ORIGINAL ARTICLE

IDENTIFICATION OF PROGNOSTIC MARKERS IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE

Akut Dekompanse Kalp Yetersizliği Olan Hastalarda Prognostik Belirteçlerin Tanımlanması

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ABSTRACT

Objective: This study aims to evaluate the effectiveness of prognostic markers in predicting 90-day mortality in patients admitted to the hospital with a diagnosis of acute decompensated heart failure (ADHF).

Material and Methods: This retrospective study analyzed data from 559 ADHF patients admitted between 01.05.2023 and 01.09.2024. Age, sex, laboratory parameters, and 90-day mortality data were collected, and independent variables affecting mortality were evaluated via logistic regression and receiver operating characteristic (ROC) analysis.

Results: Age, blood urea nitrogen, albumin, and lactate levels were identified as independent predictors of 90-day mortality. The blood urea nitrogen level demonstrated the highest area under the curve (AUC = 0.673) for a cutoff value of 30.9 mg/dL. A significant increase in mortality risk was observed for patients with lactate levels >1.45 mmol/L.

Conclusion: Age, blood urea nitrogen, albumin, and lactate levels are strong prognostic markers for 90-day mortality in patients with ADHF. These findings may contribute to early risk stratification and the development of personalized treatment strategies.

Keywords: *Albumin; BUN; Heart Failure; Lactate; Mortality; Age*

ÖZET

Amaç: Bu çalışmada akut dekompanse kalp yetmezliği (ADKY) tanısıyla hastaneye yatırılan hastalarda 90 günlük mortaliteyi öngörmede prognostik belirteçlerin etkinliği değerlendirildi.

Gereç ve Yöntemler: Bu retrospektif çalışmada 01.05.2023 ile 01.09.2024 tarihleri arasında hastaneye yatırılan 559 ADHF hastasının verileri analiz edildi. Yaş, cinsiyet, laboratuvar parametreleri ve 90 günlük mortalite verileri toplandı ve mortaliteyi etkileyen bağımsız değişkenler lojistik regresyon ve alıcı işletim karakteristiği (ROC) analizi ile değerlendirildi.

Bulgular: Yaş, kan üre azotu, albümin ve laktat düzeyleri 90 günlük mortalitenin bağımsız belirleyicileri olarak tanımlandı. Kan üre nitrojen düzeyi, 30,9 mg/dL kesme değeri için en yüksek eğri altında kalan alanı (AUC = 0,673) göstermiştir. Laktat düzeyi >1,45 mmol/L olan hastalarda mortalite riskinde anlamlı bir artış gözlenmiştir.

Sonuç: Yaş, kan üre azotu, albümin ve laktat düzeyleri ADHF hastalarında 90 günlük mortalite için güçlü prognostik belirteçlerdir. Bu bulgular erken risk tabakalandırmasına ve kişiselleştirilmiş tedavi stratejilerinin geliştirilmesine katkıda bulunabilir.

Anahtar Kelimeler: *Albümin; BUN; Kalp Yetersizliği; Laktat; Mortalite; Yaş*

INTRODUCTION

Heart failure (HF) is a major public health issue worldwide associated with high mortality and morbidity rates. In the United States, it has been reported that 10–51% of patients hospitalized with HF require intensive care, and 10.6% of these patients die (1). Acute decompensated heart failure (ADHF) is characterized by the sudden onset or progressive worsening of HF symptoms and requires urgent medical intervention (2). ADHF accounts for approximately 70% of acute heart failure syndromes and is among the leading causes of hospitalization, healthcare costs, morbidity, and mortality. According to the literature, the annual mortality rate in patients with ADHF ranges between 20% and 30% (3,4).

Identifying appropriate treatment strategies for ADHF patients is crucial for improving care and reducing morbidity, mortality, and healthcare costs (5). Various biomarkers and risk stratification tools have been investigated to predict the prognosis of HF patients (6–9). Predicting mortality at the time of admission allows for the identification of high-risk patients, facilitates personalized treatment options, reduces costs, and improves patient prognosis (10). Therefore, this study aims to identify risk factors for 90-day mortality in hospitalized ADHF patients, enabling the early recognition of high-risk individuals and a more accurate prognosis estimation.

MATERIALS AND METHODS

This study was conducted retrospectively in a tertiary hospital and included patients aged 18 years and older admitted to the emergency department (ED) with a diagnosis of ADHF between 01.05.2023 and 01.09.2024. Approval was obtained from the local clinical research and ethics committee (Decision No: 2025/10). All procedures in this study were conducted in accordance with the ethical principles and guidelines outlined in the Declaration of Helsinki.

Patients presenting to Ordu University Research Hospital between 01.05.2023 and 01.09.2024 with a known diagnosis of HF and ADHF symptoms (dyspnea, orthopnea, or body swelling) who were evaluated by a cardiology specialist and subsequently admitted with an ADHF diagnosis were included in the study.

Patients under 18 years of age, pregnant women, those newly diagnosed with HF at the time of ED admission, those with a history of malignancy, those receiving renal replacement therapy, those with incomplete data in the data recording form, and those diagnosed with acute coronary syndrome, myocarditis, or pulmonary embolism in addition to ADHF were excluded from the study.

Demographic data, such as age and sex, as well as laboratory parameters, including white blood cell count (WBC), hemoglobin, red blood cell count (RBC), platelet count, neutrophil count, eosinophil count, glucose, blood urea nitrogen (BUN), creatinine, glomerular filtration rate (GFR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), sodium, potassium, chloride, albumin, and lactate, along with 90-day mortality status, were recorded in the data collection form. The data were obtained from the hospital's automated system. Inflammatory indices were calculated from the collected data:

Neutrophil-to-lymphocyte ratio (NLR) = neutrophil count/lymphocyte count

Platelet-to-lymphocyte ratio (PLR) = Platelet count/ lymphocyte count

Systemic immune-inflammation index (SII) = neutrophil count × platelet count/lymphocyte count

Statistical Analysis

Statistical analyses were performed via the IBM® SPSS® Statistics v.26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.) software package. Descriptive statistics are presented as the means ± standard deviations, medians (25th and 75th percentiles), frequencies, and percentages (%). The normality of the variable distributions was assessed via histograms, the Kolmogorov–Smirnov test, and skewness–kurtosis parameters. Quantitative variables were compared via the independent samples t test or Mann–Whitney U test, depending on the assumption of normality, whereas categorical variables were compared via the chi–square test.

To investigate the independent effects of variables on 90-day mortality, univariate and multivariate logistic regression analyses were performed, and odds ratios (ORs) were calculated. Variables that were found to be statistically significant ($p < 0.05$) in predicting 90-day

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mortality in the univariate logistic regression analysis were included in the multivariate logistic regression analysis to assess their independent effects. The diagnostic performance of variables identified as independent predictors of 90-day mortality via multivariate logistic regression analysis was evaluated via the receiver operating characteristic (ROC) curve and area under the curve (AUC) with a 95% confidence interval (CI). The cutoff values were determined via the Youden index. A p value <0.05 was considered to indicate statistical significance.

RESULTS

The mean age of the 559 patients included in the study was determined, with 45.08% (n=252) being male. 90-day mortality occurred in 40.43% (n=226) of the patients. No significant relationship was found between 90-day mortality and sex, while the mean age of deceased patients was significantly greater (p<0.001).

The mean WBC and neutrophil counts were greater in deceased patients than in survivors, but this difference was not statistically significant (p=0.299 and p=0.095). A statistically significant relationship was found between 90-day mortality and the NLR, RBC count, and platelet count (p=0.015, p=0.001, p=0.028, respectively). The median BUN, creatinine and lactate levels were significantly greater in the deceased patient group than in the survivor group (p<0.001), whereas the median lymphocyte, GFR, chloride, and albumin levels were significantly lower (p values: 0.014, <0.001, 0.018, and <0.001, respectively). The relationships among demographic characteristics, laboratory findings, and 90-day mortality are presented in Table 1.

To evaluate the independent effects of variables on 90-day mortality, univariate and multivariate logistic regression analyses were performed. Accordingly, age (OR: 1.036, p<0.001), BUN (OR: 1.023, p<0.001), albumin (OR: 0.573, p=0.001), and lactate (OR: 1.444, p<0.001) were identified as independent predictors of 90-day mortality in multivariate analysis. Details regarding the logistic regression analysis are provided in Table 2.

ROC analysis was performed on the independent predictors of 90-day mortality identified in the logistic regression analysis. Accordingly, BUN demonstrated the best predictive performance (AUC: 0.673, p<0.001), followed by age (AUC: 0.623, p<0.001). The highest sensitivity was observed with an age of 75.7%, whereas the highest specificity was observed with a BUN level of 71.8%. The ROC analysis graph is shown in Figure 1, and the performance characteristics of the variables in predicting 90-day mortality are provided in Table 3.

DISCUSSION

In the present study, age, BUN, albumin, and lactate levels measured at the time of ED admission were identified as independent predictors of 90-day mortality in ADHF patients. The BUN level had the highest AUC (0.673) for the prediction of 90-day mortality, with a cutoff value of 30.9 mg/dL. Age demonstrated the highest sensitivity (75.7%) at a cutoff value of 71.5 years.

A significant proportion of patients admitted with a diagnosis of ADHF are aged 75 years or older (11). Studies have shown that advanced age is associated with increased comorbid conditions, physical and cognitive impairment, and decreased self-care capacity. Owing to these risk factors, ADHF is associated with increased mortality rates in elderly patients (12,13). Lombardi et al. demonstrated that advanced age is an independent predictor of both in-hospital and long-term mortality in patients with acute HF (14). Similarly, Jacob et al. identified advanced age (≥75 years) as an independent predictor of short-term mortality (15). Consistent with these findings, the present study also revealed that advanced age independently predicts mortality in ADHF patients. In the ROC analysis, an age cutoff of >70.5 years was the second strongest predictor of 90-day mortality after BUN.

HF is frequently associated with impaired renal function. Studies have reported that impaired renal function can predict mortality in HF patients (6). BUN is a metabolic byproduct synthesized in the liver and serves as an indicator of the balance between urea production and renal excretion (16). Reduced renal perfusion leads to elevated BUN levels. In HF, decreased cardiac output results in renal hypoperfusion, activating neurohormonal mechanisms, including the renal sympathetic nervous system and the renin–angiotensin–aldosterone system, leading to increased

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Table 1. Relationships with 90-day mortality and patient demographic characteristics and clinical and laboratory findings.

	90-Day Mortality		
	Alive (n=333)	Deceased (n=226)	p values
Sex; n (%)			0.501
Male	154 (61.1%)	98 (38.9%)	
Female	179 (58.3%)	128 (41.7%)	
Age (year)	72(63-82)	78(72-85)	<0.001
WBC count (cells/mm^3)	7.93(6.3-10.12)	7.6(6.05-10.65)	0.676
RBC count	4.20 (3.78-4.74)	4.01(3.55-4.50)	0.015
Hemoglobin (mg/dL)	11.80 (10.20-13.40)	11.40(9.90-13.00)	0.177
Neutrophil count (cells/mm^3)	5.5(3.95-7.4)	5.47(4.1-7.85)	0.401
Lymphocyte count (cells/µl)	1.46(0.95-2.09)	1.3(0.86-1.8)	0.014
Platelet count (cells/mm^3)	235(184-309)	212(165-282)	0.003
NLR	3.67(2.28-6.31)	4.28(2.74-7.83)	0.004
PLR	153.89(107.45-258.22)	171.75(111.67-265.15)	0.376
SII	871.33(514.1-1550.74)	899.75(562.5-1789.91)	0.230
Glucose (mg/dl)	127(104-185)	135(107-171.5)	0.888
BUN (mg/dL)	22.4(16.4-32.6)	32.6(22-51.5)	<0.001
Creatinine (IU/L)	1.01(0.81-1.37)	1.28(0.9-1.7)	<0.001
GFR	64(46.94-87)	50(38-71.98)	<0.001
Sodium	139(136-141)	138(135-141)	0.141
Potassium	4.4(4.04-4.82)	4.41(4-4.9)	0.646
Chloride	101(98.9-104)	101(97-103)	0.018
ALT	18(12-26)	17(11-28)	0.310
AST	21(16-30)	22(14-31.5)	0.712
Albumin	3.7(3.3-4.1)	3.4(3.1-3.8)	<0.001
Lactate	1.6(1.2-2.1)	1.8(1.3-2.3)	<0.001

The values are presented as the means ± SDs, medians (25th and 75th quartiles), or n (%). ALT: alanine aminotransferase, AST: aspartate aminotransferase, BUN: blood urea nitrogen, GFR: glomerular filtration rate, NLR: neutrophil–lymphocyte ratio, PLR: platelet–lymphocyte ratio, SII:, RBC: red blood cell, WBC: white blood cell.

urea reabsorption and elevated BUN levels (17). Jujo et al. reported that high BUN levels were associated with increased cardiovascular mortality rates in acute HF patients. Furthermore, in their multivariate logistic regression analysis, high BUN levels were identified as independent predictors of mortality (18). Similarly, Cauthen et al. reported that elevated BUN levels were associated with increased long-term mortality in HF patients (17). Additionally, an analysis of Acute Decompensated Heart Failure National Registry (ADHERE) data identified BUN >37 mg/dL as one of the most important predictors of mortality (19). Consistent with the literature, the present study revealed that high BUN levels were independent predictors of 90-day mortality in ADHF patients, with the highest AUC (0.673) in the ROC analysis. Moreover, BUN is a stronger predictor of adverse outcomes than both the GFR and creatinine level are (16–18).

Tissue hypoperfusion due to decreased cardiac output in ADHF leads to impaired tissue oxygenation and subsequently elevated lactate levels. Additionally, activation of the neurohormonal system and increased oxygen demand further contribute to lactate elevation (3,20). Several studies have demonstrated an association between increased lactate levels and poor outcomes in patients with acute HF (21–23). Kawase et al. identified lactate as an independent predictor of short-term mortality in ADHF patients admitted to

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Table 2. Logistic regression analysis for predicting 90-day mortality.

Parameters	Model 1		Model 2	
	OR (%95 CI)	p value	OR (%95 CI)	p value
Age	1.038(1.022-1.054)	<0.001	1.036(1.018-1.054)	<0.001
RBC	0.795(0.636-0.994)	0.044	1.038(0.8-1.346)	0.782
Lymhocyte	0.872(0.743-1.024)	0.094	*	*
Platelet	0.997(0.995-0.999)	0.002	0.998(0.996-1)	0.091
NLR	1.03(1.004-1.056)	0.026	1.017(0.995-1.039)	0.132
BUN	1.029(1.019-1.039)	<0.001	1.023(1.011-1.036)	<0.001
Creatinine	0.997(0.954-1.042)	0.883	*	*
GFR	0.984(0.978-0.991)	<0.001	1.001(0.992-1.011)	0.782
Chloride	0.957(0.926-0.99)	0.011	0.997(0.947-1.049)	0.910
Albumin	0.494(0.365-0.669)	<0.001	0.573(0.409-0.802)	0.001
Lactate	1.36(1.169-1.582)	<0.001	1.444(1.217-1.713)	<0.001

*Not applicable because these variables were not statistically significant in the univariate logistic regression analysis. Model 1: unadjusted model Model 2: Each marker was adjusted for other variables. BUN: blood urea nitrogen, CI: confidence interval, GFR: glomerular filtration rate, NLR: neutrophil–lymphocyte ratio, OR: odds ratio, PLR: platelet–lymphocyte ratio, RBC: red blood cell.

Table 3. Cutoff Points and Performance Characteristics of Variables in Predicting 90-Day Mortality

Parameters	AUC (95% CI)	Cutoff	Sensitivity	Specificity	+LR	-LR	p values
Age	0.623(0.576-0.669)	71.5	0.757	0.486	1.47	0.50	<0.001
BUN	0.673(0.628-0.719)	30.9	0.549	0.718	1.95	0.63	<0.001
Albumin	0.609(0.562-0.656)	3.45	0.509	0.667	1.53	0.74	<0.001
Lactate	0.587(0.539-0.635)	1.45	0.735	0.426	1.28	0.62	<0.001

AUC: Areas under the curve, BUN: Blood urea nitrogen, CI: Confidence interval, GFR: Glomeruler filtration rate, LR: Likehood ratio, NLR: Neutrophil-lymphocyt ratio, PLR: Platelet to lymphocyte ratio, RBC: Red blood cells.

the intensive care unit. They reported an AUC of 0.071 for a lactate cutoff of >3.2 mmol/L (24). Similarly, Zymlinski et al. reported that elevated blood lactate levels measured at hospital admission were predictive of all-cause mortality, even in the absence of peripheral hypoperfusion in acute HF patients (22). In the present study, a serum lactate cutoff of >1.45 mmol/L was used to predict 90-day mortality. Furthermore, consistent with the literature, lactate was an independent predictor of mortality according to the multivariate logistic regression analysis. Compared with that in the study by Kawase et al., the lactate cutoff value was lower (>3.2 vs. >1.45 mmol/L). This difference may be attributed to the fact that the study by Kawase et al. was conducted on a more severely ill patient population admitted to the intensive care unit, whereas the present study included hospitalized ADHF patients (24).

Hypoalbuminemia is commonly observed in HF patients. The underlying causes of hypoalbuminemia in HF patients include malnutrition, hemodilution, increased metabolic activity, proteinuria, and inflammatory mechanisms (1,25). Hypoalbuminemia has been associated with poor prognosis in ADHF patients (26). Uthamalingam et al. investigated the relationship between albumin levels and mortality in ADHF patients and reported that albumin levels <3.4 g/dL were associated with increased 1-year mortality (25). In another study, Karki et al. reported that hypoalbuminemia was associated with prolonged hospital stays and increased mortality in patients hospitalized for HF (27). A study conducted on patients admitted with acute HF revealed that those with albumin levels ≤3.4 g/dL had higher in-hospital mortality rates, and logistic regression analysis confirmed that hypoalbuminemia was an independent predictor of in-hospital mortality in acute HF patients (28). In the present study, the serum ALB

concentration was identified as an independent predictor of 90-day mortality in ADHF patients. According to the ROC analysis, the serum ALB concentration demonstrated good predictive performance for mortality, with an AUC of 0.609 at a cutoff value of <3.45 g/dL.

This study has several limitations. First, owing to its retrospective design, data collection may be subject to limitations in terms of accuracy and completeness. Second, as the study was conducted at a single center, the generalizability of the findings may be restricted. Therefore, multicenter studies with larger and more diverse patient populations are needed to validate these results and enhance their applicability to broader clinical settings. Finally, the study was conducted within a specific time frame and included a particular patient population; further studies with larger datasets are necessary.

CONCLUSION

This study highlights the prognostic significance of age and blood urea nitrogen, albumin, and lactate levels in predicting 90-day mortality in patients with acute decompensated heart failure and highlights the clinical relevance of these parameters. The findings contribute significantly to optimizing treatment strategies, improving patient outcomes, and reducing healthcare costs through the early identification of high-risk patients. However, to increase the clinical applicability of these parameters and validate them in broader patient populations, multicenter and prospective studies are needed.

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The authors declare that they have no conflict of interest to disclose.

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