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Original research

PROGNOSTIC VALUE OF THE BIOSTAT RISK SCORE FOR ALL-CAUSE MORTALITY IN PATIENTS WITH ACUTE HEART FAILURE

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ABSTRACT

Objectives: *To determine the 6-month all-cause mortality rate in patients with AHF after hospital discharge and evaluate the prognostic value of the BIOSTAT score for predicting all-cause mortality in this population.*

Methods: *A descriptive cross-sectional study with longitudinal follow-up was conducted on patients aged ≥18 years who were discharged with a diagnosis of AHF from Thong Nhat Cardiovascular Center between January 2024 and December 2024. All patients were followed for 6 months post-discharge for the outcome of all-cause mortality.*

Results: *A total of 309 patients aged ≥ 18 years diagnosed with AHF were included. The 6-month all-cause mortality rate was 18.77%. Among these, 83.17% had a BIOSTAT score between 0 and 3 (BIOSTAT scores of 0, 1, 2, and 3 accounted for 16.50%, 20.39%, 24.60%, and 21.68%, respectively), while 16.83% had a BIOSTAT score between 4 and 5 (BIOSTAT scores of 4 and 5 were 11.97% and 4.85%, respectively). Compared with patients having BIOSTAT scores of 0 - 3, those with scores of 4 - 5 had a significantly higher hazard ratio (HR) for all-cause mortality: 1.84 (p = 0.03). The area under the ROC curve (AUC) was 0.838.*

Conclusion: *A higher BIOSTAT score (4 - 5 points) was significantly associated with increased risk of mortality (p < 0.05). The area under the ROC curve (AUC) was 0.838.*

Keywords: *Acute heart failure, all-cause mortality, BIOSTAT risk score.*

I. INTRODUCTION

Acute heart failure (AHF) remains a major global health burden and is the leading cause of hospitalization in individuals aged ≥65 years in high-income countries [1]. Despite advances in the management of chronic heart failure, outcomes for patients hospitalized with AHF have not improved substantially over the past two decades. Worldwide, millions of patients are admitted each year with AHF, with reported in-hospital mortality rates ranging from 4% to 10%, 6-month mortality rates between 15% and 30%, and 1-year rehospitalization rates exceeding 50% [1,2]. The clinical complexity of AHF poses significant challenges in early risk stratification. Most patients present with multiple comorbidities, such as hypertension, diabetes, renal dysfunction, or anemia, which are independently associated with worse outcomes [3,4]. Given the high post-discharge morbidity and mortality, effective tools for early prognostication are essential to guide therapeutic decision-making, optimize resource allocation, and reduce rehospitalization rates.

In response to this need, several risk prediction models have been developed and validated in AHF populations, including ADHERE, OPTIMIZE-HF, and MAGGIC. Among them, the BIOSTAT risk score, derived from the large multicenter BIOSTAT-CHF study conducted in Europe, has

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emerged as a promising tool. This model integrates five clinically accessible parameters-age ≥ 70 years, blood urea nitrogen (BUN) > 11 mmol/L, NT-proBNP > 4000 pg/mL, hemoglobin ≤ 12 g/dL, and no prior use of beta-blockers-and has demonstrated good prognostic performance, with an area under the receiver operating characteristic (ROC) curve of 0.72 [5]. Although the BIOSTAT score has shown utility in European populations, its applicability and predictive performance in other settings, including Southeast Asia, remain unclear. In Vietnam, most existing studies on AHF have focused on short-term outcomes such as in-hospital or 30-day mortality using relatively small sample sizes [6-8]. To date, no study has specifically evaluated the BIOSTAT score in a Vietnamese population with acute heart failure.

Therefore, the objective of this study was to determine the 6-month all-cause mortality rate and assess the prognostic value of the BIOSTAT risk score in patients with acute heart failure admitted to Thong Nhat Hospital.

II. MATERIALS AND METHODS

Study design and population: We conducted a cross-sectional study with longitudinal follow-up involving patients aged 18 years and older who were diagnosed with acute heart failure (AHF) at the time of hospital discharge, in accordance with the 2021 European Society of Cardiology (ESC) guidelines [9]. Patients with malignancies or those who declined to participate were excluded.

Study Setting and Duration: The study was conducted at the Cardiovascular Center of Thong Nhat Hospital from January 2024 to December 2024. Patient recruitment was conducted from January to May 2024. The last patient was enrolled in May, and follow-up was completed in November 2024.

Sample Size Calculation: The required sample size was calculated using a prevalence (p) of 0.5 to obtain the maximum sample size, with a margin of error (d) of 0.06 and a confidence level of 95% (α = 0.05).

$$n = \frac{Z^2_{(1-\alpha/2)} p(1-p)}{d^2}$$

The estimated minimum sample size was 267 patients. Accounting for a 10% potential loss to follow-up, the final target sample size was adjusted to 294 patients.

Sampling Method: Consecutive sampling was applied throughout the study period.

Definition of Key Variables:

BIOSTAT Risk Score Components: The BIOSTAT score includes five clinical parameters, each contributing one point to the total score (Table 1):

Table 1: Definition of BIOSTAT Score Components [5]

Parameter	Definition	Score
Elevated NT-proBNP	NT-proBNP > 4000 pg/mL	1
Anemia	Hemoglobin ≤ 12 g/dL	1
Older Age	Age ≥ 70 years	1
Elevated Blood Urea Nitrogen (BUN)	BUN > 11 mmol/L	1
No Prior Beta-blocker Use	No history of beta-blocker therapy as documented in records	1

All-cause Mortality: Defined as death from any cause during the 6-month follow-up period.

Follow-up Protocol: Patients were followed monthly through the hospital's electronic medical records system or via direct phone contact. Deaths occurring at Thong Nhat Hospital were verified using the hospital database. For deaths outside the hospital or at home, confirmation was obtained by phone with the patient's family. Patients were considered lost to follow-up if contact could not be established during the 6-month observation period.

Statistical Analysis: Categorical variables were summarized as frequencies and percentages. Continuous variables were presented as mean ± standard deviation for normally distributed data or as median and

interquartile range (IQR 25-75%) for non-normally distributed data. Univariate Cox proportional hazards models were used to explore associations between predictors and all-cause mortality. Multivariate Cox regression and Kaplan-Meier survival analysis were performed to evaluate mortality risk. Discriminative ability of the BIOSTAT score was assessed using receiver operating characteristic (ROC) curves, with the area under the curve (AUC) reported. A p-value < 0.05 was considered statistically significant, with a 95% confidence interval.

III. RESULTS

During the study period and 6-month post-discharge follow-up, a total of 309 patients aged ≥18 years who were diagnosed with acute heart failure (AHF) at discharge and met the inclusion criteria were enrolled and completed follow-up. Baseline chasracteristics of the study population are summarized in Table 2, and 6-month all-cause mortality outcomes are shown in Table 3.

Table 2: Baseline Characteristics of the Study Population (N=309)

Characteristic	Number (n)	Percentage (%)
General Characteristics		
Male	111	35.92
Age (years), mean ± SD	70.75 ± 12.74	
Age ≥ 70 years	174	56.31
Medical History		
Hypertension	276	89.32
Diabetes mellitus	137	44.34
Dyslipidemia	236	76.38
Atrial fibrillation	72	23.30
Chronic kidney disease	72	23.30
Prior heart failure	227	73.46
Coronary artery disease	168	55.37
Stroke	27	8.74
No history of beta-blocker use	125	40.45
Laboratory Findings		
BUN > 11 mmol/L	38	12.30
Hemoglobin ≤ 12 g/Dl	145	46.93
NT-proBNP > 4000 pg/Ml	180	58.25
Precipitating Factors for Acute Heart Failure		
Acute coronary syndrome	154	49.84
Infection	95	30.74
CHAMPIT-related causes	221	71.52
Other causes	110	35.60
Multiple precipitating factors	28	9.06

The study cohort was characterized by an older population, with a mean age of 70.75 ± 12.74 years, and a predominance of females, as males accounted for only 35.92%. In addition to a high prevalence of prior heart failure (73.46%), the majority of patients presented with multiple comorbidities. The most frequent comorbid condition was hypertension (89.32%), followed by dyslipidemia (76.38%), coronary artery disease (55.37%), and diabetes mellitus (44.34%). Regarding precipitating factors for acute heart failure, acute coronary syndrome was the most commonly identified cause (49.84%), followed by infections (30.74%). A substantial proportion of patients (71.52%) had identifiable precipitants classified under the CHAMPIT mnemonic. Notably, 9.06% of patients presented with multiple concurrent triggers for acute decompensation.

Table 3: All-Cause Mortality Rate at 6 Months

Variable	Number of Deaths (n)	Mortality Rate (%)	p-value
All-cause mortality (N = 309)	58	18.77	–
BIOSTAT Score Groups			
BIOSTAT 0 - 3 points (n = 257)	19	7.39	0.031
BIOSTAT 4 - 5 points (n = 52)	39	75.00	

During the 6-month follow-up period, a total of 58 patients (18.77%) died from all causes. Stratification by BIOSTAT score revealed a significantly lower mortality rate in the low-score group (0 - 3 points: 7.39%) compared to the high-score group (4 - 5 points: 75.00%). This difference was statistically significant (p = 0.031), indicating that a higher BIOSTAT score was strongly associated with increased risk of mortality.

The analysis showed a trend toward increasing hazard ratios (HR) for all-cause mortality with higher BIOSTAT scores. Although individual point estimates for BIOSTAT scores of 1 to 5 did not reach statistical significance (p > 0.05), patients with a score of 4 or 5 had a notably elevated risk. When grouped, patients with a BIOSTAT score of 4 - 5 had a significantly higher risk of all-cause mortality compared to those with a score of 0 - 3 (HR = 1.81; 95% CI: 1.06 - 3.21; p = 0.031), indicating that a higher BIOSTAT score is associated with increased mortality risk (Table 4, Figure 1, Figure 2).

Table 4: Association Between BIOSTAT Score and Risk of All-Cause Mortality

BIOSTAT Score	Hazard Ratio (HR)	95% Confidence Interval	p-value
BIOSTAT = 1	1.32	0.12 - 14.64	0.82
BIOSTAT = 2	1.37	0.14 - 13.20	0.78
BIOSTAT = 3	1.73	0.23 - 13.30	0.60
BIOSTAT = 4	2.52	0.34 - 18.75	0.37
BIOSTAT = 5	3.91	0.51 - 30.21	0.19
Grouped BIOSTAT Score			
BIOSTAT 0 - 3	1	-	-
BIOSTAT 4 - 5	1.81	1.06 - 3.21	0.031

The analysis showed a trend toward increasing hazard ratios (HR) for all-cause mortality with higher BIOSTAT scores. Although individual point estimates for BIOSTAT scores of 1 to 5 did not reach statistical significance (p > 0.05), patients with a score of 4 or 5 had a notably elevated risk. When grouped, patients with a BIOSTAT score of 4 - 5 had a significantly higher risk of all-cause mortality compared to those with a score of 0 - 3 (HR = 1.81; 95% CI: 1.06 - 3.21; p = 0.031), indicating that a higher BIOSTAT score is associated with increased mortality risk.

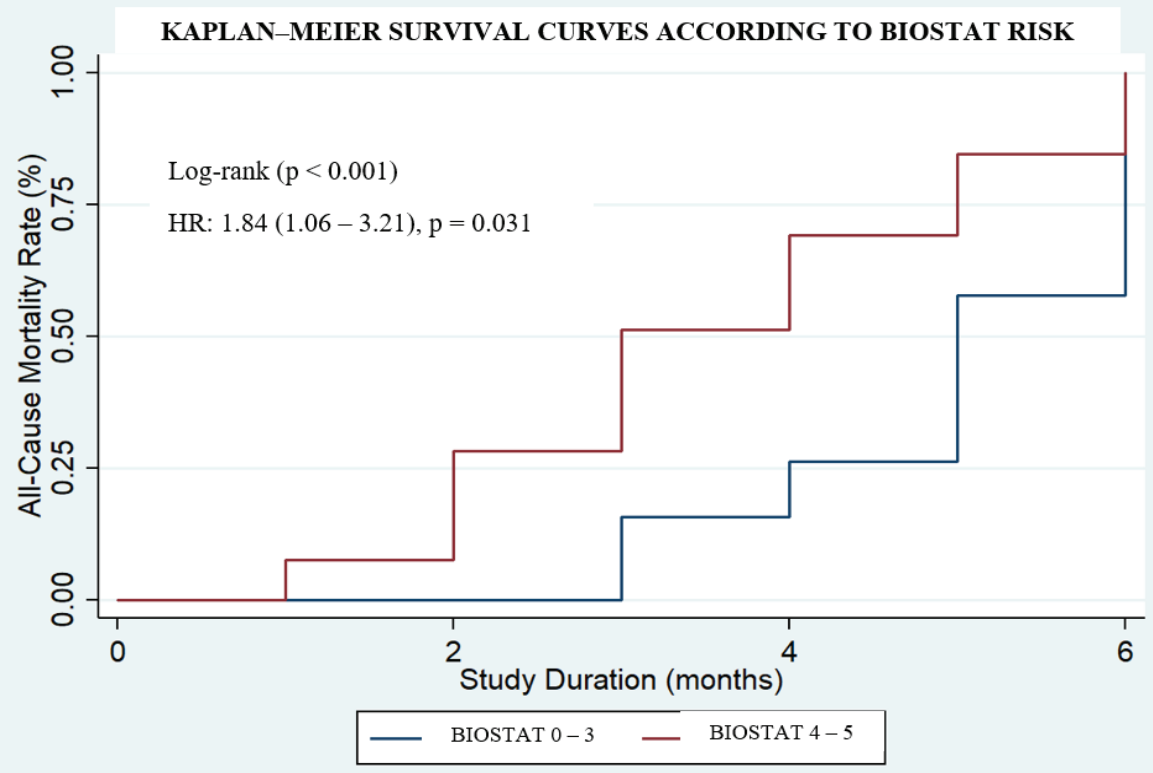

Figure 1: Kaplan-Meier Survival Curve Showing the Association Between BIOSTAT Score and All-Cause Mortality

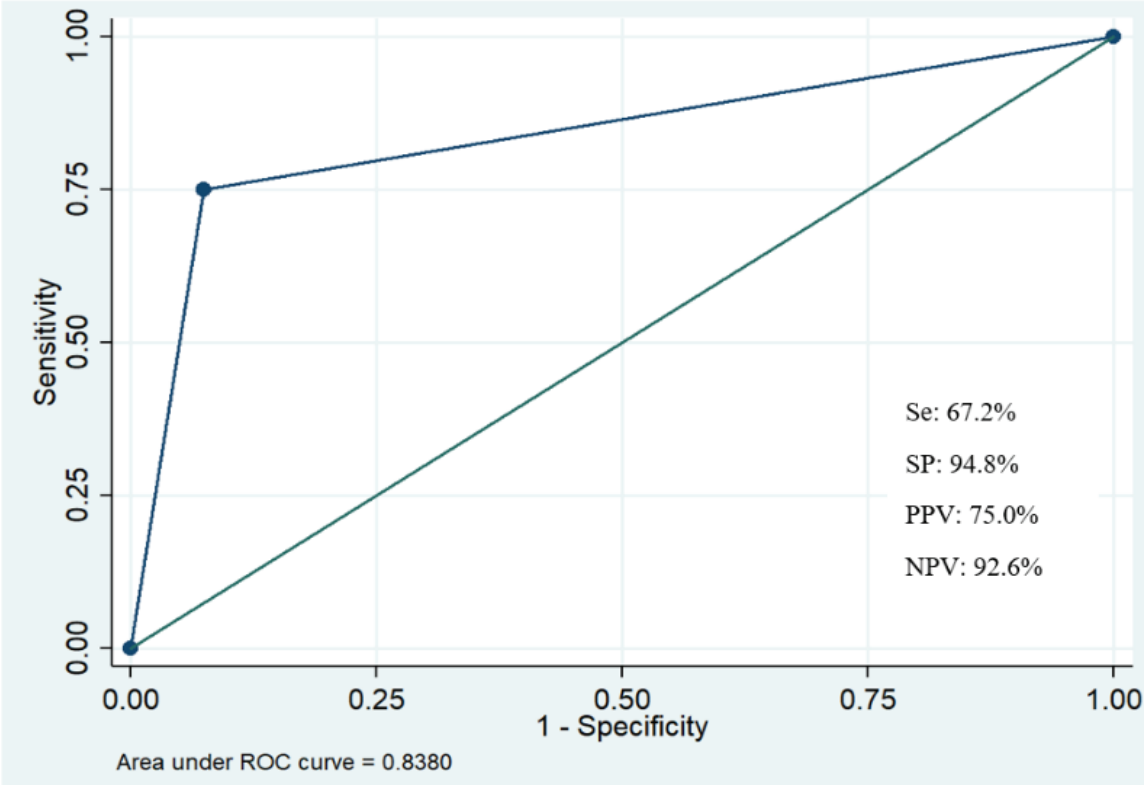

Figure 2: ROC Curve of the BIOSTAT Score for Predicting 6-Month All-Cause Mortality

IV. DISCUSSION

The present study included patients with acute heart failure (AHF) who had a relatively advanced mean age of 70.75 ± 12.74 years and a lower proportion of males (35.92%). A high burden of comorbidities was observed, particularly hypertension (89.32%), coronary artery disease (55.37%), and diabetes mellitus (44.34%). Compared with prior studies, our cohort tended to be older and more comorbid. For instance, Ho Thi Ngoc Duyen et al. (2021) reported a younger mean age of 62 ± 17.4 years and a higher proportion of males (52.3%) at Cho Ray Hospital, with lower rates of hypertension (61.9%) and chronic heart failure (59.9%) [6]. Similarly, Phuong et al. (2020) from 115 People's Hospital reported a mean age of 65.8 ± 14.8 years [7]. A more recent study by Nguyen Duc Khanh (2024) at Cho Ray Hospital documented a mean age of 71 years, 57.7% male, with comorbidities including renal dysfunction (69%), chronic anemia (59.2%), hypertension (41.8%), diabetes mellitus (28.5%), and dyslipidemia (21.1%) [8]. In our study, acute coronary syndrome (ACS) was the most frequently identified precipitating factor for decompensation, accounting for nearly half of the cases, followed by infection (30.74%). Notably, 71.52% of patients had causes classified within the CHAMPIT mnemonic, as outlined in the 2021 European Society of Cardiology (ESC) guidelines for acute heart failure [8]. Additionally, 9.06% of patients had multiple concurrent precipitants, underscoring the complex and multifactorial nature of AHF exacerbations. During the 6-month follow-up period, 58 patients (18.77%) died from all causes. Importantly, mortality was significantly higher among patients with high BIOSTAT scores (4 - 5 points) compared to those with lower scores (0–3 points), with a statistically significant difference ($p = 0.031$). This finding supports the prognostic utility of the BIOSTAT score for short-term mortality risk stratification in patients with AHF. The 2021 ESC guidelines also highlight the BIOSTAT score, developed from the BIOSTAT-CHF study, as a validated risk prediction tool incorporating clinical comorbidities and biomarkers such as NT-proBNP. Incorporating such tools into clinical practice may enable better risk stratification, guide post-discharge planning, and support individualized treatment strategies aimed at reducing mortality and rehospitalization in patients with acute heart failure.

The Kaplan-Meier survival curves in Figure 1 reveal a time-dependent divergence in all-cause mortality between patients with BIOSTAT scores of 0–3 and those with scores of 4 - 5 over a 6-month follow-up period. The survival probability in the high-risk group (BIOSTAT 4 - 5) began to decline earlier, with noticeable separation starting at month 1, suggesting early vulnerability in this population. By month 2, mortality in the high-risk group had already increased significantly, whereas the low-risk group maintained relatively stable survival. As follow-up progressed, the survival curves continued to diverge. By month 4, the cumulative mortality in the BIOSTAT 4 - 5 group had surpassed 50%, while the 0 - 3 group experienced only a modest rise. At the 6-month endpoint, mortality in the high-score group approached 75%, in contrast to less than 10% in the low-score group. The log-rank test confirmed a significant difference in survival ($p < 0.001$), and Cox regression analysis yielded a hazard ratio of 1.84 (95% CI: 1.06 - 3.21, $p = 0.031$) for high versus low BIOSTAT scores. These results underscore the time-sensitive prognostic value of the BIOSTAT score. The early and steep decline in survival among high-risk patients highlights the need for timely identification and post-discharge management strategies. Clinicians may consider enhanced follow-up, closer monitoring, and tailored interventions during the first 6 months-when mortality risk accelerates most rapidly-for patients identified as high risk at discharge.

The ROC curve analysis demonstrated good discriminatory power of the BIOSTAT score in predicting 6-month all-cause mortality among patients with acute heart failure. The area under the ROC curve (AUC) was 0.8380, indicating excellent overall performance. At the optimal cutoff point (BIOSTAT score: 4 - 5), the model yielded a sensitivity of 67.2%, a specificity of 94.8%, a positive predictive value (PPV) of 75.0%, and a negative predictive value (NPV) of 92.6%. These results suggest that the BIOSTAT score is a highly specific tool for identifying patients at high risk of death, while also maintaining a strong ability to rule out

mortality in low-risk individuals. The combination of high specificity and high NPV supports its utility in clinical decision-making, particularly for discharge planning and post-discharge surveillance. Moreover, the relatively high PPV emphasizes its value in identifying patients who may benefit from closer follow-up or more aggressive intervention.

V. CONCLUSION

The BIOSTAT risk score proved to be a valuable tool for predicting 6-month mortality risk in patients with acute heart failure. Our findings demonstrated that higher BIOSTAT scores (4 - 5 points) were significantly associated with increased risk of death.

Ethical considerations

The study protocol was reviewed and approved by the Institutional Review Board of Hue University of Medicine and Pharmacy (Approval No. H2024/013, dated January 16, 2024), the Ethics Committee in Biomedical Research of Thong Nhat Hospital, approval number 102/2023/BVTN-HDYD dated November 27, 2023

Conflict of interest

The authors declare no conflict of interest.

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