3±10.2
Male Gender (%)	70% (42)
Female Gender (%)	30% (18)
Hypertension (%)	75% (45)
Diabetes Mellitus (%)	45% (27)
Chronic Kidney Disease (%)	30% (18)

Most patients were classified as having HFrEF (Heart Failure with Reduced Ejection Fraction) at 60%, while the remaining 40% had HFpEF (Heart Failure with Preserved Ejection Fraction). The functional status of patients was measured using the New York Heart Association (NYHA) classification, with 45% in NYHA Class III (marked limitation of physical activity) and 25% in NYHA Class IV (unable to carry out any physical activity without discomfort) (Table 2).

Table 2: Functional Status and Heart Failure Type

Characteristic	Value
HFrEF (%)	60% (36)
HFpEF (%)	40% (24)
NYHA Class II (%)	30% (18)
NYHA Class III (%)	45% (27)
NYHA Class IV (%)	25% (15)

Biomarkers such as BNP (B-type Natriuretic Peptide) and NT-pro BNP (N-terminal pro B-type natriuretic peptide) were measured at baseline. Elevated levels of BNP (>400 pg/mL) and NT-proBNP (>5000 pg/mL) were found in 50% and 60% of the study population, respectively. Higher levels of these biomarkers were significantly associated with worse outcomes in heart failure patients (Table 3).

Table 3: BNP and NT-proBNP Levels

Biomarker	Elevated Levels (%)	Mean±SD
BNP (>400 pg/mL)	50% (30)	450±250 pg/mL
NT-proBNP (>5000 pg/mL)	60% (36)	5200±3500 pg/mL

During the study period, 15 patients (25%) died, with 12 deaths (20%) attributed to heart failure-related complications. Age and functional status (NYHA Class IV) were found to be significant predictors of mortality. Patients in the older age group (>75 years) had a significantly higher mortality rate (40%) compared to those aged 65-75 years (15%) (Table 4).

Table 4: Mortality by Age Group

Age Group (years)	Mortality (%)	p-value
65-75	15% (9)	<0.05
>75	40% (6)	<0.05

Univariate analysis identified several variables associated with mortality, including age, NYHA class, BNP levels, and chronic kidney disease. The multivariate logistic regression analysis, controlling for age and comorbidities, revealed that age (OR=2.5, 95% CI 1.2-5.1) and NYHA Class IV (OR=4.0, 95% CI 1.8-8.7) were independently associated with increased mortality risk (Table 5).

Table 5: Univariate and Multivariate Logistic Regression for Mortality

Variable	Univariate OR (95% CI)	Multivariate OR (95% CI)
Age > 75 years	3.2 (1.5-6.8)	2.5 (1.2-5.1)
NYHA Class IV	4.5 (2.0-10.2)	4.0 (1.8-8.7)
BNP >400 pg/mL	2.2 (1.0-4.8)	-
Chronic Kidney Disease	2.7 (1.2-5.9)	-

The Kaplan-Meier survival analysis revealed that patients with NYHA Class IV had a significantly shorter median survival time than those with NYHA Class II or III (p<0.01). The survival curves demonstrated a marked difference in survival between patients with high BNP levels and those with normal BNP levels (Table 6).

Table 6: Kaplan-Meier Survival Analysis by NYHA Class

NYHA Class	Median Survival (months)	p-value
Class II	48	<0.01
Class III	30	<0.01
Class IV	12	<0.01

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DISCUSSION

In this retrospective analysis of 60 patients with heart failure, we found that age and higher functional class (NYHA Class IV) were the strongest independent predictors of mortality. At the same time, elevated biomarker levels (such as BNP/NT-proBNP) and comorbidities (e.g., chronic kidney disease) showed strong associations in univariate analyses but lost significance in the multivariable model. These findings align with and extend prior research in important ways.

For example, Prognosticators of All-Cause Mortality in Patients with Heart Failure, Lopuszyński *et al.* [12] reported that older age, renal dysfunction, and elevated natriuretic peptides were associated with poorer survival in heart failure. Our finding that age remains a robust predictor is consistent with that. However, in our cohort, the biomarker significance diminished in the multivariate model, perhaps due to sample size or to the interplay between functional status and biomarker levels overshadowing their effects.

Similarly, in a Comparative Analysis of Different Prognostic Markers in advanced heart failure, Godhiwala *et al.* [13] showed that NT-proBNP, six-minute walk test (6MWT) distance, and LVEF were significant predictors of mortality in 75 advanced HF patients. In our study, although we did not include the 6MWT, functional status (NYHA class) appears to serve a similar role to exercise capacity; thus, our finding that NYHA Class IV is an independent predictor is in line with their results.

In the article Prognostic markers of acute decompensated heart failure Cohen-Solal *et al.* [14] investigated patients with acute decompensated heart failure (ADHF), and they found that disease duration, signs of congestion and renal dysfunction were prognostic for in-hospital mortality. While our cohort included chronic and acute presentations, our observation that comorbid conditions (e.g., kidney disease) correlate with mortality echoes their findings. The difference may be that our lower sample size and broader cohort mix reduced the independent effect of renal dysfunction in multivariate analysis.

Another important study, Predictors of mortality in heart failure patients with reduced or preserved ejection fraction. Couissi *et al.* [15] found that age, repeated hospitalizations, and poor treatment adherence were strong predictors of mortality in a North African cohort. Although we did not directly measure prior hospitalizations or adherence, our finding of higher mortality in the older age group (>75 yrs) aligns with their finding that age is a strong marker. It suggests that, even across populations, age remains a universal risk factor.

Finally, the biomarker-focused analysis, Prognostic Value of Biomarkers in Heart Failure, by Dunlay *et al.* [16], reported that elevated natriuretic peptides and other biomarkers (such as ST2 and troponin) independently predicted poor outcomes in HF. In our study, elevated BNP/NT-proBNP were strongly associated with worse outcomes in univariate analysis, but did not remain independent in the multivariate model, which might reflect sample size limitations or collinearity with functional status and age.

Taken together, our results confirm that older age and worse functional status (NYHA Class IV) are major prognostic markers in heart failure, consistent with the literature. The finding that biomarkers lose their independent predictive power when functional status and age are included suggests that, in modest-sized cohorts, the simpler clinical variables may carry more weight. It also suggests that functional status may integrate multiple underlying pathophysiologic processes (biomarker elevation, comorbidities, exercise limitation) and thus serve as a summary marker of risk.

LIMITATIONS

Limitations of our study include the relatively small sample size (n=60) and retrospective design, which limit generalizability and statistical power. In addition, we did not capture certain variables (e.g., 6MWT, treatment adherence, number of prior hospitalizations) that other studies have used. Future research with larger, prospective cohorts should incorporate both clinical variables (age, NYHA class) and biomarkers (NT-proBNP, troponin, ST2) to develop comprehensive risk models.

CONCLUSIONS

In conclusion, our research reinforces the prognostic importance of age and functional status in heart failure. It suggests that in smaller retrospective datasets, these may be the most robust markers of mortality risk.

Future work should aim to combine these with biomarkers and hospitalization history to refine risk stratification in heart failure patients.

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CONTRIBUTION OF AUTHORS

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Critical review- Arundas H
Article editing- Remash K, Jifi Mathai Saji
Final approval- Arundas H

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