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Original Article

Diuretic resistance during emergency treatment of acute heart failure: incidence and correlation with 30-day readmission

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Abstract: Objectives: To investigate the incidence of diuretic resistance (DR) during emergency treatment of acute heart failure (AHF) and its correlation with 30-day readmission. Methods: We retrospectively collected data from 198 AHF patients admitted to Beijing Chao-Yang Hospital, Capital Medical University between 2021 and 2025. Patients were allocated into a DR group and non-DR group according to the presence of diuretic resistance. Baseline characteristics, laboratory values, echocardiographic indices, and readmission rate were compared between the two groups. Logistic regression was performed to analyze the correlation between DR and short-term readmission rate. A nomogram was constructed to develop a clinical prediction model for readmission, and SHapley Additive exPlanations (SHAP) were used for model interpretation. Results: DR occurred in 48 patients (24.24%). The 30-day readmission rate was higher in the DR group than in the non-DR group (37.5% vs. 18.0%, $P<0.05$). Multivariate logistic regression analysis identified DR (OR=4.69, 95% CI: 2.17-10.16, $P<0.001$), New York Heart Association (NYHA) functional class (OR=5.05, 95% CI: 2.26-11.26, $P<0.001$), and left ventricular ejection fraction (LVEF) (OR=0.90, 95% CI: 0.86-0.94, $P<0.001$) as independent risk factors for readmission. The combined model demonstrated a significantly higher area under the receiver operating characteristic curve (ROC-AUC) compared to individual predictors ($P<0.05$). Conclusions: The incidence of DR in AHF patients during emergency treatment is closely associated with an increased risk of 30-day readmission. Early identification and intervention for DR may improve short-term prognosis.

Keywords: Acute heart failure, emergency, diuretic resistance, incidence rate, short-term readmission rate, correlation

Introduction

Acute heart failure (AHF) is defined as the new onset or exacerbation of heart failure symptoms and signs, and is the most common cause of unplanned hospitalization in patients over 65 years of age [1]. AHF is associated with high in-hospital mortality (4%-10%), high 1-year mortality (20%-30%), and substantial readmission rates [2]. Regionally, one-year mortality rate is highest in Africa (34%) and India (23%), intermediate in Southeast Asia (15%), and relatively lower in China (7%), South America (9%), and the Middle East (9%) [3]. AHF typically develops on the basis of underlying structural or functional cardiac disease, such as ischemic heart disease and hypertension [4]. The clinical manifestations of AHF are mainly characterized by the symptoms and signs of systemic congestion. The increase of ventricular filling pressure causes the accumulation of extracellular fluid [5, 6]. Therefore, initial management in most AHF patients includes non-invasive ventilation and intravenous diuretic therapy. The therapeutic effect of diuretics is primarily dependent on sodium and fluid excretion [7]. Clinical evidence indicates that patients with AHF remain at high risk of readmission after discharge, with approximately 20%-25% experiencing unplanned readmission within 30 days [8].

Although there is no uniform definition of diuretic resistance (DR), it is often interpreted as the failure to achieve adequate diuresis or sodium

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excretion despite appropriate diuretic treatment [9]. The pathophysiology of DR is multifactorial, involving neurohormonal activation [10], inflammatory responses [11], and renal function fluctuations [12]. In addition, long-term exposure to loop diuretics may induce nephron remodeling and hypertrophy of distal renal tubular cells, thereby enhancing compensatory sodium reabsorption and attenuating diuretic responsiveness [13]. Patients with DR tend to present with lower blood pressure, more comorbidities, reduced hemoglobin levels, decreased estimated glomerular filtration rate (eGFR), lower sodium content, and elevated uric acid content at admission [14]. Patients with DR have a 37% higher risk of death within 1 year [15]. Therefore, accurate identification and effective treatment of DR are needed for improving the clinical outcome in AHF patients.

This retrospective study analyzed DR incidence and its association with short-term readmission rate. The novelty of this study lies in three aspects: (1) reporting the incidence of DR specifically during the emergency treatment phase of AHF, (2) quantifying the association between DR and 30-day readmission, and (3) developing a nomogram and SHAP-based predictive model for early risk identification. The clinical significance lies in the potential for early recognition of DR in the emergency department to guide individualized diuretic therapy and optimize post-discharge management, thereby reducing short-term readmission rates and improving patient outcome.

Materials and methods

Subjects

A total of 198 patients with AHF who were treated and subsequently hospitalized at Beijing Chao-Yang Hospital, Capital Medical University between January 2021 and December 2025 were retrospectively selected. Inclusion criteria: ① meeting the diagnostic criteria of AHF [16]; ② receipt of standard diuretic therapy after emergency treatment (e.g., furosemide, torasemide); ③ availability of complete clinical data, including baseline characteristics and treatment data; ④ age ≥18 years old; ⑤ presentation to the Emergency Department as the initial point of contact, followed by hospital admission for AHF. Exclusion criteria: ① electrolyte disorder and acid-base imbalance caused by other reasons; ② endocrine disorders affecting urinary sodium (Na^+) excretion, including hypothalamus-pituitary diseases, primary aldosteronism, and pheochromocytoma; ③ in-hospital death or loss to follow-up; ④ pregnancy or lactation; ⑤ primary liver disease or uncontrolled autoimmune diseases; ⑥ eGFR <30 mL/(min·1.73 m^2); ⑦ malignant neoplasia with life expectancy <6 months, severe cognitive impairment, or frailty with markedly reduced functional reserve; ⑧ severe uncorrected valvular stenosis, left ventricular outflow obstruction, or hypertrophic/restrictive cardiomyopathy; or ⑨ incomplete clinical data.

Diuretic resistance (DR) was defined as persistent signs and symptoms of congestion despite administration of intravenous furosemide at a dose of 80 mg/d (or equivalent loop diuretic dosage) [17].

The primary endpoint was unplanned 30-day readmission due to cardiovascular events after discharge. A flow chart of patient selection is shown in **Figure 1**. This study was approved by the Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University (2026-6-15-K2), and the requirement for informed consent was waived due to the retrospective nature of the study.

Data collection

All clinical data were extracted from the electronic case system of the hospital. Baseline variables included demographic characteristics (e.g., age, sex, body mass index [BMI]) and comorbid conditions (e.g., hypertension, diabetes, renal insufficiency, atrial fibrillation). Clinical severity was assessed using the New York Heart Association (NYHA) classification.

Laboratory values included serum creatinine (Scr), blood urea nitrogen (BUN), brain natriuretic peptide (BNP), serum potassium, serum sodium, eGFR, urinary sodium, Cystatin C, and interleukin-6 (IL-6). Echocardiographic indices included left atrial diameter, left ventricular diastolic diameter (LVEDD), left ventricular systolic diameter (LVESD), and left ventricular ejection fraction (LVEF).

Treatment-related variables and prognosis indicators included diuretic regimen, length of hospital stay, and 30-day readmission. Laboratory

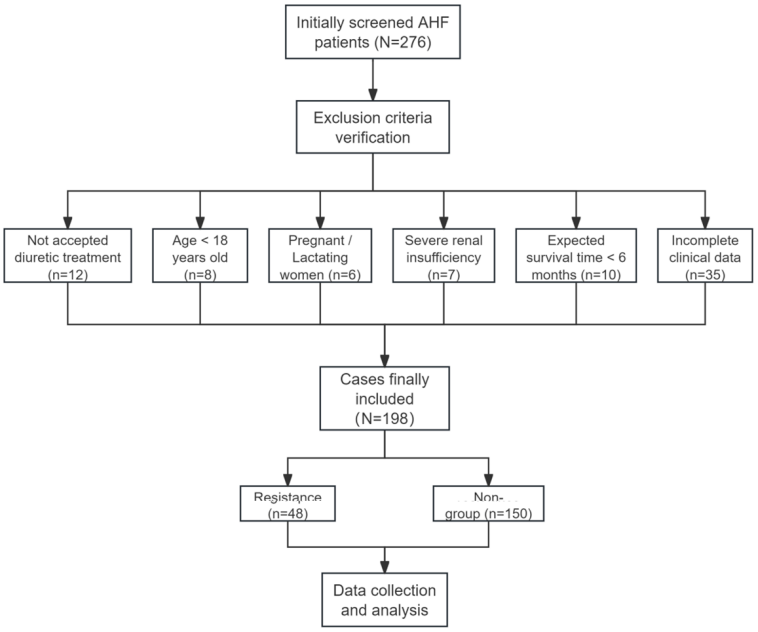

Figure 1. Flow chart of patient screening. Note: AHF: acute heart failure.

indicators were collected within 2 hours after Emergency Department admission and before administration of any diuretic therapy. Echocardiographic indices were measured within 24 hours of admission.

Outcome measures

Primary outcomes: (1) unplanned 30-day readmission due to cardiovascular events after discharge from the index hospitalization; (2) the incidence of DR during emergency treatment; and (3) the relationship between DR and 30-day readmission rate.

Secondary outcomes: (1) identification of risk factors for DR; and (2) identification of risk factors for 30-day readmission rate.

Statistical analysis

SPSS 27.0 statistical software was used for data analysis. Continuous variables were tested for normality using the Shapiro-Wilk test, with $P>0.05$ indicating a normal distribution. Normally distributed continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent-samples t-test. Non-normally distributed continuous variables were expressed as [M (IQR)] and compared using the Mann-Whitney U test. Categorical variables were expressed as counts and percentages [n (%)] and compared using the chi-square test or Fisher's exact test, as appropriate. Univariate analysis was first performed to identify potential predictors of 30-day readmission. Variables with P<0.1 in univariate analysis were included in multivariate logistic regression analysis to identify independent predictors for 30-day readmission, which were further adopted to develop a nomogram predictive model. Receiver operating characteristic (ROC) curve was performed to evaluate the predictive performance of the model. All statistical tests were two-sided, and a P value <0.05 was considered significant.

Results

Comparison of baseline characteristics between the two groups of patients

Among the 198 patients with AHF included in this study, DR occurred in 48 patients during emergency treatment, with an incidence of 24.24% (48/198). Among these, 32 patients required escalation of diuretic dosage, while 16 patients required combination diuretic therapy to achieve adequate decongestion. Patients were divided into a DR group (n=48) and a non-DR group (n=150) according to the presence of DR. Baseline characteristics, including age, sex, BMI, NYHA functional class, and comorbidities, were comparable between the two groups ($P>0.05$) (**Table 1**).

Comparison of laboratory values between the two groups

Compared to the non-DR group, patients in the DR group had significantly lower serum sodium, urinary sodium, and eGFR.However, BNP, BUN, SCr, serum potassium, Cystatin C, and IL-6 were significantly higher ($P<0.05$) (**Table 2**).

Comparison of echocardiographic indices between the two groups

Regarding echocardiographic findings, LVESD in the DR group was significantly higher than

Table 1. Comparison of baseline characteristics between DR and non-DR groups

Baseline indicator	DR group (n=48)	Non-DR group (n=150)	t/χ^2	*P*
Age (years)	76.81±7.93	74.61±8.13	1.641	0.103
Gender Sex (n, %)			0.125	0.724
Male	27 (56.3)	80 (53.3)		
Female	21 (43.8)	70 (46.7)		
BMI (kg/m^2)	24.58±3.72	24.12±3.56	0.769	0.443
NYHA Classification (n, %)			0.931	0.335
II-III	26 (54.2)	93 (62.00)		
IV	22 (45.8)	57 (38.00)		
Underlying disease (n, %)				
Hypertension	33 (68.8)	99 (66.0)	0.124	0.725
Diabetes	22 (45.8)	67 (44.7)	0.020	0.888
Renal insufficiency	21 (43.8)	48 (32.0)	2.211	0.137
Atrial fibrillation	16 (33.3)	47 (31.3)	1.579	0.209
Smoking history	19 (39.6)	53 (35.3)	0.284	0.594

Notes: DR: diuretic resistance; BMI: body mass index; NYHA: New York Heart Association.

that in the non-DR group, while the LVEF was significantly lower than that in the non-DR group (*P*<0.05) (**Table 3**).

Univariate and multivariate logistic regression of diuretic resistance

To identify factors associated with diuretic resistance, logistic regression analysis was performed with DR as the dependent variable. Candidate independent variables included demographic characteristics (e.g., age), laboratory indicators (e.g., Scr), and cardiac function indicators (e.g., LVEF).

Univariate analysis showed that Scr, BUN, BNP, serum potassium, serum sodium, LVESD, LVEF, urinary sodium, cystatin C, IL-6, and eGFR were associated with DR at a threshold of P<0.10. In multivariate logistic regression analysis, lower eGFR, serum sodium, and urinary sodium, as well as higher Scr, BUN, BNP and LVESD, were identified as independent risk factors for DR in patients with AHF (all *P*<0.05) (**Tables 4**, **5**).

Comparison of short-term readmission rates between the two groups of patients

Among the 198 AHF patients, 45 patients were readmitted within 30 days after discharge, corresponding to a short-term readmission rate of 16.16%. In the DR group, 18 patients (18/48) experienced 30-day readmission, with a readmission rate of 37.5%; In contrast, 27 patients (27/150) in the non-DR group were readmitted within 30 days, with a readmission rate of 18.0%. The short-term readmission rate in the DR group was significantly higher than that of the non-DR group (χ^2=7.873, *P*=0.005) (**Figure 2**).

We further compared baseline characteristics, including age, sex, BMI, NYHA functional classification, between the readmission and non-readmission groups, and found significant differences in age, NYHA class, and renal insufficiency between the two groups (*P*<0.05) (**Table 6**).

Univariate logistic regression analysis of 30-day readmission

Binary logistic regression analysis was performed with 30-day readmission as the dependent variable, and demographic characteristics, laboratory values, and echocardiographic indices as independent variables. The results showed that DR, NYHA classification, renal insufficiency, age, Scr, LVEF, BNP and LVESD were associated with 30-day readmission (*P*<0.1) (**Table 7**).

Multivariate logistic regression analysis of 30-day readmission

Variables with *P*<0.1 in the univariate analysis (DR, NYHA classification, renal insufficiency, age, Scr, LVEF, BNP, LVESD) were entered into the multivariate logistic regression model. The results showed that DR, NYHA classification and LVEF were independent predictors of 30-day readmission in patients with AHF (*P*<0.05) (**Figure 3**; **Table 8**).

Construction of a nomogram-based risk prediction model for readmission

A nomogram model was constructed to predict the risk of 30-day readmission based on the risk factors identified by multivariate analysis (**Figure 4**). For each predictor, a corresponding

Table 2. Comparison of laboratory values between DR and non-DR groups

Laboratory indicator	DR group (n=48)	Non-DR group (n=150)	t	*P*
Scr (μmol/L)	142.36±35.78	110.26±29.78	6.181	<0.001
BUN (mmol/L)	10.25±2.69	8.78±2.95	3.081	0.002
BNP (ng/L)	1928.56±325.78	1679.50±321.08	4.661	<0.001
Serum potassium (mmol/L)	4.08±0.62	3.81±0.54	2.932	0.004
Blood sodium (mmol/L)	139.19±5.12	141.65±4.76	3.062	0.003
Urinary sodium (mmol/L)	42.36±8.52	48.75±8.25	4.636	<0.001
Cystatin C (mg/L)	1.86±0.42	1.71±0.35	2.321	0.021
IL-6 (pg/mL)	7.58±3.66	6.32±2.18	2.901	0.004
eGFR (mL/(min·1.73 m^2))	62.64±11.38	70.95±12.66	4.054	<0.001

Notes: DR: diuretic resistance; BNP: brain natriuretic peptide; BUN: blood urea nitrogen; Scr: serum creatinine; IL-6: interleukin-6; eGFR: estimated glomerular filtration rate.

Table 3. Comparison of echocardiographic indicators between DR and non-DR groups

Echocardiographic indicator	DR group (n=48)	Non-DR group (n=150)	t	*P*
LVEDD (mm)	58.50±5.46	56.95±6.45	1.497	0.136
LVESD (mm)	48.52±7.51	45.49±8.56	2.194	0.030
Left atrial diameter (mm)	45.75±2.94	46.19±2.99	0.884	0.378
LEVF (%)	38.13±7.89	44.50±10.33	3.921	<0.001

Notes: DR: diuretic resistance; LVEDD: left ventricular diastolic diameter; LVESD: left ventricular systolic diameter; LVEF: left ventricular ejection fraction.

Table 4. Univariate and multivariate logistic regression of diuretic resistance

Variable	β	S.E	Z	*P*	OR (95% CI)	Assignment
Scr	0.03	0.01	5.03	<.001	1.03 (1.02-1.05)	Original value
BUN	0.18	0.06	2.95	0.003	1.19 (1.06-1.34)	Original value
BNP	0.01	0	4.15	<.001	1.01 (1.01-1.01)	Original value
Serum potassium	0.86	0.31	2.81	0.005	2.36 (1.30-4.29)	Original value
Blood sodium	-0.11	0.04	-2.94	0.003	0.90 (0.84-0.96)	Original value
LVESD	0.04	0.02	2.15	0.031	1.05 (1.01-1.09)	Original value
LVEF	-0.07	0.02	-3.67	<.001	0.93 (0.90-0.97)	Original value
Urinary sodium	-0.09	0.02	-4.22	<.001	0.91 (0.87-0.95)	Original value
Cystatin C	1.04	0.46	2.26	0.024	2.83 (1.15-6.99)	Original value
IL-6	0.18	0.06	2.77	0.006	1.20 (1.05-1.36)	Original value
eGFR	-0.06	0.01	-3.74	<.001	0.95 (0.92-0.97)	Original value

Notes: BNP: brain natriuretic peptide; BUN: blood urea nitrogen; Scr: serum creatinine; IL-6: interleukin-6; eGFR: estimated glomerular filtration rate; LVESD: left ventricular systolic diameter; LVEF: left ventricular ejection fraction.

score was assigned according to its position on the nomogram scale. The total score was obtained by summing the individual scores of all predictors. A higher total score indicated a higher predicted risk of 30-day readmission.

ROC curve analysis of risk factors for 30-day readmission

To further evaluate the predictive performance of independent risk factors for 30-day readmission in patients with AHF, ROC curve analysis was performed. The area under the curve (AUC) for DR in predicting 30-day readmission was 0.665 (95% *CI*: 0.558-0.772, *P*<0.05), with a sensitivity of 51.4% and a specificity of 81.6%. The AUC for LVEF was 0.749 (95% *CI*: 0.652-0.847, *P*<0.001), with an optimal cutoff value of 34.4%, yielding a sensitivity of 48.6% and a specificity of 92.6%. The AUC for NYHA class was 0.691 (95% *CI*: 0.595-0.788, *P*<0.001), with an optimal cutoff of grade IV, correspond-

Table 5. Multivariate logistic regression of diuretic resistance

Variable	β	S.E	Z	*P*	OR (95% CI)	Assignment
Scr	0.04	0.01	4.09	<.001	1.04 (1.02-1.06)	Original value
BUN	0.21	0.1	2.04	0.041	1.24 (1.01-1.52)	Original value
BNP	0.01	0	3.23	0.001	1.01 (1.01-1.01)	Original value
Serum potassium	0.82	0.44	1.86	0.063	2.27 (0.96-5.38)	Original value
Blood sodium	-0.11	0.05	-1.98	0.048	0.90 (0.81-0.99)	Original value
LVESD	0.07	0.03	2.12	0.034	1.07 (1.01-1.13)	Original value
LVEF	-0.05	0.03	-1.52	0.130	0.96 (0.90-1.01)	Original value
Urinary sodium	-0.1	0.03	-3.13	0.002	0.90 (0.84-0.96)	Original value
Cystatin C	0.24	0.74	0.32	0.751	1.26 (0.30-5.39)	Original value
IL-6	0.15	0.1	1.43	0.154	1.16 (0.95-1.42)	Original value
eGFR	-0.07	0.02	-2.91	0.004	0.93 (0.89-0.98)	Original value

Notes: BNP: brain natriuretic peptide; BUN: blood urea nitrogen; Scr: Serum creatinine; IL-6: Interleukin-6; eGFR: estimated Glomerular Filtration Rate; LVESD: left ventricular systolic diameter; LVEF: left ventricular ejection fraction.

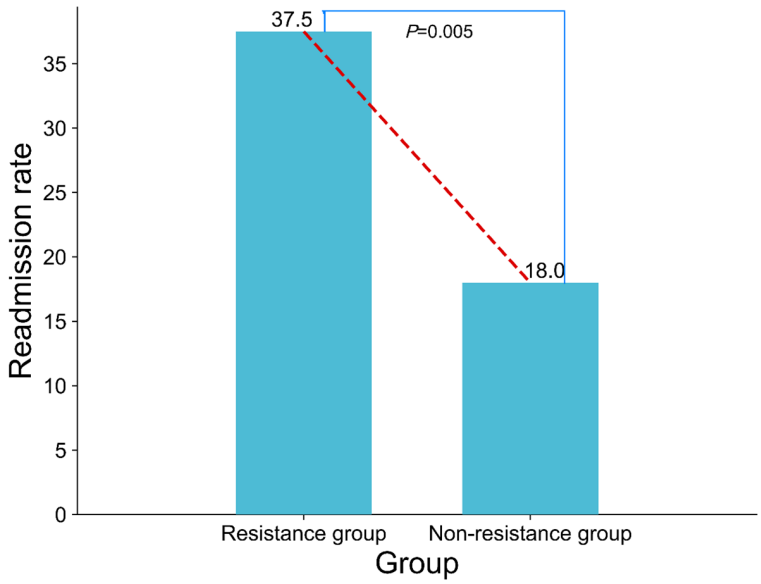

Figure 2. Comparison of short-term readmission rates between the resistance and non-resistance groups.

ing to a sensitivity of 71.4% and a specificity of 66.9%.

The AUC of the combined predictive model (DR + NYHA classification + LVEF) was 0.839 (95% *CI*: 0.759-0.919, *P*<0.001), with a sensitivity of 74.3%, a specificity of 80.4%, and a Youden index of 0.547, suggesting improved discriminative performance (**Figure 5**).

Model interpretation using SHAP analysis

SHAP analysis was applied to interpret the contribution of each variable in the predictive model. LVEF was identified as the most important predictor based on the mean absolute SHAP value (**Figure 6A**). **Figure 6B** illustrates the impact of each metric on readmission at the threshold. Specifically, patients with higher LVEF values (>52%), NYHA class III, and absence of DR exhibited a lower risk of 30-day readmission.

External validation of the predictive model

In the external validation cohort, 21 patients experienced 30-day readmission, while 17 patients did not. The predictive model was further evaluated in this independent external cohort.

The model demonstrated an AUC of 0.69 (95% CI: 0.51-0.87), which was slightly lower than the AUC obtained from the training set (0.84 [95% CI: 0.76-0.92]), but still indicated satisfactory discriminative ability (**Figure 7A**). Calibration curve analysis showed good agreement between predicted and observed probabilities across all risk strata (Hosmer-Lemeshow test, P>0.05) (**Figure 7B**). Additionally, decision curve analysis demonstrated that the model provided a net clinical benefit when the threshold probability ranged from approximately 0.4 and 0.8 (**Figure 7C**).

Table 6. Comparison of baseline characteristics between the readmission and non-readmission groups

Baseline indicator	Readmission group (n=45)	Non-readmission group (n=153)	t/χ^2	*P*
Age (years)	77.97±8.35	74.54±7.96	2.293	0.023
Sex (n, %)			3.271	0.070
Male	19 (42.2)	92 (60.1)		
Female	26 (56.8)	71 (39.9)		
BMI (kg/m^2)	24.13±4.01	24.26±3.51	0.199	0.842
NYHA (n, %)			20.410	<0.001
II-III	14 (31.1)	105 (68.6)		
IV	31 (68.9)	48 (31.4)		
Underlying disease (n, %)				
Hypertension	27 (60.0)	105 (68.6)	1.165	0.281
Diabetes	21 (46.7)	68 (44.4)	0.069	0.792
Renal insufficiency	23 (51.1)	46 (30.1)	6.784	0.009
Atrial fibrillation	17 (37.8)	46 (30.1)	0.953	0.329
Smoking history	21 (46.7)	51 (33.3)	2.671	0.102

Notes: BMI: body mass index; NYHA: New York Heart Association.

Discussion

Heart failure (HF) affects more than 64 million individuals worldwide, and this burden is expected to further increase with improved survival from cardiovascular diseases and advances in the management of underlying cardiac conditions [18, 19]. Congestion represents the main pathophysiologic and clinical feature of HF and remains the leading cause of HF-related hospitalization [20]. AHF affects more than 10 million individuals annually [21].

In patients with AHF, persistent congestion after discharge is strongly associated with early readmission and adverse clinical outcomes [22]. Therefore, achieving safe and effective decongestion remains a primary goal in AHF treatment [23]. Diuretics, particularly loop diuretics, constitute the first-line treatment for AHF patients [24]. However, some patients exhibit an insufficient response to standard diuretic therapy, leading to the development of DR. Despite its clinical relevance, most current treatment strategies largely rely on experience [25]. In this context, the present study provides real-world evidence regarding the incidence of DR and its association with early readmission risk, which may contribute to the optimization of individualized treatment strategies and reduce short-term readmission risk.

In this study, clinical data of 198 AHF patients were retrospectively analyzed. The results showed that the incidence of DR during emergency treatment was 24.24%, which is broadly consistent with previously reported rates of about 20% in domestic studies [26, 27]. This consistency supports the robustness of our findings and indicates that the observed incidence is representative of the emergency AHF population. Nevertheless, treatment protocols, diuretic prescribing strategies, and population characteristics may cause minor variations across studies, reflecting the inherent heterogeneity of clinical settings. The development of DR is multifactorial, involving pharmacokinetic and hemodynamic mechanisms [28]. In patients with acute compensatory heart failure, intestinal wall edema may reduce the bioavailability of diuretics. Even when adequate drug delivery is achieved, therapeutic efficacy may be weakened by compensatory sodium reabsorption. Long-term use of diuretics can induce structural and functional adaptations in the distal nephron, thereby shifting the dose-response relationship to the lower right [29-31]. In AHF patients, even if diuretics are sufficiently delivered, the kidney will functionally choose to store sodium rather than excrete sodium under long-term neurohormone activation and renal adaptation to volume overload [25].

In the present study, multivariate regression analyses identified elevated serum creatinine, BNP, BUN, and LVESD, as well as decreased serum sodium, urinary sodium, and eGFR, as

Table 7. Univariate logistic regression analysis of short-term readmission rate

Variable	β	S.E	Z	*P*	*OR* (95% *CI*)	Assignment
Group						
Non-resistance group					1.00 (Reference)	1
Resistance group	1.55	0.39	3.92	<.001	4.69 (2.17-10.16)	2
Gender						
Male					1.00 (Reference)	1
Female	0.55	0.38	1.45	0.146	1.73 (0.83-3.61)	2
NYHA classification						
III					1.00 (Reference)	1
IV	1.62	0.41	3.95	<.001	5.05 (2.26-11.26)	2
Hypertension						
No					1.00 (Reference)	0
Yes	-0.35	0.38	-0.92	0.358	0.70 (0.33-1.49)	1
Diabetes						
No					1.00 (Reference)	0
Yes	0.04	0.37	0.1	0.920	1.04 (0.50-2.16)	1
Smoking history						
No					1.00 (Reference)	0
Yes	0.48	0.38	1.26	0.207	1.61 (0.77-3.37)	1
Renal insufficiency						
No					1.00 (Reference)	0
Yes	0.84	0.38	2.23	0.026	2.33 (1.11-4.88)	1
Atrial fibrillation						
No					1.00 (Reference)	0
Yes	0.29	0.39	0.74	0.457	1.34 (0.62-2.86)	1
Age	0.05	0.02	2.24	0.025	1.05 (1.01-1.11)	Original value
BMI	-0.01	0.05	-0.2	0.841	0.99 (0.89-1.10)	Original value
SCr	0.01	0.01	2.51	0.012	1.01 (1.01-1.03)	Original value
BNP	0	0	1.72	0.086	1.00 (1.00-1.00)	Original value
BUN	0.04	0.06	0.66	0.507	1.04 (0.92-1.18)	Original value
Serum potassium	0.22	0.33	0.66	0.509	1.24 (0.65-2.36)	Original value
Serum sodium	-0.04	0.04	-0.97	0.330	0.96 (0.89-1.04)	Original value
LVEDD	0.02	0.03	0.7	0.483	1.02 (0.96-1.08)	Original value
LVESD	0.04	0.02	1.87	0.061	1.04 (1.00-1.09)	Original value
Left atrial diameter	-0.02	0.06	-0.37	0.715	0.98 (0.86-1.11)	Original value
LVEF/%	-0.11	0.02	-4.35	<.001	0.90 (0.86-0.94)	Original value

Notes: BMI: body mass index; NYHA: New York Heart Association; BNP: brain natriuretic peptide; BUN: blood urea nitrogen; SCr: serum creatinine; LVEDD: left ventricular diastolic diameter; LVESD: left ventricular systolic diameter; LVEF: left ventricular ejection fraction. The non-resistance group was used as the reference group.

independent risk factors for DR. Elevated Scr and BUN, along with decreased eGFR, indicate varying degrees of renal impairment. Such impairment directly limits sodium excretion and attenuates the renal response to diuretics [32]. Reduced urinary sodium levels further reflect impaired sodium excretion capacity and persistent sodium-water retention, serving as a direct marker of poor diuretic response [33]. Hyponatremia is often associated with excessive neuroendocrine activation and effective circulating volume depletion, and may further aggravate fluid overload by affecting osmotic pressure regulation, thereby forming a vicious cycle [34]. Elevated BNP levels reflect increased ventricular wall stress and more severe volume overload [35], indicating advanced cardiac dysfunction with significantly impaired

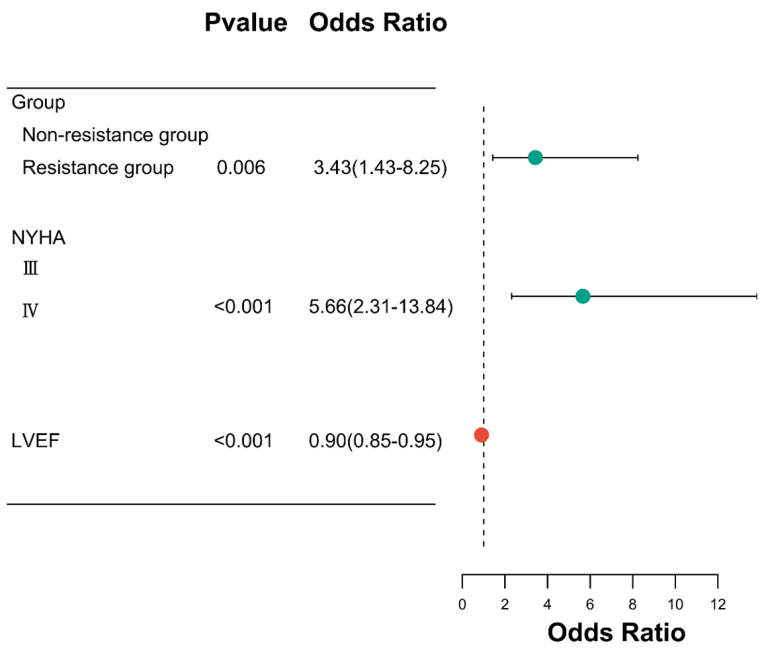

Figure 3. Forest plot of multivariate logistic regression.

myocardial systolic and diastolic function. The decrease of cardiac output will lead to the decrease of renal performance. Reduced cardiac output subsequently leads to renal hypoperfusion, further exacerbating renal dysfunction and diminishing diuretic efficacy, thereby forming a pathophysiologic cascade linking cardiac dysfunction, renal impairment, and diuretic resistance. Furthermore, increased LVESD reflects averse left ventricular remodeling and chamber dilation, which are associated with reduced myocardial contractility and mechanical efficiency. This not only impairs cardiac pump function but also exacerbates renal hypoperfusion through hemodynamic compromise, thereby contributing to reduced diuretic responsiveness and progression toward diuretic resistance [36, 37].

Regarding the association between DR and short-term readmission rate in patients with AHF, this study showed that the 30-day readmission rate was significantly higher in the DR group (37.5%) than in the non-DR group (18.0%). Multivariate logistic regression analysis confirmed that DR, high NYHA classification, and low LVEF were associated with an increased risk of short-term readmission. These findings are generally consistent with previous reports [38]. Notably, the effect size in our study (OR=3.43) appears higher than that reported in some prior studies (OR ranging from 1.8 to 2.5). This difference may be explained by our exclusive focus on the emergency treatment phase, when diuretic responsiveness is first assessed. In addition, the inclusion of SHAP-based model interpretation may have improved risk stratification and contributed to more pronounced effect estimation.

NYHA functional class was also identified as an important predictor of readmission. Patients with NYHA class IV exhibited a significantly higher readmission risk than those of grade II-III patients. NYHA classification reflects the severity of functional limitation in patients with heart failure and is primarily based on the main symptoms burden, including dyspnea, fatigue, and exercise intolerance [39]. Higher NYHA class indicates more advanced cardiac dysfunction, impaired myocardial contractility, and reduced cardiac reserve, all of which contribute to an increased risk of clinical deterioration and rehospitalization. These findings are consistent with previous studies [40, 41]. In addition, patients with NYHA class IV often have more severe sodium and water retention, myocardial remodeling, worse diuretic treatment effect, and higher incidence of DR, further aggravating the risk of readmission, and forming a vicious cycle of 'cardiac function deterioration → DR occurrence → poor treatment effect → readmission'.

As a core indicator of left ventricular systolic function, reduced LVEF reflects impaired cardiac output and is a well-established predictor of adverse outcomes in patients with AHF [42]. The results of this study showed that lower LVEF was associated with a higher risk of 30-day readmission. This may be explained by the fact that reduced baseline cardiac function renders patients more vulnerable to recurrent decompensation, even after apparent symptom improvement, particularly in response to minor triggers such as fatigue and infection.

Table 8. Multivariate logistic regression analysis of short-term readmission rate

Variable	β	S.E	Z	P	OR (95% CI)	Assignment
Group						
Non-resistance group					1.00 (Reference)	1
Resistance group	1.23	0.45	2.76	0.006	3.43 (1.43-8.25)	2
NYHA						
III					1.00 (Reference)	1
IV	1.73	0.46	3.79	<.001	5.66 (2.31-13.84)	2
LVEF/%	-0.11	0.03	-3.71	<.001	0.90 (0.85-0.95)	Original value

Notes: NYHA: New York Heart Association; LVEF: left ventricular ejection fraction.

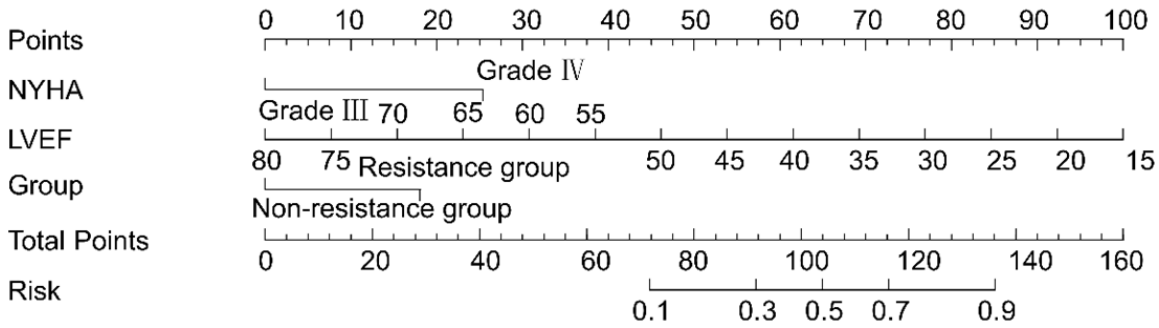

Figure 4. Nomogram model for predicting the risk of 30-day readmission. Notes: NYHA: New York Heart Association; LVEF: left ventricular ejection fraction.

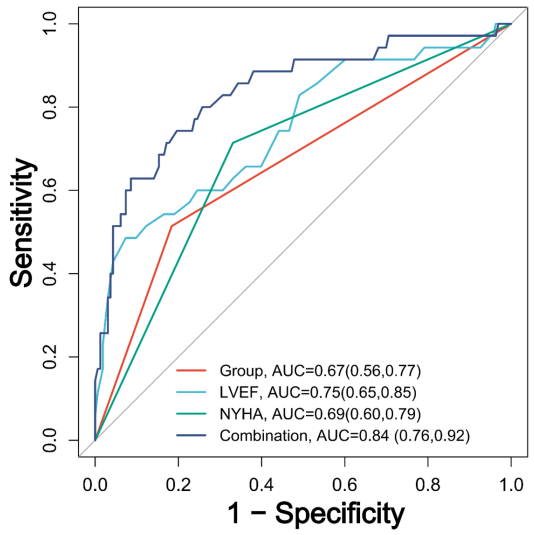

Figure 5. ROC curves for each predictor and their combined model for predicting 30-day readmission in patients with AHF. Notes: AUC: Area under the curve; DR: Diuretic resistance; NYHA: New York Heart Association; LVEF: Left ventricular ejection fraction. The combined model includes DR, NYHA classification and LVEF.

Furthermore, ROC curve analysis confirmed that DR, NYHA class, and LVEF each demonstrated good predictive value for 30-day readmission in patients with AHF. the combined model incorporating all three variables significantly improved predictive performance compared to individual predictors. These findings provided objective evidence for early risk stratification of high-risk population and may facilitate individualized intervention.

For the clinical management of DR in patients with AHF during emergency treatment, the following measures can be considered: ① Optimization of diuretic therapy is essential, such as dose escalation of loop diuretics, sequential nephron blockade through combination therapy (e.g., loop diuretics + thiazide diuretics), or switching between different loop diuretics when appropriate [43]. ② In patients with hypotension and insufficient renal perfusion, vasodilators or positive inotropic drugs can be appropriately used to increase renal blood flow and enhance diuretic responsiveness. ③ Active management of underlying comorbidities, including control of blood pressure and blood glucose levels, preservation or improvement of renal function, and reduction of cardiac load, may contribute to improved vol-

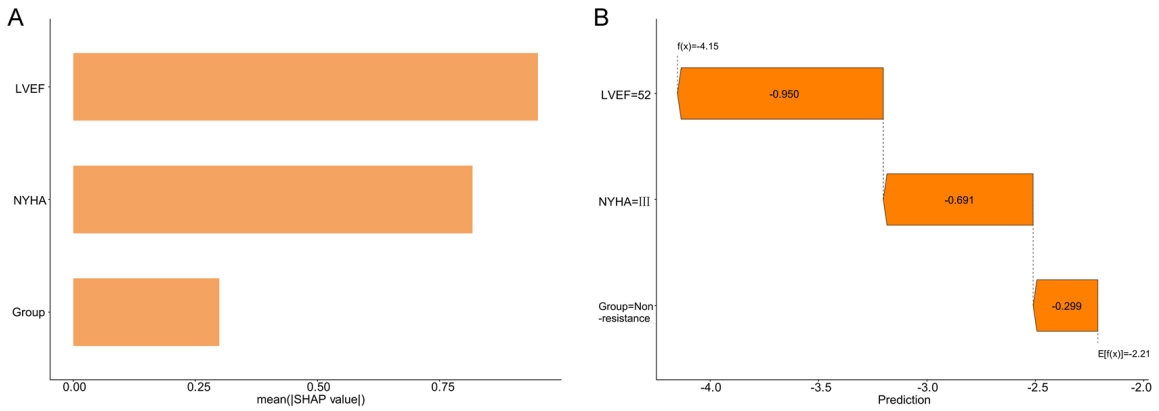

Figure 6. Model interpretation using SHAP. A. Importance of each feature as determined by mean absolute SHAP values. B. SHAP waterfall diagram of various influencing factors on readmission prediction. The horizontal axis represents SHAP prediction values. Negative values indicate protective factors associated with reduced adverse prognosis risk. Each orange bar shows the independent contribution of LVEF=52%, NYHA class III and non-diuretic resistance to the final prediction outcome. SHAP: SHapley Additive exPlanations.

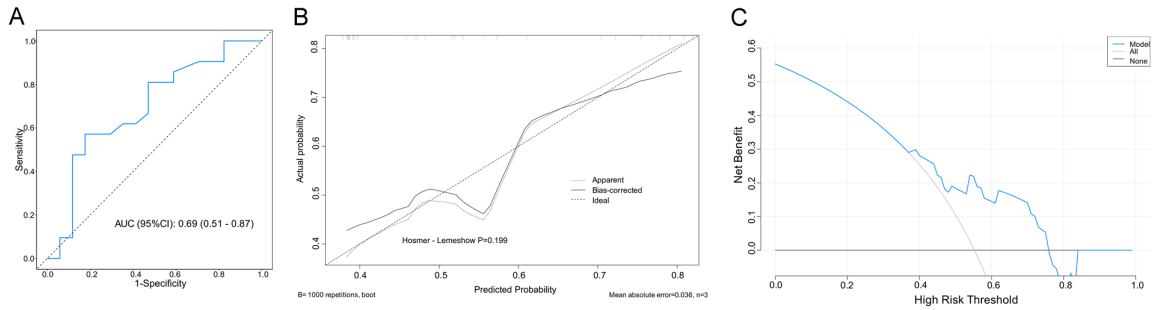

Figure 7. External validation of the predictive model. A. ROC curve demonstrating the discriminative performance of the model. B. Calibration plots showing the agreement between predicted probabilities and observed outcomes. C. DCA illustrating the net clinical benefit of the model across different threshold probabilities. Notes: ROC: Receiver operating characteristic; DCA: Decision curve analysis.

ume management and diuretic efficacy. ④ Structured post-discharge follow-up is of critical importance. Patients should be educated regarding medication adherence and dietary sodium restriction, and encouraged to monitor body weight and urine output regularly.

There were several limitations to this study. First, this was a single-center retrospective study, which inevitably introduces selection bias and information bias. Moreover, the retrospective design precluded prospective screening and standardized intervention, and may have resulted in incomplete data collection potentially affecting the generalizability of the findings. Second, the underlying mechanisms linking NYHA class and LVEF with the occurrence of DR and 30-day readmission were not directly analyzed. Our discussion of mechanisms is largely inferred from published literature rather than directly tested in this study. Future studies combining basic research and prospective clinical designs are warranted to further elucidate the biological mechanisms underlying these associations. Third, the follow-up period was relatively short, with outcomes limited to 30-day readmission. Long-term outcomes, including 6-month, 1-year readmission rates, mortality, and changes in cardiac function, were not assessed. Fourth, although multivariate regression analysis was performed, residual confounding cannot be fully excluded. Key variables such as nutritional status, detailed dosing and duration of combined medication (e.g., angiotensin- converting enzyme inhibitors, β-blockers) and post-discharge rehabilitation were not comprehensively included. In addition, detailed information

regarding concomitant medications during hospitalization was not systematically collected. These unmeasured factors may have influenced diuretic responsiveness and clinical outcomes through effects on renal hemodynamics, sodium reabsorption, and cardiac function, thereby potentially introducing bias. Finally,patients with severe renal insufficiency, advanced valvular heart disease, malignancy, pregnancy, or lactation were excluded; therefore, the findings may not be generalizable to these special AHF subgroups. Moreover, although external verification of the prediction model was performed, the sample was relatively small. Larger, multi-center prospective studies are needed to further validate the robustness and generalizability of the proposed model.

Conclusion

The incidence of DR during emergency treatment in patients with AHF is relatively high. DR, NYHA classification, and LVEF are closely associated with the risk of 30-day readmission. Early identification of DR during the emergency period is therefore of great clinical importance. Comprehensive assessment incorporating NYHA classification and LVEF level may facilitate more accurate risk stratification and support individualized treatment plans aimed at improving cardiac function, reducing the occurrence of DR and related adverse events, and ultimately reducing short-term readmission rates while improving overall prognosis.

Disclosure of conflict of interest

None.

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