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ORIGINAL ARTICLE

Stress Hyperglycemia Ratio Predicts 6-Month Mortality in Patients with Acute Heart Failure: a Retrospective Cohort Study

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ABSTRACT

Background: **Stress hyperglycemia is frequently observed in patients with acute heart failure (AHF) and reflects metabolic responses to acute physiological stress. The stress hyperglycemia ratio (SHR), calculated using admission blood glucose and glycated hemoglobin (HbA1c), has been proposed as a novel indicator of stress-related hyperglycemia. This study aimed to investigate the association between SHR and 6-month readmission and mortality in patients with AHF.**

Methods: **A total of 305 patients diagnosed with AHF at Xichong County People's Hospital between January 2021 and June 2024 were retrospectively included. Clinical characteristics and laboratory parameters were extracted from electronic medical records. Univariate and multivariate logistic regression analyses were performed to identify factors associated with readmission and mortality within 6 months after discharge. Patients were stratified into low- and high-SHR groups according to the median SHR value. Kaplan-Meier survival analysis was conducted to compare outcomes between groups.**

Results: **Among the 305 patients, 94 (30.82%) experienced readmission and 53 (17.38%) died within 6 months after discharge. Multivariate logistic regression analysis showed that age, serum uric acid, N-terminal pro-brain natriuretic peptide (NT-proBNP), and SHR were independent risk factors for 6-month readmission after discharge, while New York Heart Association (NYHA) functional class and lymphocyte count were protective factors. For 6-month mortality after discharge, independent risk factors included age, serum uric acid, neutrophil count, NT-proBNP, and SHR, whereas NYHA class II, left ventricular ejection fraction, lymphocyte count, and estimated glomerular filtration rate were protective factors. Kaplan-Meier analysis demonstrated that mortality within 6 months was significantly higher in the high-SHR group than in the low-SHR group ($p = 0.008$), whereas no significant difference in readmission rates was observed between the groups ($p = 0.136$).**

Conclusions: **SHR is associated with an increased risk of 6-month mortality in patients with acute heart failure and may serve as a useful laboratory indicator for early risk stratification.**

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KEYWORDS

stress hyperglycemia ratio, emergency, acute heart failure, readmission, mortality, predictor

LIST OF ABBREVIATIONS

AHF - Acute heart failure
BMI - Body mass index
SHR - Stress hyperglycemia ratio
HbA1c - Glycated hemoglobin
NT-proBNP - N-terminal pro-brain natriuretic peptide

NYHA - Percutaneous coronary intervention
PCI - Chronic obstructive pulmonary disease
COPD - Left ventricular ejection fraction
LVEF - Left ventricular ejection fraction
eGFR - Estimated glomerular filtration rate
CI - Confidence interval
SPSS - Statistical Package for the Social Sciences
OR - Odds ratio

INTRODUCTION

Acute heart failure (AHF) is a critical cardiovascular syndrome associated with high morbidity, frequent hospitalizations, and substantial mortality [1]. Despite advances in diagnostic techniques and therapeutic strategies, the long-term prognosis of patients with AHF remains poor. In particular, readmission and mortality rates within 6 months after discharge remain persistently high, imposing a considerable burden on healthcare systems and significantly affecting patient outcomes. Stress-induced hyperglycemia is a common metabolic response during the acute phase of AHF and has been associated with myocardial injury, impaired cardiac function, and adverse clinical outcomes [2]. Acute stress responses involving sympathetic activation, inflammatory processes, and hormonal changes may contribute to transient elevations in blood glucose levels. Therefore, laboratory indicators reflecting stress-related glycemic disturbances may provide valuable information for early risk stratification in patients with AHF. The stress hyperglycemia ratio (SHR), defined as the ratio of admission blood glucose to glycated hemoglobin (HbA1c), integrates acute glucose levels with chronic glycemic status. Compared with isolated blood glucose measurements, SHR may provide a more accurate assessment of stress-induced hyperglycemia. Increasing evidence indicates that SHR is associated with clinical outcomes in several cardiovascular and cerebrovascular diseases [3,4]. However, the prognostic value of SHR in patients with AHF, particularly regarding readmission and mortality after discharge, remains insufficiently investigated. Therefore, this retrospective study aimed to evaluate the association between SHR and the risks of readmission and mortality within 6 months after discharge in patients with AHF, and to explore the potential role of SHR as a laboratory indicator for risk stratification in this population.

MATERIALS AND METHODS

Study participants

A total of 462 patients with suspected acute heart failure (AHF) identified from the medical records of Xichong County People's Hospital between January 1, 2021, and June 30, 2024, were screened for eligibility. Because this was a retrospective study, the study size was determined by including all consecutive patients who met the prespecified eligibility criteria during the predefined study period, rather than by an a priori sample size calculation. The diagnosis of AHF was established based on echocardiographic findings, clinical manifestations, and medical history, in accordance with the Chinese Clinical Practice Guidelines for the Diagnosis and Management of Acute Heart Failure in the Emergency Department (2017) [5]. The inclusion criteria were as follows: 1) fulfillment of the diagnostic criteria for AHF; 2) presentation to the emergency department; and 3) availability of complete laboratory data obtained immediately after admission. The exclusion criteria were as follows: 1) presence of severe comorbidities, including endocrine disorders, bronchial asthma, severe neurological disorders, or significant dysfunction of major organs, including the liver, kidneys, heart, or lungs; 2) self-discharge or incomplete clinical and medical records; 3) absence of 6-month follow-up information; and 4) missing key variables required for the analyses. Of the 462 patients screened, 157 were excluded according to the predefined eligibility criteria, leaving 305 patients for the final analysis. The patient selection process is shown in Figure 1.

The final analytical cohort comprised 305 patients, including 94 patients with readmission and 53 patients who died during the 6-month follow-up. The observed number of events was considered adequate for the planned multivariable logistic regression analyses, with more than 10 events per covariate in each model.

Data collection

The medical record number was used as a unique identifier to extract demographic, clinical, and laboratory data obtained after admission, including age, sex, body mass index (BMI), history of percutaneous coronary intervention (PCI), presence of atrial fibrillation, presence of diabetes mellitus, underlying diseases (coronary artery disease, hypertension, chronic obstructive pulmonary disease (COPD), chronic renal insufficiency, and others), precipitating factors (infection, arrhythmia, acute changes in blood volume, electrolyte disturbances, and others), New York Heart Association (NYHA) functional class (I, II, III, or IV), Killip class (II, III, or IV), heart rate, oxygen saturation, mean arterial pressure, left ventricular ejection fraction (LVEF), hemoglobin, serum uric acid, blood urea nitrogen, creatinine, serum potassium, neutrophil count, lymphocyte count, red cell distribution width, estimated glomerular filtration rate (eGFR), N-terminal pro-brain natriuretic peptide (NT-proBNP), and the SHR. The stress hyperglycemia ratio was calculated using a validated mathematical model incorporating admission blood glucose and HbA1c, according to the following formula: SHR = admission blood glucose/[(28.7 x HbA1c%) - 46.7].

Outcome events and follow-up

The study endpoints included readmission and mortality events. Readmission was defined as rehospitalization due to AHF or other related complications within 6

months after discharge. Mortality was defined as death from AHF or any other cause within 6 months after discharge.

Statistical analysis

Statistical analyses were performed using SPSS software (version 25.0, IBM Corp., Armonk, NY, USA). Continuous variables with a normal distribution are presented as mean ± standard deviation and were compared between groups using the independent-samples *t*-test. Categorical variables are presented as proportions and were compared using the χ^2 test.

Binary logistic regression analysis was performed to identify independent factors associated with readmission and mortality within 6 months after discharge among emergency patients with AHF. Follow-up duration was calculated from the date of discharge to the date of death, the date of censoring (e.g., loss to follow-up), or the 6-month study endpoint, whichever occurred first. The total person-time was derived by summing individual follow-up times across all patients. Kaplan–Meier survival analysis was used to compare cumulative readmission and mortality rates within 6 months after discharge between patients with different SHR levels, with between-group comparisons performed using the log-rank test. A two-sided p-value < 0.05 was considered statistically significant. All primary analyses, including the logistic regression models and the Kaplan-Meier survival comparisons, were prespecified.

Ethical statement

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments. The study protocol was reviewed and approved by the Medical Ethics Committee of Xichong County People's Hospital (Approval No. 202505). Due to the retrospective nature of the study, the requirement for informed consent was waived by the ethics committee. Patient data were anonymized and de-identified prior to analysis to ensure confidentiality.

RESULTS

Differences in baseline characteristics between groups

Among the 462 patients with suspected AHF identified during the study period, 157 were excluded. Specifically, 3 patients did not meet the diagnostic criteria for AHF, 10 did not present to the emergency department, and 28 had incomplete laboratory data at admission. In addition, 52 patients had severe comorbidities or major organ dysfunction, 19 were self-discharged or had incomplete medical records, 24 had no available 6-month follow-up information, and 21 had missing key variables required for the analyses. Consequently, 305 patients were included in the final analysis. After these exclusions, the final analytical dataset of 305 patients contained no missing data for any of the variables of interest. Follow-up status at 6 months (or at the time of death) was ascertainable for all 305 patients. The median follow-up time was 6.0 months (range: 57 - 180 days; approximately 1.9 - 6.0 months), and the total effective follow-up time was 47,507 person-days (equivalent to approximately 1,563 person-months, based on 30.4 days per month). Within 6 months after discharge, 94 patients (30.82%) experienced readmission, and 53 patients (17.38%) died. The patient selection process is illustrated in Figure 1.

Among all patients, the primary underlying diseases were coronary artery disease (n = 98, 32.13%), hypertension (n = 79, 25.90%), chronic obstructive pulmonary disease (n = 58, 19.02%), chronic renal insufficiency (n = 33, 10.82%), and other conditions (n = 37, 12.13%). The main precipitating factors included infection (n = 168, 55.08%), arrhythmia (n = 85, 27.87%), acute changes in blood volume and electrolyte disturbances (n = 46, 15.08%), and other factors (n = 6, 1.97%) (Table 1).

Multivariate logistic regression analysis of risk factors for 6-month readmission

Six-month readmission after discharge among emergency patients with AHF was defined as the dependent variable. Variables demonstrating statistical significance in univariate analyses were subsequently incorporated as covariates into a multivariable binary logistic regression model. The analysis identified age (OR = 1.052, 95% CI: 1.013 - 1.092, p = 0.008), serum uric acid (OR = 1.005, 95% CI: 1.001 - 1.008, p = 0.017), NT-proBNP (OR = 1.001, 95% CI: 1.000 - 1.001, p = 0.047), and SHR (OR = 3.703, 95% CI: 1.062 - 12.918, p = 0.040) as independent risk factors for readmission within 6 months following discharge.

Conversely, NYHA functional class II (OR = 0.217, 95% CI: 0.099 - 0.476, p < 0.001), NYHA functional class III (OR = 0.411, 95% CI: 0.210 - 0.804, p = 0.009), and lymphocyte count (OR = 0.265, 95% CI: 0.085 - 0.831, p = 0.023) were independently associated with a reduced risk of 6-month readmission (Table 2).

Multivariate logistic regression analysis of risk factors for 6-month mortality

Using 6-month post-discharge mortality in emergency patients with AHF as the dependent variable, variables that were statistically significant in the univariate analysis were included as covariates in a multivariable binary logistic regression model. The analysis revealed that age (OR = 1.112, 95% CI: 1.049 - 1.180, p < 0.001), serum uric acid (OR = 1.014, 95% CI: 1.008 - 1.020, p < 0.001), neutrophil count (OR = 2.131, 95% CI: 1.035 - 4.386, p = 0.040), NT-proBNP (OR = 1.001, 95% CI: 1.000 - 1.002, p = 0.004), and SHR (OR = 9.230, 95% CI: 1.588 - 53.645, p = 0.013) were identified as independent risk factors for mortality within 6 months after discharge in emergency patients with AHF.

Table 1. Baseline characteristics of patients with AHF stratified by 6-month readmission and mortality.

Variables	Readmission (n = 94)	Non-readmission (n = 211)	p	Death (n = 53)	Survival (n = 252)	p
Age (years)	68.87 ± 7.42	65.73 ± 7.56	0.001	70.45 ± 6.92	65.91 ± 7.57	< 0.001
Sex (male/female)	65/29	130/81	0.206	37/16	158/94	0.327
BMI (kg/m^2)	23.95 ± 0.22	23.96 ± 0.25	0.674	23.92 ± 0.21	23.97 ± 0.24	0.219
History of PCI	14	25	0.462	7	32	0.920
Atrial fibrillation	21	45	0.843	12	54	0.845
Diabetes mellitus	42	106	0.370	23	125	0.411
Underlying diseases			0.910			0.679
Coronary artery disease	29	59		14	84	
Hypertension	24	55		16	63	
COPD	17	41		11	47	
Chronic renal insufficiency	10	23		4	29	
Others	14	23		8	29	
Precipitating factors			0.935			0.701
Infection	54	114		29	139	
Arrhythmia	24	61		15	70	
Acute changes in blood volume and electrolyte disturbances	14	32		9	37	
Others	2	4		0	6	
NYHA functional class			< 0.001			< 0.001
Class II	17	81		6	92	
Class III	40	101		21	120	
Class IV	37	29		26	40	
Heart rate (/min)	81.63 ± 7.37	79.57 ± 7.60	0.029	81.91 ± 6.93	79.85 ± 7.67	0.072
Oxygen saturation (%)	98.10 ± 2.08	97.84 ± 1.92	0.293	98.26 ± 2.03	97.85 ± 1.96	0.170
Mean arterial pressure (mmHg)	99.94 ± 11.95	97.88 ± 10.52	0.132	100.36 ± 11.14	98.12 ± 10.96	0.178
LVEF (%)	38.97 ± 3.87	39.76 ± 3.78	0.096	38.24 ± 3.70	39.79 ± 3.80	0.007
Hemoglobin (g/L)	126.45 ± 17.09	126.09 ± 16.21	0.861	125.09 ± 17.44	126.44 ± 16.27	0.589
Serum uric acid (μmol/L)	511.43 ± 83.53	476.24 ± 70.11	< 0.001	546.21 ± 73.21	474.65 ± 70.82	< 0.001
Blood urea nitrogen (mmol/L)	9.21 ± 4.13	9.25 ± 3.93	0.934	8.92 ± 3.90	9.31 ± 4.01	0.525
Creatinine (μmol/L)	98.80 ± 10.50	98.74 ± 9.98	0.960	98.40 ± 9.62	98.83 ± 10.24	0.781
Serum potassium (mmol/L)	4.08 ± 0.81	4.07 ± 0.87	0.924	3.96 ± 0.80	4.09 ± 0.86	0.309
Neutrophil count (x 10^9/L)	5.57 ± 0.67	5.49 ± 0.50	0.297	5.76 ± 0.68	5.46 ± 0.52	0.005
Lymphocyte count (x 10^9/L)	0.99 ± 0.29	1.06 ± 0.22	0.024	0.96 ± 0.30	1.06 ± 0.23	< 0.001
Red cell distribution width	14.85 ± 2.16	14.26 ± 1.95	0.019	15.22 ± 1.84	15.25 ± 2.04	0.002
eGFR (mL x min^{-1} x 1.73m^{-2})	78.41 ± 7.04	80.68 ± 6.30	0.005	76.61 ± 7.04	80.69 ± 6.30	< 0.001
NT-ProBNP (pg/mL)	3,894.22 ± 563.90	3,657.59 ± 573.11	0.001	4,045.30 ± 583.23	3,664.31 ± 557.97	< 0.001
SHR	1.05 ± 0.28	0.96 ± 0.19	0.001	1.11 ± 0.30	0.97 ± 0.20	< 0.001

In contrast, NYHA functional class II (OR = 0.141, 95% CI: 0.040 - 0.495, p = 0.002), LVEF (OR = 0.894, 95% CI: 0.800 - 0.998, p = 0.046), lymphocyte count (OR = 0.131, 95% CI: 0.025 - 0.694, p = 0.017), and eGFR (OR = 0.930, 95% CI: 0.874 - 0.990, p = 0.022) were identified as independent protective factors against 6-month mortality (Table 3).

Table 2. Multivariable logistic regression analysis of risk factors for 6-month readmission in emergency patients with AHF.

Variables	B	SE	Wald $\chi 2$	p	OR	95% CI
Age	0.051	0.019	7.108	0.008	1.052	1.013 - 1.092
NYHA functional class			14.857	0.001		
Class II	-1.527	0.400	14.547	< 0.001	0.217	0.099 - 0.476
Class III	-0.890	0.343	6.745	0.009	0.411	0.210 - 0.804
Heart rate	0.033	0.019	2.895	0.089	1.033	0.995 - 1.073
Serum uric acid	0.005	0.002	5.670	0.017	1.005	1.001 - 1.008
Lymphocyte count	-1.327	0.583	5.185	0.023	0.265	0.085 - 0.831
Red cell distribution width	0.106	0.070	2.289	0.130	1.112	0.969 - 1.276
eGFR	-0.030	0.022	1.932	0.165	0.970	0.930 - 1.012
NT-ProBNP	0.001	0.000	3.949	0.047	1.001	1.000 - 1.001
SHR	1.309	0.637	4.218	0.040	3.703	1.062 - 12.918
Constant	-9.244	3.181	8.445	0.004	0.000	

Table 3. Multivariable logistic regression analysis of risk factors for 6-month mortality in emergency patients with AHF.

Variables	B	SE	Wald $\chi 2$	p	OR	95% CI
Age	0.106	0.030	12.595	< 0.001	1.112	1.049 - 1.180
NYHA functional class			9.812	0.007		
Class II	-1.961	0.641	9.350	0.002	0.141	0.040 - 0.495
Class III	-0.920	0.470	3.832	0.050	0.399	0.159 - 1.001
LVEF	-0.112	0.056	3.981	0.046	0.894	0.800 - 0.998
Serum uric acid	0.014	0.003	19.603	< 0.001	1.014	1.008 - 1.020
Neutrophil count	0.756	0.368	4.219	0.040	2.131	1.035 - 4.386
Lymphocyte count	-2.035	0.852	5.709	0.017	0.131	0.025 - 0.694
Red cell distribution width	0.162	0.110	2.182	0.140	1.176	0.948 - 1.458
eGFR	-0.073	0.032	5.235	0.022	0.930	0.874 - 0.990
NT-ProBNP	0.001	0.000	8.446	0.004	1.001	1.000 - 1.002
SHR	2.222	0.898	6.125	0.013	9.230	1.588 - 53.645
Constant	-16.195	5.651	8.212	0.004	0.000	

Kaplan-Meier survival analysis based on the median SHR

Patients were stratified into low- and high-SHR groups according to the median stress hyperglycemia ratio (SHR < 1.01 and SHR ≥ 1.01, respectively). Kaplan-Meier survival curves were constructed to evaluate the associations between SHR levels and clinical outcomes after discharge. The analysis demonstrated no statistically significant difference in the 6-month readmission rate between the high-SHR and low-SHR groups ($p = 0.136$). In contrast, patients in the high-SHR group exhibited a significantly higher 6-month post-discharge mortality rate compared with those in the low-SHR group ($p = 0.008$) (Figure 2).

DISCUSSION

In the present study, 305 patients with acute heart failure were included, of whom 94 (30.82%) experienced readmission and 53 (17.38%) died within 6 months after discharge. These findings indicate that patients with AHF remain at a considerable risk of readmission and mortality during the early post-discharge period. Multivariable logistic regression analysis identified the SHR as an independent risk factor for both 6-month readmission and mortality in emergency patients with AHF, with progressively higher risks observed at increasing SHR levels. Furthermore, Kaplan-Meier survival curve analysis demonstrated that patients with SHR ≥ 1.01

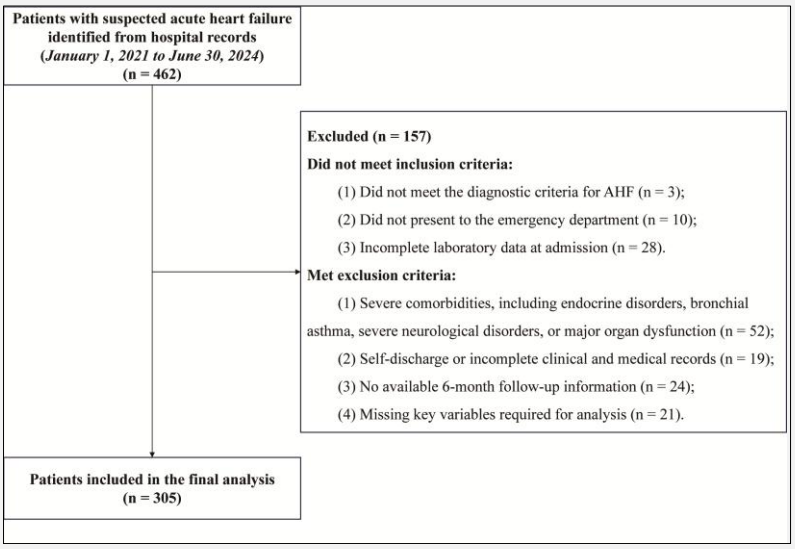


Figure 1. Flow diagram explaining the inclusion and exclusion criteria.

AHF: acute heart failure. The numbers (n) will be filled in according to the actual data.

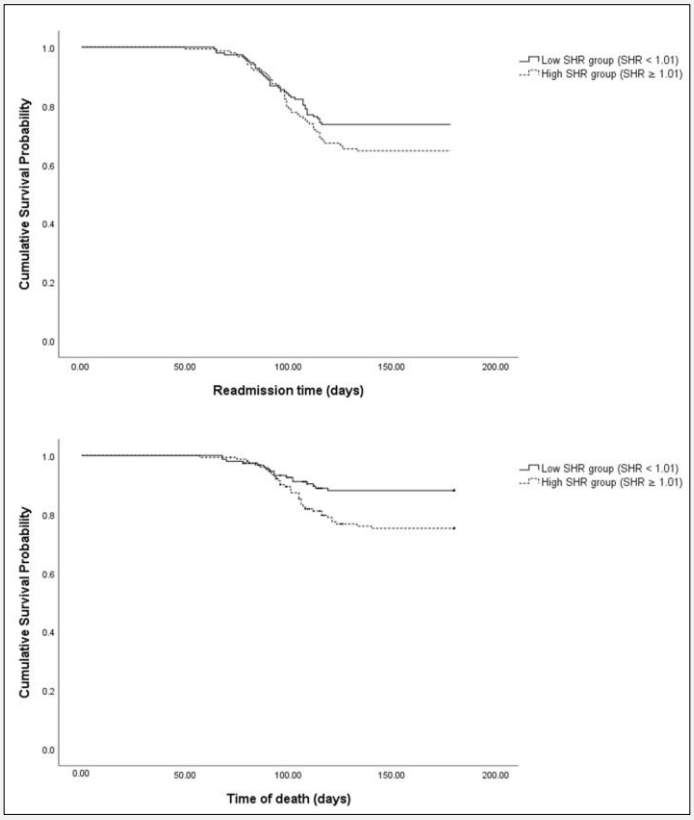


Figure 2. Kaplan-Meier survival curves stratified by the median SHR. A: 6-month readmission; B: 6-month mortality.

had a significantly higher 6-month post-discharge mortality rate compared with those with SHR < 1.01, underscoring the prognostic value of SHR for short-term mortality after discharge. Collectively, these results suggest that monitoring SHR may assist in the early identification of emergency patients with AHF who are at high risk for adverse outcomes, thereby facilitating timely risk stratification and the implementation of targeted post-discharge management strategies.

SHR is an indicator used to assess glucose metabolism under stress conditions and is generally attributed to enhanced stress responses, which lead to increased secretion of catecholamines and cortisol, thereby promoting hepatic gluconeogenesis and inhibiting insulin action [6]. Patients with AHF presenting to the emergency department often experience pronounced stress responses due to impaired cardiac function, accompanied by reduced glycemic regulatory capacity and subsequent stress-induced hyperglycemia [7,8].

Accumulating evidence suggests that SHR is closely associated with the prognosis of patients with AHF [9,10]. A retrospective study involving 559 patients with AHF demonstrated a positive association between SHR and all-cause mortality within three months after discharge; however, among patients with concomitant diabetes mellitus, those with SHR ≤ 0.88 exhibited a more than two-fold increase in three-month mortality risk [11], findings that are not entirely consistent with those of the present study. This discrepancy may be explained by differences in study design, patient characteristics, follow-up duration, SHR stratification thresholds, and the proportion of patients with diabetes mellitus. In contrast, a long-term follow-up study focusing on non-surgical heart failure patients with type 2 diabetes mellitus reported a U-shaped association between SHR and adverse in-hospital outcomes, including composite cardiac events, severe acute kidney injury, and severe systemic infection; patients with baseline renal dysfunction were at increased risk when SHR was either excessively high or low [12]. Furthermore, Mohammed et al. [13] demonstrated that elevated SHR was an independent predictor of adverse long-term outcomes in patients with heart failure with preserved ejection fraction, with higher SHR independently associated with increased risks of composite all-cause events, cardiovascular mortality, and HF-related readmission.

In this retrospective analysis of emergency AHF patients, we observed that the risks of readmission and mortality within six months after discharge were closely associated. After categorizing the continuous variable SHR into two groups according to its median value, survival analysis revealed that patients in the high-SHR group had a significantly higher six-month mortality rate compared with the low-SHR group ($p = 0.008$). This finding suggests that SHR has a robust predictive effect on long-term survival, which is consistent with previously published findings. Although the underlying mechanisms have not been fully elucidated, several plausible explanations may account for these observations. First, during acute episodes of AHF, myocardial injury triggers the release of large amounts of inflammatory cytokines and reactive oxygen species, leading to enhanced systemic inflammation and oxidative stress. These pathological processes further exacerbate myocardial damage and impair the function of other organs, thereby contributing to adverse clinical outcomes [14]. Second, the decline in cardiac pump function during AHF results in systemic circulatory dysfunction. Such hemodynamic impairment may subsequently disrupt glucose metabolism and compromise multi-organ function, ultimately increasing the risks of both readmission and mortality [15]. Third, sustained hyperglycemia may increase cardiac workload and impair cardiomyocyte function, while also inducing internal homeostatic disturbances, including electrolyte imbalance and acid-base disorders, which collectively contribute to an elevated risk of death [16].

This study has several limitations that should be acknowledged. First, the study population was predominantly composed of Han Chinese individuals from a single region, and the follow-up period was limited to six months, which may limit the generalizability of the findings and preclude evaluation of long-term outcomes. Second, the present study primarily evaluated the prognostic value of SHR at discharge; therefore, the potential impact of SHR measured at admission and its dynamic fluctuations during hospitalization on patient outcomes was not further investigated. Third, the prognosis of patients with AHF may be affected by several unmeasured or uncontrollable factors, including individual heterogeneity and variability in treatment adherence during and after hospitalization. Finally, given the single-center retrospective design of this study, the observed associations between SHR and prognosis in patients with AHF should be interpreted with caution, as causal inferences cannot be drawn.

CONCLUSION

In conclusion, the present study demonstrated that SHR was independently associated with adverse outcomes in patients with acute heart failure after discharge. Elevated SHR levels were significantly associated with an increased risk of 6-month mortality. These findings suggest that SHR may serve as a useful laboratory indicator for early risk stratification in patients with acute heart failure.

Declaration of Generative AI in Scientific Writing:

During the preparation of this manuscript, the author used ChatGPT for translation and language editing. After using this tool, the author carefully reviewed and revised the content as necessary and takes full responsibility for the accuracy and integrity of the final manuscript.

Declaration of Interest:

There is no competing interest in this study.

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