

ORIGINAL ARTICLE

The correlation between ejection fraction values and blood urea nitrogen levels and blood urea nitrogen/creatinine ratios in heart failure

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ABSTRACT

Background: Heart failure is a condition with high mortality characterized by a decrease in the heart's ability to pump blood. Decreased EF can affect renal perfusion and trigger renal dysfunction, as reflected in increased BUN and altered BUN/Cr ratio. Therefore, the relationship between EF and these biochemical parameters is important to support clinical assessment in patients with heart failure. The purpose of this study was to determine the correlation between EF values and BUN levels and BUN/Cr ratio in patients with heart failure.

Materials and Methods: An analytical observational study with a cross-sectional design involving 456 patients with heart failure at Wahidin Sudirohusodo Hospital, Makassar, Indonesia. EF values were obtained from echocardiography, and BUN and creatinine levels were measured through laboratory tests.

Result: Patients with HFrEF showed significantly higher mean BUN levels compared to HFmrEF and HFpEF (55.08 ± 38.49 mg/dL vs. 50.87 ± 35.31 mg/dL vs. 37.78 ± 21.50 mg/dL, respectively; $p < 0.001$). HFrEF patients showed significantly higher mean BUN/Cr ratios compared to HFmrEF and HFpEF (48.94 ± 28.10 mg/dL vs. 45.56 ± 24.63 mg/dL vs. 41.25 ± 22.41 mg/dL, respectively; $p = 0.04$).

Conclusion: Patients with heart failure with low ejection fraction (HFrEF) had the highest BUN levels and BUN/creatinine ratios compared to the HFmrEF and HFpEF groups. These findings confirm that renal dysfunction is more common in patients with low ejection fraction, and monitoring BUN parameters and BUN/creatinine ratios can be important indicators in assessing the severity of heart failure. (www.actabiomedica.it)

Key words: heart failure, blood urea nitrogen, creatinine



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Introduction

Heart failure is a complex clinical syndrome characterized by structural or functional disorders that cause the ventricles to be unable to fill or pump blood adequately (1). The Global Burden of Disease (GBD) study reported a 29.4% increase in the prevalence of heart failure from 2010 to 2019 (2). Indonesia has a relatively high prevalence of heart failure, with an age-standardized rate (ASR) of approximately 900.90 cases per 100,000 population, making it one of the countries with the highest prevalence of heart failure in Asia (3). Blood urea nitrogen (BUN) is the end product of protein metabolism synthesized in the liver and excreted primarily through the kidneys (4,5). Several studies have shown that elevated BUN levels are associated with poor clinical outcomes in patients with heart failure, particularly in the context of acute decompensation. BUN is more sensitive in reflecting the progression of heart failure than serum creatinine, as it reflects more dynamic changes in renal perfusion (6). The blood urea nitrogen to creatinine ratio (BUN/Cr) is a marker of neurohormonal activation that plays a role in hemodynamic regulation in patients with heart failure. Although data on its relationship with prognosis are still limited, several studies have shown that an increased BUN/Cr ratio is associated with poor prognosis in patients with heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). Activation of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS) in patients with acute heart failure (AHF) increases sodium and water reabsorption and causes passive reabsorption of BUN in the renal tubules. In addition, renal vasoconstriction due to neurohormonal activation decreases glomerular filtration rate (GFR) and BUN excretion, thereby contributing to an increase in the BUN/Cr ratio (7). This study aims to determine the correlation between EF values and BUN levels and BUN/Cr ratios in patients with heart failure.

Methods and Materials

An observational analytical study with a cross-sectional design. The target population was all patients diagnosed with heart failure based on echocardiography

who were treated at Wahidin Sudirohusodo Hospital. Samples were selected using consecutive sampling based on the inclusion criteria, namely adult patients with complete data on EF, BUN, and creatinine levels. Patients with advanced chronic kidney disease or incomplete clinical data were excluded from the study. This study used secondary data taken from the medical records of patients diagnosed with heart failure from January 2023 to May 2025. Only data already recorded in the patients' electronic medical record system was used; there were no new interventions or measurements taken on the patients. Demographic data such as age, gender, and history of comorbidities were collected from the identity section and medical notes in each patient's medical record. Patient comorbidities such as hypertension, type 2 diabetes mellitus, and dyslipidemia were determined based on diagnoses in medical records and received treatment according to their diseases. To confirm the diagnosis, medical records were also reviewed to check for a history of blood pressure measurements $>140/100$ mmHg, HbA1c tests $>6.5\%$, and LDL tests >130 mg/dl or TG tests >200 mg/dl. Creatinine value is defined based on blood test results when the patient has been diagnosed with heart failure. BUN value is defined using the formula $\text{BUN (mg/dL)} = \text{Urea (mg/dL)} \times 0.467$. The BUN/creatinine ratio is defined based on the result of dividing BUN by creatinine. EF values were taken from the latest echocardiography (Philips Sparq) report available in the medical record. BUN and creatinine levels were taken from the patient's latest laboratory results. The BUN/creatinine ratio was calculated after extraction. The data analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Subject characteristics are presented in the form of frequencies and percentages. Statistical analysis used the Kruskal-Wallis Test, considered significant if $p < 0.05$. The results are presented in narrative format, accompanied by tables to clarify and facilitate understanding of the findings.

Result

This study involved 456 patients with heart failure. The average age of patients was 58.16 ± 10.9 years. The majority of patients were male, 368 (80.7%) patients, and female, 88 (19.3%) patients. Most patients

had HFrEF, 188 (41.2%) patients, followed by HFmrEF, 149 (32.7%) patients, and HFpEF, 119 (26.1%) patients. Hypertension was the most common comorbidity, with 261 (57.2%) patients, diabetes mellitus 146 (32%) patients, and dyslipidemia 171 (37.5%) patients (Table 1).

Comparison of BUN levels based on EF values shows that HFrEF patients had significantly higher mean BUN levels than HFmrEF and HFpEF patients (55.08 ± 38.49 mg/dL vs. 50.87 ± 35.31 mg/dL vs. 37.78 ± 21.50 mg/dL, respectively; p < 0.001) (Table 2).

Comparison of BUN/Cr ratios based on ejection fraction values shows that HFrEF patients had significantly higher mean BUN/Cr ratios than HFmrEF

and HFpEF patients (48.94 ± 28.10 mg/dL vs. 45.56 ± 24.63 mg/dL vs. 41.25 ± 22.41 respectively mg/dL; p = 0.04) (Table 3).

Discussion

Heart failure is a global health problem with high morbidity and mortality rates. The role of the kidneys in the pathophysiology of heart failure is very important, because the hemodynamic disturbances that occur lead to decreased renal perfusion, activation of the renin-angiotensin-aldosterone system, fluid and urea nitrogen retention. BUN has long been used as one of the laboratory parameters that predict renal function status, and increased BUN values are associated with the severity of heart failure and the clinical prognosis of patients (8). Several studies have reported that elevated BUN levels are an independent predictor of mortality in patients with heart failure, regardless of whether ejection fraction is reduced or preserved (9). In addition, the BUN-to-creatinine ratio is increasingly being used as an additional biomarker because it is considered more stable and reflects the complex interaction between renal function and cardiovascular status. Studies show that the BUN/Cr ratio is associated with an increased risk of mortality and rehospitalization in patients with heart failure. BUN and the BUN/Cr ratio play an important role not only in evaluating kidney function, but also in risk stratification and clinical monitoring of patients with heart failure (10). This study shows a significant difference in BUN levels in heart failure patients based on ejection fraction. Patients with HFrEF showed

Table 1. Characteristics of the study.

Variable	n = 456	%
Age (years)		
Mean + SD	58.16 + 10.9	
Median (min-max)	58 (33-87)	
Gender		
Male	368	80.7
Female	88	19.3
Degrees of Heart Failure		
HFpEF	119	26.1
HFmrEF	149	32.7
HFrEF	188	41.2
Comorbidities		
Hypertension	261	57.2
Diabetes	146	32
Dyslipidemia	171	37.5

Table 2. Comparison of BUN levels based on ejection fraction values.

Variable	n	Mean	SD	Median (min-max)	p
HFpEF	119	37.78	21.50	31.0 (12-127)	<0.001
HFmrEF	149	50.87	35.31	35.3 (9-178)	
HFrEF	188	55.08	38.49	43.0 (4-284)	

*Kruskal-Wallis Test(p<0.05). *Abbreviations:* HFpEF: Heart failure with preserved ejection fraction; HFmrEF: Heart failure with mildly reduced ejection fraction; HFrEF: Heart failure with reduced ejection fraction.

Table 3. Comparison of BUN/Cr ratio based on ejection fraction values.

Variable	n	Mean	SD	Median (min-max)	p
HFpEF	119	41.25	22.41	34 (15-134)	0.04
HFmrEF	149	45.56	24.63	38 (8-128)	
HFrEF	188	48.94	28.10	42 (10-174)	

*Kruskal-Wallis Test (p<0.05). *Abbreviations:* HFpEF: Heart failure with preserved ejection fraction; HFmrEF: Heart failure with mildly reduced ejection fraction; HFrEF: Heart failure with reduced ejection fraction.

significantly higher BUN levels compared to patients with HFpEF and HFmrEF. These results are consistent with the study by Oswald et al. (2024), which found that patients with low ejection fraction had higher BUN levels compared to patients with preserved ejection fraction. Furthermore, it was reported that increased BUN is a strong predictor of mortality in heart failure patients, particularly in the HFrEF group (11). Similar results were also reported by Yingchoncharoen et al. (2024), who found that high BUN was associated with an increased risk of death in nearly 3,000 heart failure patients in Thailand, especially in patients with EF <40% (12). In a therapeutic perspective, a study by El Amrawy (2025) provides evidence that BUN levels may decrease as heart failure patients improve clinically. In his study, administering ivabradine to patients with chronic heart failure not only increased ejection fraction but also significantly decreased BUN levels. This reinforces the view that BUN can be used as a parameter to monitor the effectiveness of therapy in heart failure patients (13). Thus, the findings of this study are consistent with existing literature, showing that BUN levels increase in patients with low ejection fraction, while confirming its potential as a modality for prognosis and therapeutic response in heart failure. In addition to BUN, the BUN/Cr ratio was also found to be higher in patients with HFrEF. A number of studies support these findings. Parhizkar Roudsari et al (2024) in a systematic review confirmed that renal biomarkers, including BUN, creatinine, and the BUN/creatinine ratio, have important prognostic value in predicting mortality in heart failure patients, both in HFpEF and HFrEF (8). Another study by İnce et al (2025) also showed that renal biomarker values were closely related to ejection fraction and NT-proBNP levels, reinforcing the evidence that decreased EF correlates with an increased BUN/Cr ratio (14). In addition, a retrospective study by Yu et al (2025) also reported that BUN/Cr levels were associated with the degree of heart failure based on ejection fraction, where patients with HFrEF had higher renal biomarker values than those with HFmrEF and HFpEF (15). Another study by Fukuta et al (2024) added that changes in EF in heart failure patients are associated with changes in metabolic and renal biomarkers, including BUN/creatinine, which contribute to long-term prognosis

(16). Thus, the findings of this study are consistent with current scientific evidence that an increase in the BUN/creatinine ratio reflects the severity of heart failure and can be used as a prognostic marker and for therapy evaluation. This study has several limitations, such as creatinine and BUN values being measured only once, so it cannot describe the dynamics of changes in these biomarkers over the course of the disease or in response to therapy. In addition, this study did not take into account confounding factors that could potentially affect BUN and creatinine levels, such as age, gender, nutritional status, degree of hypertension, diabetes mellitus, chronic kidney disease, and the use of certain medications. The absence of analysis of these variables may reduce the validity of the study results, as these confounding factors play an important role in influencing kidney function and the clinical status of patients with heart failure.

Conclusion

The results of this study indicate that patients with heart failure with low ejection fraction (HFrEF) have the highest BUN levels and BUN/Cr ratios compared to the HFmrEF and HFpEF groups. These findings confirm that renal dysfunction is more common in patients with low ejection fraction, and monitoring BUN parameters and BUN/Cr ratios can be important indicators in assessing the severity of heart failure.

Ethics Approval: This study has been approved by the Research Ethics Committee of the Faculty of Medicine, Hasanuddin University through the publication of an ethical approval letter number 349/un4.6.4.5.31/pp36/2025. The study adhered to the ethical principles, ensuring the protection of participants' rights and confidentiality.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interests, patent/licensing, arrangement etc-) that might pose a conflict of interest in connection with the submitted article.

Declaration on the Use of AI: None.

Authors Contribution: DFJ, IM, and HR drafted the manuscript. IM, HR, AMA and SB designed and conceived the study. DFJ and AAZ collected and analyzed and interpreted the data. HR, AMA, and SB revised manuscript critically for important intellectual content. All authors participated in the final draft preparation, manuscript revision, and critical evaluation of the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

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