

Original Article

Risk factors for heart failure in critically ill patients with COVID-19: a retrospective study

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Abstract: Objective: To investigate the clinical characteristics and risk factors for heart failure (HF) in critically ill patients with coronavirus disease 2019 (COVID-19). Methods: Medical records of 230 critically ill COVID-19 patients admitted from January 2022 to January 2026 were retrospectively analyzed. Patients were assigned to HF (n=106) and control (n=124) groups. The HF group was further subdivided into the HF with preserved ejection fraction (HFpEF) group (n=94) and the HF with reduced and mildly reduced ejection fraction (HFr+mEF) group (n=12). Clinical characteristics and therapeutic interventions were compared. Univariate and multivariate logistic regression identified factors independently linked to HF. Results: Among 230 patients, 106 (46.09%) developed HF. The HF group had older age, and higher rates of hypertension and coronary artery disease rates (all $P < 0.05$). Subgroup analysis revealed no baseline differences between the HFpEF and HFr+mEF groups (all $P > 0.05$), but corticosteroid use was significantly more frequent in HFpEF group (62.77% vs. 25.00%, $P = 0.026$). Multivariate analysis identified heart rate (OR=1.052), neutrophil-to-lymphocyte ratio (NLR) (OR=4.848), and platelet count (OR=0.952) as factors independently linked to HF (all $P < 0.01$). Their combination yielded an area under the curve of 0.944 (sensitivity: 95.16%, specificity: 83.96%) for predicting HF. Conclusion: The incidence of HF in critically ill COVID-19 patients is high, with HFpEF being the predominant subtype. Heart rate, NLR, and platelet count are independently associated with HF in critically ill COVID-19 patients, and their combination demonstrates good predictive value.

Keywords: Critically ill COVID-19, heart failure, reduced ejection fraction, related factors, advanced age

Introduction

As a global public health emergency, coronavirus disease 2019 (COVID-19) has placed enormous strain on public health systems and caused unprecedented social and economic consequences [1]. Although the overall pathogenicity of COVID-19 has changed with viral mutations and shifts in population immunity, critically ill COVID-19 patients still face an extremely high risk of death [2]. Critical COVID-19 often manifests as shock, respiratory failure, or multiple organ dysfunction, with the core pathophysiological mechanisms including virus-induced hyperinflammation, endothelial injury, and microthrombus formation [3]. This severe systemic inflammatory state not only damages the pulmonary parenchyma but also imposes a significant burden on the cardiovascular system.

Heart failure (HF) is a common cardiovascular complication of COVID-19 [4]. Specifically, myocardial injury, myocarditis, and coronary plaque instability caused by the virus can all trigger acute HF [5]. Once HF occurs, cardiac workload increases, and the risks of cardiovascular events and multiple organ dysfunction significantly rise [5]. HF is highly prevalent in the elderly, with primary characteristics of pulmonary and/or systemic congestion [6]. When HF coexists with pulmonary infection, the infection can increase pulmonary vascular resistance and right ventricular afterload, exacerbating myocardial hypoxia and injury, and thus substantially increasing mortality rate compared with that in patients with HF alone [7, 8]. COVID-19 is essentially a viral pulmonary infection, and its associated HF faces the same risks. Notably, the clinical presentation of COVID-19-associated HF is often atypical and can be

masked by symptoms of respiratory failure, leading to delayed or missed diagnosis [9]. However, the clinical characteristics of HF specifically in critically ill patients remain poorly defined, and the impact of critical care interventions - such as corticosteroids, mechanical ventilation, and prone positioning - on HF development has received insufficient attention. Therefore, systematically analyzing the clinical characteristics of HF in critically ill COVID-19 patients is of significant value. Critically ill patients often require invasive mechanical ventilation, prone positioning, blood purification, and immunomodulatory therapies, which confer unique features on the development and progression of HF [10]. Additionally, these patients are generally older, with a high burden of cardiovascular comorbidities [11], and medications such as corticosteroids may cause fluid/sodium retention and blood pressure fluctuations, indirectly affecting cardiac function [12]. Furthermore, the distribution and prognosis of HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF) may differ in critically ill patients [13], but this issue has received insufficient attention. Clarifying the clinical characteristics of different HF subtypes will facilitate individualized treatment, and identifying risk factors is key to preventing HF.

Against this background, we conducted a retrospective analysis of 230 critically ill COVID-19 patients, aiming to provide evidence-based support for early clinical warning, stratified management, and optimized treatment.

Data and methods

Data source

This study was conducted after approval by the Medical Ethics Committee of Shijiazhuang Second Hospital.

The clinical data of 256 critically ill COVID-19 patients admitted to Shijiazhuang Second Hospital between January 2022 and January 2026 were retrospectively analyzed. Following the specified inclusion and exclusion criteria, 230 patients were finally included.

Patient selection

Inclusion criteria: complete clinical data; age >18 years; confirmed diagnosis of COVID-19

(positive nucleic acid polymerase chain reaction (PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from nasal or throat swab specimens) and chest computed tomography (CT) imaging findings consistent with viral pneumonia; met the criteria for critical illness. The classification of critical illness was based on the criteria set forth in *Guidance for Corona Virus Disease 2019 Prevention, Control, Diagnosis and Management* issued by the National Health Commission of the People's Republic of China [14]. Patients meeting any of the conditions below were classified as critically ill: (1) Respiratory failure requiring mechanical ventilation (including non-invasive or invasive ventilation); (2) Presence of shock; (3) Failure of other organs requiring intensive care unit (ICU) admission.

Exclusion criteria: pregnant or peripartum COVID-19 patients; patients who died within 24 hours of hospitalization; patients with a prior diagnosis of chronic HF (New York Heart Association [NYHA] class III-IV) before COVID-19 onset; patients with end-stage renal disease requiring maintenance hemodialysis; patients with malignant tumors or other terminal illnesses with life expectancy <6 months; patients who were transferred from other hospitals with incomplete baseline data; patients with missing key variables (heart rate, NLR, or platelet count).

Sample size

This sample size of this retrospective study was determined by case availability. Among the 230 enrolled patients, 106 developed heart failure (HF), providing 106 events for the primary multivariate logistic regression analysis. With 4 candidate variables (age, heart rate, neutrophil-to-lymphocyte ratio, and platelet count) entered into the final model, the events-per-variable (EPV) ratio was 26.5 (106 events/4 variables). This ratio substantially exceeds the recommended minimum threshold of 10 events per variable proposed by Peduzzi et al. [15], and also surpasses the more conservative threshold of 15-20 suggested in recent methodological guidelines [16]. Therefore, the primary regression model was adequately powered to identify independent factors associated with HF in this cohort.

However, for the HF subtype comparison (HFpEF, n=94 vs. HFr+mEF, n=12), the small

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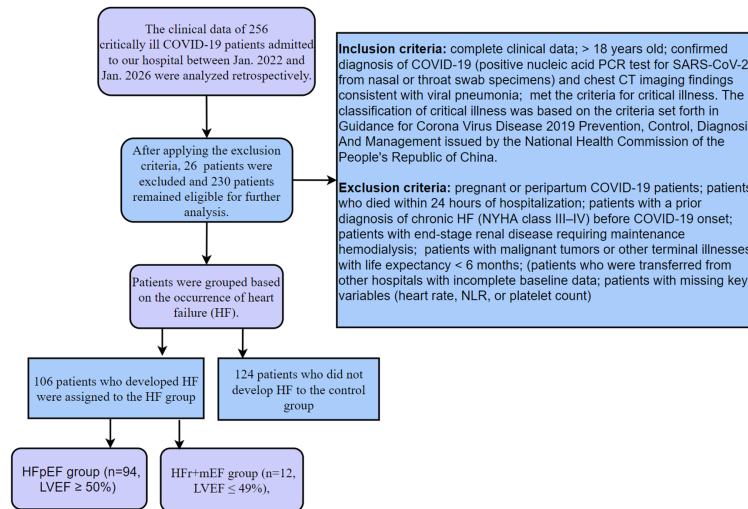


Figure 1. Patients selection and grouping. Notes: COVID-19, Corona Virus Disease 2019; PCR, polymerase chain reaction; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; CT, computed tomography; HF, heart failure; NYHA, New York Heart Association; HFpEF, heart failure with preserved ejection fraction; HFr+mEF, heart failure with reduced ejection fraction + mid-range ejection fraction; LVEF, left ventricular ejection fraction; NLR, neutrophil-to-lymphocyte ratio.

sample size in the HFr+mEF subgroup precludes formal power calculation and limits the robustness of any statistical inferences drawn from these comparisons. These subgroup analyses are therefore considered hypothesis-generating, and the findings require validation in larger cohorts. No additional HFr+mEF cases could be included due to the predefined study period and single-center design, which we acknowledge as a major limitation.

Group assignment

Patients were grouped based on the occurrence of HF: 106 patients who developed HF were assigned to the HF group, and the remaining 124 patients who did not develop HF were assigned to the control (Con) group. The HF group was further subdivided according to left ventricular ejection fraction (LVEF) into a HFr+mEF group (n=12) and a HFpEF group (n=94). HF was defined according to the 2021 European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of HF [17]. Based on LVEF, HF subtypes were classified as: heart failure with reduced ejection fraction (HFrEF, LVEF ≤40%), heart failure with mildly reduced ejection fraction (HFmrEF, LVEF 41-49%), and heart failure with preserved ejection fraction (HFpEF, LVEF ≥50%). Because the numbers of patients with HFrEF and HFmrEF were small,

these two groups were combined into the HFr+mEF group (LVEF ≤49%). Patient selection and grouping details can be found in **Figure 1**.

Data extraction

We reviewed inpatient medical records from Shijiazhuang Second Hospital and extracted clinical data, including demographics (age, body mass index [BMI], sex, diabetes mellitus [DM], hypertension, smoking, coronary artery disease [CAD]), admission vitals (heart rate and blood pressure) recorded at the time of ICU admission, symptoms (fever and cough) that were documented within the first 24 hours of ICU admission, initial laboratory parameters (neutrophil-to-lymphocyte ratio [NLR] and

platelet count) obtained from the first blood draw performed within 24 hours of ICU admission, and in-hospital treatments (continuous renal replacement therapy (CRRT), prone positioning, corticosteroids, immunoglobulins, non-invasive/invasive mechanical ventilation, and anticoagulants).

Outcome measures

Primary outcomes: (1) Analysis of independent influencing factors: Univariate and multivariate logistic regression analyses were carried out for identifying independent factors linked to HF in critically ill COVID-19 patients. Variables included in the analysis were age, heart rate, NLR, and platelet count. (2) Predictive efficacy of associated factors: Receiver operating characteristic (ROC) curves were generated to evaluate the predictive value of heart rate, NLR, platelet count, and the combined model of these three factors for HF in critically ill COVID-19 cases.

Secondary outcomes: (1) General clinical characteristics and baseline data: The HF and Con groups were compared in age, sex, BMI, history of smoking, hypertension, CAD, DM, heart rate, blood pressure, NLR, platelet count, and the incidence rates of symptoms including fever, and cough. (2) Subgroup comparison of HF: The

HFpEF and HFr+mEF groups were compared in baseline data (age, sex, BMI, comorbidities, symptoms, etc.) and treatment interventions, including the modality of oxygen therapy (non-invasive/invasive mechanical ventilation), the proportion of patients with respiratory failure at the initial visit, and the utilization rates of prone position ventilation, CRRT, corticosteroids, and human immunoglobulin.

Statistical analyses

Statistical analyses were performed via SPSS 20.0 (IBM Corp, Armonk, NY, USA), and graphs were generated using GraphPad Prism 7 software (GraphPad Software Inc., San Diego, CA, USA). After testing for normality, continuous variables that followed a normal distribution were expressed as mean $\pm$ standard deviation, with inter-group comparisons conducted using the independent samples t-test. Count variables were expressed by number (percentage) [n (%)], with inter-group comparisons conducted using the chi-square test or Fisher's exact test, as appropriate. Univariate logistic regression was first performed to screen potential factors. Variables with $P < 0.05$ in univariate analysis were then entered into the multivariate logistic regression model using the Enter method (forced entry), and no stepwise selection was applied. Age, heart rate, NLR, and platelet count were all entered into the multivariate model as continuous variables with their original measured values. These variables were selected for multivariate analysis based on univariate screening ($P < 0.05$). ROC curves were plotted for the predictive efficacy evaluation of risk factors, and the AUC was calculated. $P < 0.05$ indicates a conspicuous discrepancy.

Results

Baseline characteristics of the HF and Con groups

As presented in **Table 1**, compared with the Con group, the HF group had notably older age, and higher heart rate and NLR (all $P < 0.001$), but a notably lower platelet count ($P < 0.001$). Regarding comorbidities, the HF group had notably higher proportions of patients with a history of hypertension and CAD than the Con group (both $P < 0.05$). No significant inter-group differences were observed in sex, BMI, smoking history, DM, blood pressure, fever, or cough (all $P > 0.05$).

Baseline characteristics of HF subgroups

As summarized in **Table 2**, there were no significant differences between the HFpEF and HFr+mEF groups in terms of age, sex, BMI, heart rate, blood pressure, NLR, platelet count, smoking history, history of hypertension, DM, or CAD, and symptoms such as fever and cough (all $P > 0.05$).

Comparison of treatment interventions between HF subgroups

As summarized in **Table 3**, regarding the modality of oxygen therapy, the HFr+mEF group showed a non-significantly higher proportion of patients receiving invasive mechanical ventilation than the HFpEF group (83.33% vs. 68.09%, $P = 0.340$), and also showed a non-significantly higher proportion of patients presenting with respiratory failure at the initial visit than the HFpEF group (83.33% vs. 68.09%, $P = 0.203$). Moreover, no significant inter-group differences were observed in the use of prone position ventilation ($P = 0.289$), CRRT ($P = 0.471$), and human immunoglobulin ($P = 0.529$). Notably, the HFpEF group showed a notably higher proportion of patients using corticosteroids than the HFr+mEF group (62.77% vs. 25.00%, $P = 0.026$).

Factors associated with HF in critically ill COVID-19 patients

Assignment for all variables included in the logistic regression models is presented in **Table 4**. According to univariate logistic regression, age, heart rate, NLR, and platelet count were all potential associated factors linked to HF in critically ill COVID-19 patients (all $P < 0.05$; **Table 5**). All four variables were included in the multivariate logistic regression analysis. Multivariate analysis results (**Table 6**) identified heart rate (OR=1.052, 95% CI 1.012-1.093, $P = 0.010$), NLR (OR=4.848, 95% CI 2.784-8.442, $P < 0.001$), and platelet count (OR=0.952, 95% CI 0.936-0.968, $P < 0.001$) as factors independently associated with HF in critically ill COVID-19.

Predictive efficacy of influencing factors for HF in critically ill COVID-19 patients

ROC curves were generated for predictive value assessment of heart rate, NLR, platelet count, and the combined model of these three factors

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Table 1. Comparison of baseline characteristics between HF and control groups

	HF group (n=106)	Control group (n=124)	χ^2/t	P
Age (years)	66.38±11.69	61.15±10.92	3.505	<0.001
BMI (kg/m ²)	23.29±1.75	23.18±2.21	0.409	0.683
Sex			0.208	0.648
Male	63 (59.43%)	70 (56.45%)		
Female	43 (40.57%)	54 (43.55%)		
Heart rate (HR)	95.86±13.54	87.15±10.79	5.428	<0.001
Systolic blood pressure (mmHg)	129.54±9.83	130.91±8.52	1.132	0.259
Diastolic blood pressure (mmHg)	74.16±12.44	72.13±11.50	1.288	0.199
NLR	5.30±1.05	3.51±0.59	16.190	<0.001
Platelet count (×10 ⁹ /L)	167.67±21.29	220.54±22.90	18.020	<0.001
History of smoking			0.107	0.744
Yes	32 (30.19%)	35 (28.23%)		
No	74 (69.81%)	89 (71.77%)		
Underlying diseases				
History of hypertension			4.105	0.043
Yes	49 (46.23%)	44 (35.48%)		
No	57 (53.77%)	88 (64.52%)		
History of diabetes mellitus			0.281	0.596
Yes	28 (26.42%)	29 (23.39%)		
No	78 (73.58%)	95 (76.61%)		
Coronary artery disease			13.621	<0.001
Yes	42 (39.62%)	22 (17.74%)		
No	64 (60.38%)	102 (82.26%)		
Symptoms				
Fever			0.261	0.609
Yes	85 (80.19%)	96 (77.42%)		
No	21 (19.81%)	28 (22.58%)		
Cough			0.161	0.688
Yes	85 (80.19%)	102 (82.26%)		
No	21 (19.81%)	22 (17.74%)		

Note: HR: heart rate; BMI: body mass index; NLR: neutrophil-to-lymphocyte ratio.

for predicting HF in critically ill COVID-19 cases. As shown in **Figure 2** and **Table 7**, the AUC for heart rate, NLR, platelet count, and the combined model in predicting HF in critically ill COVID-19 patients were 0.684, 0.888, 0.879, and 0.944, respectively. The optimal cutoff value for NLR was 4.235, with a sensitivity of 86.29% and a specificity of 81.13%. The optimal cutoff value for platelet count was 191.75×10⁹/L, with a sensitivity of 86.29% and a specificity of 83.96%. The combined model had the best predictive efficacy, with an AUC of 0.944, a sensitivity of 95.16%, a specificity of 83.96%, and an accuracy of 90.00%. The confusion matrix for the combined model based on the optimal cutoff value is presented in **Table 8**.

Discussion

COVID-19 critically ill patients exhibit a high incidence of HF, and its clinical manifestations are frequently masked by respiratory failure symptoms, posing substantial challenges for early identification [18]. Through a retrospective analysis of 230 critically ill COVID-19 patients, this study systematically investigated the clinical characteristics, influencing factors, and predictive value of HF in these patients, providing evidence-based support for early identification and intervention.

In the present study, the proportion of critically ill COVID-19 patients complicated with HF was

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Table 2. Comparison of baseline characteristics between HFpEF and HFr+mEF groups

	HFpEF group (n=94)	HFr+mEF group (n=12)	χ^2/t	P
Age (years)	66.57±11.70	64.91±11.96	0.461	0.646
BMI (kg/m ²)	23.27±1.65	23.41±2.50	0.247	0.805
Sex			0.450	0.480
Male	57	6		
Female	37	6		
Heart rate (HR)	96.31±13.10	92.32±16.81	0.963	0.338
Systolic blood pressure (mmHg)	129.22±9.95	132.06±8.83	0.940	0.349
Diastolic blood pressure (mmHg)	74.69±12.62	70.03±10.50	1.226	0.223
NLR	5.27±1.03	5.49±1.22	0.666	0.507
Platelet count (×10 ⁹ /L)	168.09±20.64	164.35±26.68	0.572	0.569
History of smoking			-	0.358
Yes	27	5		
No	67	7		
Underlying diseases				
History of hypertension			0.078	0.781
Yes	43	6		
No	51	6		
History of diabetes mellitus			-	0.729*
Yes	24	4		
No	70	8		
Coronary heart disease			-	0.878*
Yes	37	5		
No	57	7		
Symptoms				
Fever			-	0.249*
Yes	77	8		
No	17	4		
Cough			-	0.701*
Yes	76	9		
No	18	3		

Note: * indicates the Fisher's exact test is used for analysis. HFpEF: heart failure with preserved ejection fraction; HFr+mEF: heart failure with reduced ejection fraction + mid-range ejection fraction; HR: heart rate; BMI: body mass index; NLR: neutrophil-to-lymphocyte ratio.

Table 3. Treatment modalities in critically ill COVID-19 patients with heart failure [n (%)]

Items	Items (106)	HFpEF group (n=94)	HFr+mEF group (n=12)	P
Oxygen therapy modality				0.340*
Non-invasive ventilation	32 (30.19%)	30 (31.91%)	2 (16.67%)	
Invasive ventilation	74 (69.81%)	64 (68.09%)	10 (83.33%)	
Presence of respiratory failure at the initial visit	67 (63.21%)	57 (60.64%)	10 (83.33%)	0.203*
Ventilation in prone position	27 (25.47%)	26 (27.66%)	1 (8.33%)	0.289*
Use of CRRT	25 (23.58%)	21 (22.34%)	4 (33.33%)	0.471*
Corticosteroids	62 (58.49%)	59 (62.77%)	3 (25.00%)	0.026*
Use of human immunoglobulin	39 (36.79%)	36 (38.30%)	3 (25.00%)	0.529*

Notes: * indicates the Fisher's exact test is used for analysis. COVID-19: Corona Virus Disease 2019; HFpEF: heart failure with preserved ejection fraction; HFr+mEF: heart failure with reduced ejection fraction + mid-range ejection fraction; CRRT: continuous renal replacement therapy.

Table 4. Variable assignment for logistic regression analysis

Variable	Assignment
Heart failure (dependent)	0 = no, 1 = yes
Age	Continuous (per 1 year)
Heart rate	Continuous (per 1 bpm)
NLR	Continuous (per 1 unit)
Platelet count	Continuous (per $1 \times 10^9/L$)

Note: NLR: neutrophil-to-lymphocyte ratio.

46.09%, which is higher than previously reported incidence of HF in the general hospitalized COVID-19 population. For example, Gomez-Mesa et al. [10], based on the CARDIO-COVID registry study encompassing 8,045 patients from 84 hospitals across 32 countries, reported an acute HF incidence of 5.4%. An age-stratified analysis of the same registry study reported an incidence of 15.2% in HF in elderly COVID-19 patients [11]. The substantially elevated incidence in our critically ill cohort is consistent with the principle that disease severity amplifies cardiovascular risk, as our patients exhibited more severe systemic inflammation, higher prevalence of underlying cardiovascular comorbidities, and greater hemodynamic stress from mechanical ventilation and other ICU interventions. This comparison validates that critical illness status is a key determinant of HF risk. The HF group was significantly older and had higher rates of hypertension and CAD than those in the con group, which is consistent with the traditional epidemiological characteristics of HF. Notably, fever and cough showed no between-group differences. Regarding HF subtypes, HFpEF was predominant (88.68%), with HFr+mEF accounting for only 11.32%. This distribution pattern aligns with the pathophysiology of COVID-19-associated HF, as viral infection is more likely to cause diastolic than severe systolic dysfunction [13, 19]. This predominance may also reflect the demographic profile of our cohort, as older age and hypertension both are overrepresented in the HF group, and are well-established risk factors for diastolic dysfunction. Clinically, this finding suggests that in critically ill COVID-19 patients, volume management and afterload reduction should take priority over inotropic support, as the latter may be less beneficial and potentially harmful in HFpEF. Furthermore, invasive mechanical ventilation and corticosteroid therapy may induce blood pressure fluctuations and fluid/sodium retention, thereby further precipitating

or exacerbating HFpEF [12, 20]. Comparison of treatment interventions between the two subgroups showed no significant differences in the use of invasive mechanical ventilation, prone position ventilation, CRRT, or human immunoglobulin, suggesting that the overall disease severity was comparable between patients

regardless of HF subtype. However, the proportion of patients receiving corticosteroids was significantly higher in the HFpEF group than that in the HFr+mEF group, which may be related to clinicians' greater caution with medication in patients with HFpEF due to their higher sensitivity to hemodynamic changes, or alternatively, may reflect a tendency to reserve corticosteroids for patients perceived as having a stronger inflammatory component, such as those with HFpEF.

Multivariate logistic regression identified heart rate, NLR, and platelet count as independent influencing factors for HF in critically ill COVID-19 patients. Tachycardia is an important compensatory mechanism in HF, but it also indicates a decline in cardiac functional reserve [21]. In critically ill COVID-19 patients, fever, hypoxemia, anxiety, and cytokine storm can all lead to tachycardia. The mechanistic pathway by which tachycardia contributes to HF is well-established: persistent tachycardia increases myocardial oxygen consumption, shortens diastolic coronary perfusion time, during which most coronary blood flow occurs, and thereby exacerbates myocardial ischemia and injury, creating a vicious cycle of worsening cardiac function [22, 23]. In the specific context of COVID-19, tachycardia may also reflect virus-induced autonomic dysfunction, as SARS-CoV-2 can affect central cardiovascular regulatory centers via systemic inflammation or neuroinvasion. This underscores the importance of heart rate monitoring in ICU settings, although beta-blocker use must be carefully balanced against the risk of hypotension in critically ill patients. NLR, as an important indicator reflecting the degree of systemic inflammatory response, is linked to poor prognosis in various diseases [24, 25]. For example, Sandor-Keri et al. [26] pointed out that NLR has been established as an independent prognostic predictor in acute coronary syndrome and systemic

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Table 5. Univariate analysis of factors associated with heart failure in critically ill COVID-19 patients

	Univariate analysis				
	β	S.E	Z	P	OR (95% CI)
Age (per 1 year)	0.042	0.012	3.351	<0.001	1.042 (1.017-1.068)
Heart rate (per 1 bpm)	0.058	0.012	4.868	<0.001	1.060 (1.036-1.085)
NLR (per 1 unit)	1.898	0.249	7.629	<0.001	6.675 (4.099-10.871)
Platelet count (per $1 \times 10^9/L$)	-0.057	0.007	-7.826	<0.001	0.945 (0.931-0.958)

Notes: COVID-19: Corona Virus Disease 2019; NLR: neutrophil-to-lymphocyte ratio.

Table 6. Multivariate logistic regression analysis of factors associated with heart failure in critically ill COVID-19 patients

	Multivariate analysis				
	β	S.E	Z	P	OR (95% CI)
Age (per 1 year)	0.033	0.02	1.643	0.1	1.034 (0.994-1.075)
Heart rate (per 1 bpm)	0.051	0.02	2.59	0.01	1.052 (1.012-1.093)
NLR (per 1 unit)	1.579	0.283	5.579	<0.001	4.848 (2.784-8.442)
Platelet count (per $1 \times 10^9/L$)	-0.049	0.009	-5.714	<0.001	0.952 (0.936-0.968)

Note: All continuous variables were entered as original numerical values without categorization; COVID-19: Corona Virus Disease 2019; NLR: neutrophil-to-lymphocyte ratio.

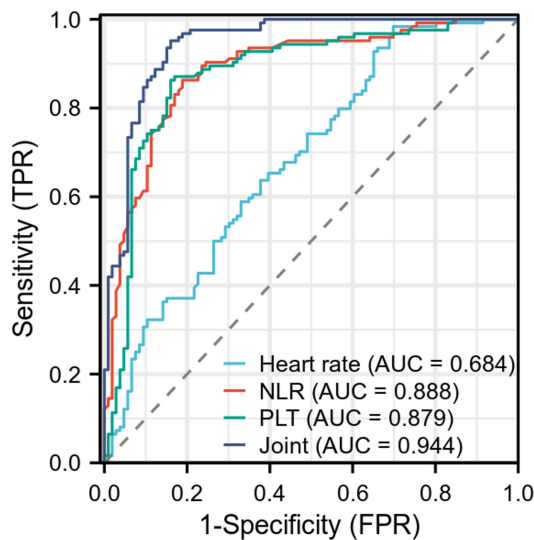


Figure 2. ROC curves of heart rate, NLR, platelet count, and the combined model for predicting heart failure in critically ill COVID-19 patients. Notes: AUC, area under the curve; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet.

inflammatory diseases, and may also be applicable for assessing disease severity in COVID-19 infection. The results of this study show a significant positive correlation between the intensity of the inflammatory response measured by NLR and the risk of developing HF. One of the core pathological mechanisms of COVID-19 is the virus-induced hyperinflammatory

response. Inflammatory cytokines can directly inhibit myocardial contractile function, induce cardiomyocyte apoptosis, and promote microthrombus formation through activation of the coagulation system [27, 28]. Therefore, NLR is not only an inflammatory marker but may also directly participate in the pathophysiology of HF. Dynamic monitoring of NLR changes may contribute to the early identification of high-risk HF cases. Platelet count was identified as an independent influencing factor in this study, which may be related to the following mechanisms. First, severe COVID-19 is often accompanied by consumptive thrombocytopenia, and a decrease in platelet count is a reflection of disease severity [29]. Second, thrombocytopenia is strongly linked to disseminated intravascular coagulation and microthrombus formation, which are important triggers of HF [30]. The concurrent elevation of NLR and reduction in platelet count observed in our HF group reflects the immunothrombosis phenomenon characteristic of severe COVID-19, wherein inflammation and coagulation are mutually reinforcing. This mechanistic interplay provides a biological rationale for why the combined model of these markers yielded superior predictive performance compared with any single indicator. These findings from the multivariate regression analysis are similar to previous studies. For instance, Gu et al. [31]

Table 7. Predictive efficacy of heart rate, NLR, platelet count, and the combined model for heart failure in critically ill COVID-19 patients

Predictors	cut-off	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
Heart rate	105.1	98.39	30.19	66.96	0.684
NLR	4.235	86.29	81.13	83.91	0.888
PLT	191.75	86.29	83.96	85.22	0.879
Joint	0.6144	95.16	83.96	90.00	0.944

Notes: COVID-19: Corona Virus Disease 2019; NLR: neutrophil-to-lymphocyte ratio; PLT: platelet count; AUC: area under the curve. Sensitivity, specificity, and accuracy for the combined model were calculated based on **Table 8**: TP=101, FP=20, FN=5, TN=104 (actual HF, n=106; actual non-HF, n=124). Sensitivity = TP/(TP+FN) = 101/(101+5)=95.16%; Specificity = TN/(TN+FP) = 104/(104+20)=83.96%; Accuracy = (TP+TN)/Total = (101+104)/230=90.00%.

Table 8. Confusion matrix of the combined prediction model for HF in critically ill COVID-19 patients

	Predicted HF	Predicted Non-HF	Total
Actual HF	101	5	106
Actual Non-HF	20	104	124
Total	121	109	230

Notes: Calculations are based on the case numbers in this table. For formulas, see **Table 7** footnote. COVID-19: Corona Virus Disease 2019; HF: heart failure.

reported that significant platelet dysfunction and endothelial injury existed in COVID-19 patients, and thrombocytopenia was closely linked to adverse cardiovascular outcomes. Similarly, a review by Ramadan et al. [32] also indicated that cardiac complications (including HF) in COVID-19 patients were directly associated with systemic hyperinflammation and a hypercoagulable state.

This study further assessed the predictive value of the above indicators for HF using ROC curves. According to the results, heart rate, NLR, and platelet count each had certain predictive value when used alone, with NLR and platelet count performing well, achieving AUCs of 0.888 and 0.879, respectively. The predictive efficacy of heart rate was relatively lower (AUC=0.684), which may be related to its susceptibility to various confounding factors. Notably, the combined model of the three indicators achieved an AUC of 0.944 (sensitivity: 95.16%; specificity: 83.96%; accuracy: 90.00%), outperforming any single indicator. This finding suggests that the combined model can more comprehensively reflect the patient's hemodynamic status, inflammatory level, and coagulation function, thereby enabling accurate assessment of HF risk.

However, this study has several limitations. First, the single-center retrospective study may be subject to selection bias, and the generalizability of the conclusions needs to be validated by multicenter prospective research. Second, the sample size of patients with HFr+mEF in the HF group was small (only 12 cases), and cardiac-specific biomarkers such as brain natriuretic peptide were not included, which may affect the diagnostic accuracy of HF and the stability of the subgroup analysis results. Third, this study did not conduct long-term follow-up for prognosis, nor did it analyze the impact of corticosteroids or anticoagulant drugs on the prognosis of HF, precluding an analysis of the effects of various risk factors and treatment regimens on hard endpoints

such as mortality. Fourth, the optimal cutoff values identified by ROC analysis require external validation in independent cohorts. Finally, the findings are based on patients treated during a specific period and may not be fully applicable to other settings or future SARS-CoV-2 variants.

In conclusion, the incidence of HF in critically ill COVID-19 patients is high, with HFpEF being the predominant subtype. Heart rate, NLR, and platelet count are independent factors associated with the development of HF, and the combined model of these three indicators demonstrates good predictive efficacy for HF.

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Disclosure of conflict of interest

None.

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