Article

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From Inflammatory Burden to Metabolic Imbalance: A Predictive Analysis of the Impact of Inflammation and Metabolic Indicators on Prognosis in Patients With Heart Failure—A Single-Center Retrospective Study

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Background: Prognostic heterogeneity is significant in patients with heart failure (HF), and traditional risk assessment remains limited. Chronic inflammation activation and metabolic homeostasis imbalance are considered core pathophysiological processes driving HF progression, but evidence for predicting HF prognosis based on the combined use of conventional inflammatory and metabolic markers is still insufficient. This study aimed to evaluate the association of combined inflammatory and metabolic markers with short-term adverse cardiovascular events in HF patients.

Methods: This was a single-center retrospective cohort study that consecutively enrolled 350 patients with heart failure hospitalized between July 2021 and July 2024. Baseline demographic, clinical history, and laboratory parameters were collected. Neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), systemic immune inflammation index (SII), and triglyceride-glucose index (TyG) were calculated. All patients were followed up for 12 months. The primary endpoint was cardiac death or serious events related to the progression of heart failure. Univariate and multivariate logistic regression analyses were used to screen for independent risk factors, and a combined risk model was constructed. The discriminative ability was evaluated using Receiver Operating Characteristic (ROC) curves.

Results: Multivariate logistic regression analysis showed that smoking history (odds ratio (OR) = 2.96, 95% confidence intervals (95% CI): 1.51–5.79), diabetes history (OR = 4.56, 95% CI: 2.35–8.84), elevated NLR (OR = 1.23, 95% CI: 1.08–1.41), elevated C-reactive protein (CRP) (OR = 1.12, 95% CI: 1.04–1.19), and elevated TyG index (OR = 2.57, 95% CI: 1.43–4.61) were independent risk factors for endpoint events in HF patients. The combined risk model constructed from these five factors showed good discriminative ability, with an area under the ROC curve (AUC) of 0.79 (95% CI: 0.72–0.85).

Conclusions: In patients with heart failure, NLR and CRP, reflecting systemic inflammatory burden, and the TyG index, a marker of insulin resistance/metabolic imbalance, are important independent prognostic factors in addition to traditional risk factors such as smoking and diabetes. An assessment strategy integrating inflammatory and metabolic markers holds promise as a simple and practical clinical tool for risk stratification and individualized management of HF patients.

Keywords: heart failure; insulin resistance; inflammatory markers; metabolic markers

Introduction

Heart failure (HF) is a common clinical manifestation of the end stage of various cardiovascular diseases. It is characterized by structural or functional impairment of the heart, resulting in insufficient cardiac output to meet the body's metabolic needs and accompanied by complex neuroendocrine and immune regulatory disorders [1]. With the current aging of the population and the improvement of cardiovascular disease survival rate, the global disease burden of HF continues to rise. Epidemiological data show that the number of people with HF worldwide has exceeded 64 million, and will continue to rise in the coming decades [2]. Patients with HF not only have a high risk of all-cause mortality and rehospitalization, but also impose a long-term and heavy burden on the medical system and socio-economic system, which has become one of the key issues that urgently need to be addressed in the field of cardiovascular disease prevention and treatment [3]. Traditional risk assessment relies on indicators such as clinical classification, left ventricular ejection fraction (LVEF) and symptom grading. These factors still have some obvious limitations in explaining the heterogeneity of outcomes among individuals [4,5]. In recent years, an increasing number of studies have suggested that the occurrence and progression of HF is not simply a hemodynamic abnormality, but a systemic disease process driven by the interaction of chronic inflammation activation and metabolic homeostasis imbalance [6–8].

Against this backdrop, inflammation and metabolic-related biological markers are increasingly recognized as key factors linking cardiac dysfunction to poor prognosis.

Chronic low-grade inflammation is considered to be one of the core links in the pathophysiology of HF [9]. Whether ischemic or non-ischemic HF, persistent inflammatory activation can aggravate myocardial damage through multiple pathways, including inducing myocardial cell apoptosis, promoting myocardial interstitial fibrosis and destroying vascular endothelial function [9,10]. Previous studies have found that elevated levels of inflammatory markers such as C-reactive protein (CRP) are closely related to the risk of HF, disease severity and mortality [11,12]. At the same time, the dynamic changes in peripheral blood cell components, such as the imbalance of the proportions of neutrophils, lymphocytes, monocytes and platelets, are considered to reflect the overall burden of the body's inflammatory-immune status and show potential value in the risk stratification of various cardiovascular diseases [13]. Inflammation ratio indicators derived from routine blood tests have gradually become a focus of attention in cardiovascular prognosis research due to their ease of acquisition and good reproducibility [14]. In addition to inflammatory response, metabolic abnormalities also play an important role in the occurrence and progression of HF. Glucose metabolism disorders, lipid metabolism abnormalities, and elevated uric acid levels are common in patients with HF and have been shown to be closely associated with adverse outcomes [15,16]. In some patients with diabetes, not only is blood glucose level an important risk factor for HF, but it can also accelerate myocardial remodeling through mechanisms such as insulin resistance, oxidative stress, and microvascular dysfunction [17]. It is noteworthy that even in patients without a confirmed diagnosis of diabetes, underlying insulin resistance may adversely affect cardiac function [18]. The triglyceride-glucose (TyG) index and its derivatives, proposed in recent years, are considered to be able to reflect insulin resistance levels relatively stably and have shown good prognostic value in a variety of cardiovascular diseases [19].

More importantly, inflammation and metabolic abnormalities do not occur in isolation but instead form a vicious cycle that mutually exacerbates the pathological process of HF [20]. On the one hand, chronic inflammation can exacerbate metabolic imbalance by interfering with insulin signaling pathways and lipid metabolism; on the other hand, metabolic disorders can further activate chronic inflammatory responses in patients, amplifying myocardial damage and functional deterioration. This persistent imbalance may be an important biological basis for the progression of HF and poor prognosis. Therefore, a comprehensive assessment of inflammatory burden and metabolic status from a holistic perspective is expected to provide new ideas for risk stratification and individualized management of HF. However, most current studies focus on individual inflammatory or metabolic parameters, and the integrated analysis combining these domains remains relatively insufficient. The prognostic value of the combined application of different indicators and their potential in clinical application still lack sufficient evidence.

Based on this, this study adopted a single-center retrospective study design to systematically evaluate inflammation and metabolic-related indicators in HF patients and explore their relationship with clinical prognosis. This study aimed to further improve the risk assessment system for HF patients and provide a basis for early clinical identification of high-risk groups and the development of more refined management strategies.

Methods

Patients

This is a single-center, retrospective cohort study. Patients with heart failure who were hospitalized at Xianju People's Hospital between July 2021 and July 2024 were consecutively included. Clinical data for all subjects were obtained from the hospital's electronic medical record system. The diagnosis of heart failure was based on current domestic and international guidelines, combined with a comprehensive assessment of the patient's clinical symptoms and/or signs, elevated natriuretic peptide levels, and objective evidence of cardiac structural or functional abnormalities. Study subjects included patients with acute decompensated heart failure and hospitalized patients with chronic heart failure. Even if a patient's symptoms improved during hospitalization, they were still included if they were clearly diagnosed with heart failure upon admission.

Inclusion criteria were: (1) age $\geq$18 years; (2) meeting the clinical diagnostic criteria for heart failure; (3) completing the laboratory tests required for the study, such as fasting blood glucose, glycated hemoglobin, lipid profile, uric acid, complete blood count, and C-reactive protein, during hospitalization; (4) having complete baseline clinical data; and (5) having clear follow-up outcome information. Exclusion criteria were: (1) patients with active malignant tumors, severe infections, or systemic inflammatory diseases; (2) patients with severe hematologic or autoimmune diseases; (3) patients with missing key laboratory indicators; and (4) patients with incomplete follow-up data or lost to follow-up. All patients were followed up for 12 months from the date of initial admission and diagnosis of heart failure. Follow-up methods included outpatient follow-up, inpatient medical record tracking, and telephone follow-up. The primary outcome of the study was defined as a composite of adverse cardiovascular events (CVEs), including cardiac death or rehospitalization due to worsening heart failure. If a patient dies during the follow-up period, they are directly assigned to the CVE group (event group), with the time of death as the endpoint; patients who do not develop CVE are followed up until the end of the 12-month follow-up period (non-event group).

This study was approved by the Ethics Committee of Xianju People's Hospital (Ethics Approval No.: 2026-06) and carried out following the principles expressed in the Declaration of Helsinki. Given the retrospective design of this study, which relied solely on previous medical records and did not involve any interventions, the Ethics Committee has approved a waiver of written informed consent. All data were anonymized during the analysis to ensure patient confidentiality.

Collection of Clinical Biomarkers

All clinical and laboratory data in this study were retrospectively extracted from the hospital's electronic medical record system. Baseline biological indicators were defined as routine clinical laboratory test results completed within 24 hours of the patient's first admission. All relevant examinations were routine procedures performed during clinical diagnosis and treatment, and no intervention was made to the patient's treatment process or testing procedures during the study.

Inflammation-related markers included CRP and peripheral blood routine parameters such as neutrophil count, lymphocyte count, monocyte count, and platelet count, all derived from routine laboratory test records during admission. Based on these blood cell parameters, further derived inflammatory markers were calculated, including the Neutrophil/lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte/lymphocyte ratio (MLR), to comprehensively reflect the body's inflammatory burden and immune status.

Metabolic indicators were also obtained retrospectively, including fasting blood glucose, glycated hemoglobin, lipid profile indicators (total cholesterol, LDL cholesterol), and serum uric acid levels. All of these indicators were derived from the results of routine biochemical tests performed for the first time during the patient's hospitalization. Based on these results, the insulin resistance-related index, the TyG, was calculated using the following formula:

TyG = ln [fasting triglycerides (mg/dL) $\times$ fasting blood glucose (mg/dL) / 2].

All laboratory indicators were analyzed based on the initial admission results to minimize the potential impact of interventions during treatment on relevant parameters, thereby providing a more accurate reflection of the patient's underlying inflammation and metabolic status.

Data Processing and Analysis

All statistical analyses were conducted in accordance with SPSS 24.0 (IBM Corp., Armonk, NY, USA). The results were completed using R 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). This study employed a complete case analysis approach; only patients with complete baseline clinical data, laboratory indicators, and 12-month follow-up information were included. Cases with missing values for variables of interest were excluded to ensure data integrity and minimize potential bias associated with imputation methods. First, normality was tested for continuous variables using the Kolmogorov–Smirnov method to assess data distribution. Variables conforming to a normal distribution were expressed as mean $\pm$ standard deviation ($\bar{x} \pm$ SD), and differences between groups were compared using an independent samples *t*-test. Variables not conforming to a normal distribution were expressed as median and interquartile range [M(Q_1, Q_3)], and the Mann–Whitney U test was used. Categorical variables were expressed as numbers and percentages, and the χ^2 test was used. To explore the factors associated with adverse cardiovascular events in patients with heart failure, univariate logistic regression was first performed. Variables with $p < 0.05$ in univariate analysis were subsequently entered into a multivariate logistic regression analysis. To mitigate potential multicollinearity in the subsequent multivariable analysis, composite inflammatory and metabolic indices were used in place of their constituent components. Specifically, NLR, PLR, MLR, and systemic immune inflammation index (SII)—which integrate different immune cell populations—were included rather than individual cell counts (neutrophils, lymphocytes, monocytes, platelets). Similarly, the TyG index was used as a surrogate marker of insulin resistance instead of including fasting glucose and triglycerides separately. This approach ensures that the multivariable model does not simultaneously contain highly correlated variables that could distort coefficient estimates and inflate standard errors. Following these adjustments, multicollinearity among the independent variables was assessed using the variance inflation factor (VIF), with values greater than 5 considered indicative of significant multicollinearity. Results were reported as odds ratios (OR) and 95% confidence intervals (95% CI).

Results

Baseline Data Analysis

This study ultimately included 350 patients with heart failure, who were divided into two groups based on their follow-up status: a non-event group (n = 292, 83.43%) and an event group (n = 58, 16.57%). Among inflammatory markers, the event group showed significantly higher neutrophil count and monocyte count than the non-event group, and also higher CRP levels ($p < 0.05$). Regarding metabolic markers, the event group had significantly higher fasting blood glucose and TyG levels than the non-event group ($p < 0.05$). Furthermore, the event group had a significantly higher proportion of patients with a history of smoking ($p < 0.05$) and a significantly higher proportion of patients with diabetes ($p < 0.001$) than the non-event group. Detailed baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics of participants.

Variables	Non-event group (n = 292)	Event group (n = 58)	Statistic	*p*
Age (years)	58.30 ± 10.75	61.28 ± 13.03	$t = -1.64$	0.106
BMI (kg/m^2)	25.20 ± 2.33	25.13 ± 2.01	$t = 0.19$	0.852
UA (umol /L)	400.46 ± 54.96	405.74 ± 56.65	$t = -0.67$	0.506
Neutrophils (10^9/L)	4.36 ± 1.24	5.04 ± 1.46	$t = -3.66$	<0.001
Lymphocytes (10^9/L)	1.51 ± 0.53	1.52 ± 0.65	$t = -0.09$	0.926
Monocytes (10^9/L)	0.41 ± 0.09	0.45 ± 0.11	$t = -2.39$	0.020
Platelets (10^9/L)	164.51 ± 52.81	154.46 ± 54.84	$t = 1.32$	0.189
Total cholesterol (mmol/L)	3.97 ± 0.96	4.09 ± 1.09	$t = -0.85$	0.394
LDL (mmol/L)	2.21 ± 0.76	2.34 ± 0.93	$t = -1.01$	0.314
Triglycerides (mg/dL)	124.84 ± 48.99	134.17 ± 54.33	$t = -1.30$	0.194
Blood glucose level (mg/dL)	89.18 (64.76, 116.24)	114.18 (84.19, 139.61)	Z = –3.97	<0.001
CRP (mg/L)	5.20 (2.56, 7.80)	7.06 (2.98, 10.83)	Z = –2.19	0.029
HbA1C	5.97 (5.36, 6.56)	6.17 (5.45, 6.97)	Z = –1.44	0.151
SBP (mmHg)	139.24 ± 21.85	136.09 ± 20.03	$t = 1.01$	0.311
DBP (mmHg)	86.49 ± 18.24	86.67 ± 19.76	$t = -0.07$	0.945
Average heart rate	86.18 (75.86, 99.91)	88.18 (77.18, 102.37)	Z = –1.09	0.274
NLR	2.96 (2.02, 4.11)	3.25 (2.25, 5.41)	Z = –1.80	0.073
PLR	106.23 (77.56, 153.09)	93.01 (74.98, 148.97)	Z = –0.96	0.338
MLR	0.28 (0.21, 0.37)	0.33 (0.21, 0.45)	Z = –1.31	0.191
SII	465.34 (297.28, 702.12)	473.79 (317.21, 807.20)	Z = –0.85	0.396
TyG	8.54 (8.15, 8.92)	8.84 (8.27, 9.19)	Z = –2.95	0.003
Gender, n (%)			$\chi^2 = 0.11$	0.736
Female	99 (33.90)	21 (36.21)		
Male	193 (66.10)	37 (63.79)		
Smoking, n (%)			$\chi^2 = 4.18$	0.041
No	215 (73.63)	35 (60.34)		
Yes	77 (26.37)	23 (39.66)		
Drinking, n (%)			$\chi^2 = 0.35$	0.554
No	248 (84.93)	51 (87.93)		
Yes	44 (15.07)	7 (12.07)		
Hypertension, n (%)			$\chi^2 = 1.27$	0.259
No	124 (42.47)	20 (34.48)		
Yes	168 (57.53)	38 (65.52)		
Diabetes, n (%)			$\chi^2 = 20.41$	<0.001
No	233 (79.79)	30 (51.72)		
Yes	59 (20.21)	28 (48.28)		
Dyslipidemia, n (%)			$\chi^2 = 2.05$	0.152
No	261 (89.38)	48 (82.76)		
Yes	31 (10.62)	10 (17.24)		
Chronic kidney disease, n (%)			$\chi^2 = 1.66$	0.198
No	238 (81.51)	43 (74.14)		
Yes	54 (18.49)	15 (25.86)		
Atrial fibrillation, n (%)			$\chi^2 = 2.23$	0.136
No	176 (60.27)	41 (70.69)		
Yes	116 (39.73)	17 (29.31)		
Ischemic heart disease, n (%)			$\chi^2 = 0.12$	0.730
No	128 (43.84)	24 (41.38)		
Yes	164 (56.16)	34 (58.62)		
NYHA, n (%)			$\chi^2 = 0.12$	0.942
II	44 (15.07)	9 (15.52)		
III	133 (45.55)	25 (43.10)		
IV	115 (39.38)	24 (41.38)		

CRP, C-reactive protein; NLR, neutrophil/lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte/lymphocyte ratio; SII, systemic immune inflammation index; TyG, triglyceride-glucose index.

Results of Univariate Logistic Regression Analysis

To preliminarily screen factors associated with poor prognosis in heart failure, univariate logistic regression analysis was performed on various indicators. The analysis included comprehensive inflammatory markers (NLR, PLR, MLR, SII) and metabolic markers (TyG index), along with traditional clinical variables. The results are shown in Table 2. Smoking and diabetes were significant risk factors for the occurrence of endpoint events in patients. Elevated NLR, MLR, and CRP levels were significantly associated with increased event risk. Regarding metabolic indicators, elevated TyG levels were also associated with increased risk ($p < 0.05$).

Results of Multivariate Logistic Regression Analysis

To control for potential confounding factors and identify independent risk factors, variables with $p < 0.05$ in the univariate analysis were included in a multivariate logistic regression analysis. The final model was constructed using stepwise regression.

The final model (see Table 3) included five independent risk factors: smoking history (OR = 2.96, 95% CI: 1.51–5.79, $p = 0.002$), history of diabetes (OR = 4.56, 95% CI: 2.35–8.84, $p < 0.001$), elevated NLR (OR = 1.23, 95% CI: 1.08–1.41, $p = 0.002$), elevated CRP (OR = 1.12, 95% CI: 1.04–1.19, $p = 0.002$), and elevated TyG index (OR = 2.57, 95% CI: 1.43–4.61, $p = 0.002$).

ROC Curve Analysis and Model Discriminative Ability

To evaluate the discriminative ability of the identified risk factors for poor prognosis in patients with heart failure, a risk score model was constructed based on the multivariate logistic regression coefficients, and Receiver Operating Characteristic (ROC) curves were plotted (Fig. 1). The analysis showed that the area under the ROC curve (AUC) of this combined model was 0.79 (95% CI: 0.72–0.85). The optimal cutoff value was 0.19, at which point the model achieved a sensitivity of 72% and a specificity of 78%. To further evaluate the discriminative ability of individual risk factors identified in the multivariate analysis, their respective AUC values, sensitivity, and specificity were calculated. The results are summarized in Table 4. The combined model integrating all five factors achieved an AUC of 0.79, outperforming any individual indicator, suggesting that integrating inflammation into metabolic markers provides incremental value for risk stratification in patients with heart failure.

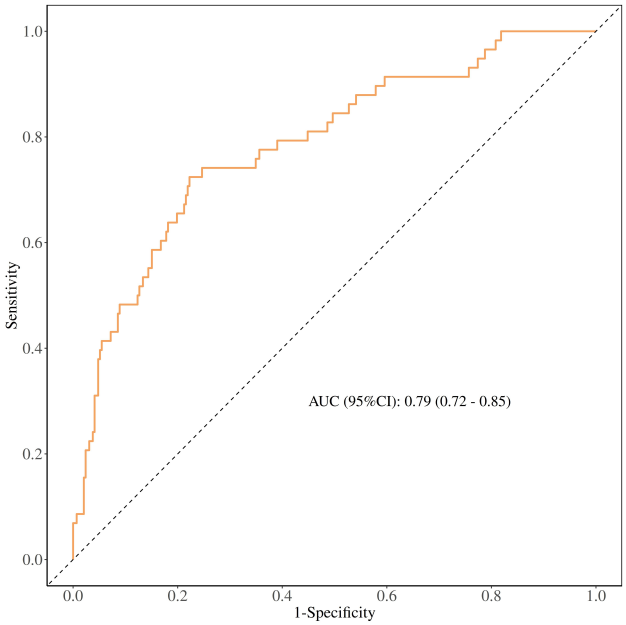

Fig. 1. Receiver operating characteristic curve.

Discussion

As the end stage of many cardiovascular diseases, heart failure is not simply driven by hemodynamic abnormalities, but is a complex systemic pathological process involving inflammatory activation, immune imbalance and metabolic remodeling [21]. Traditional risk assessment models based on left ventricular ejection fraction, NYHA classification and clinical symptoms have limitations in explaining this prognostic heterogeneity. Therefore, finding simple, stable and reproducible biomarkers to achieve early risk identification in patients with heart failure has become an important focus of current clinical research. This study systematically evaluated the predictive value of inflammation- and metabolic-related indicators for short-term adverse cardiovascular events based on a single-center real-world cohort of hospitalized heart failure patients. The results showed that during the 12-month follow-up period, smoking history, diabetes history, elevated NLR, CRP and TyG index were all significantly associated with adverse cardiovascular events in patients with heart failure, and remained independent risk factors after multivariate adjustment. The combined model incorporating the above indicators demonstrated good discriminative ability, with an area under the ROC curve of 0.79, suggesting that prognosis assessment of heart failure from an integrated perspective of inflammatory burden and metabolic imbalance holds high clinical utility.

The role of inflammation in the pathophysiology of heart failure has been widely confirmed [11]. In this study, NLR and CRP both showed independent associations with prognosis, further supporting the association of chronic low-grade inflammation with adverse outcomes. NLR integrates two opposing immune pathways: neutrophils release pro-inflammatory cytokines (e.g., IL-1β and TNF-α) that impair myocardial contractility and promote fibrosis, while lymphocytes play a protective role in modulating inflammation and facilitating tissue repair [22]. Consequently, an elevated NLR reflects both exaggerated in-

Table 2. Results of logistic regression analysis.

Variables	β	SE	Z	p	OR (95% CI)
Gender					
Female					1.00 (Reference)
Male	–0.10	0.30	–0.34	0.736	0.90 (0.50∼1.63)
Smoking					
No					1.00 (Reference)
Yes	0.61	0.30	2.03	0.043	1.83 (1.02∼3.30)
Drinking					
No					1.00 (Reference)
Yes	–0.26	0.43	–0.59	0.555	0.77 (0.33∼1.81)
Hypertension					
No					1.00 (Reference)
Yes	0.34	0.30	1.13	0.261	1.40 (0.78∼2.53)
Diabetes					
No					1.00 (Reference)
Yes	1.30	0.30	4.34	<0.001	3.69 (2.05∼6.64)
Dyslipidemia					
No					1.00 (Reference)
Yes	0.56	0.40	1.42	0.156	1.75 (0.81∼3.81)
Chronic kidney disease					
No					1.00 (Reference)
Yes	0.43	0.34	1.28	0.200	1.54 (0.80∼2.97)
Atrial fibrillation					
No					1.00 (Reference)
Yes	–0.46	0.31	–1.48	0.138	0.63 (0.34∼1.16)
Ischemic heart disease					
No					1.00 (Reference)
Yes	0.10	0.29	0.34	0.730	1.11 (0.62∼1.96)
NYHA					
II					1.00 (Reference)
III	–0.08	0.43	–0.20	0.843	0.92 (0.40∼2.12)
IV	0.02	0.43	0.05	0.963	1.02 (0.44∼2.37)
Age	0.02	0.01	1.85	0.065	1.02 (1.00∼1.05)
BMI	–0.01	0.06	–0.19	0.852	0.99 (0.87∼1.12)
UA	0.00	0.00	0.67	0.505	1.00 (1.00∼1.01)
NLR	0.17	0.06	2.72	0.006	1.18 (1.05∼1.33)
PLR	0.00	0.00	0.34	0.731	1.00 (1.00∼1.00)
MLR	1.46	0.69	2.12	0.034	4.30 (1.12∼16.58)
SII	0.00	0.00	1.65	0.098	1.00 (1.00∼1.00)
CRP	0.11	0.03	3.38	<0.001	1.12 (1.05∼1.19)
Total cholesterol	0.13	0.15	0.85	0.393	1.13 (0.85∼1.51)
TyG	0.91	0.28	3.30	<0.001	2.49 (1.45∼4.27)
LDL	0.21	0.18	1.16	0.245	1.24 (0.86∼1.77)
SBP	–0.01	0.01	–1.01	0.311	0.99 (0.98∼1.01)
DBP	0.00	0.01	0.07	0.945	1.00 (0.99∼1.02)
Average heart rate	0.01	0.01	1.23	0.218	1.01 (0.99∼1.03)
HbA1C	0.27	0.16	1.69	0.092	1.30 (0.96∼1.78)

OR, odds ratios; CI, confidence intervals.

flammation and relative immunosuppression, thereby perpetuating myocardial injury [23]. Similarly, CRP not only mirrors systemic inflammation but also actively contributes to disease progression by activating complement, inducing endothelial dysfunction, and promoting leukocyte infiltration into the myocardium. Previous studies have shown that elevated CRP levels are positively correlated with an increased risk of mortality and hospital readmission rate in

Table 3. Results of multivariate logistic regression analysis.

Variables	β	SE	Z	p	VIF	OR (95% CI)
Smoking						
No						1.00 (Reference)
Yes	1.08	0.34	3.17	0.002	1.026	2.96 (1.51∼5.79)
Diabetes						
No						1.00 (Reference)
Yes	1.52	0.34	4.50	<0.001	1.025	4.56 (2.35∼8.84)
NLR	0.21	0.07	3.03	0.002	2.549	1.23 (1.08∼1.41)
CRP	0.11	0.03	3.14	0.002	1.015	1.12 (1.04∼1.19)
TyG	0.94	0.30	3.16	0.002	1.026	2.57 (1.43∼4.61)

VIF, variance inflation factor.

Table 4. Discriminative ability of individual factors and the combined model for adverse cardiovascular events.

Variables	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Smoking	0.57 (0.50–0.63)	0.74 (0.69–0.79)	0.40 (0.27–0.52)
Diabetes	0.64 (0.57–0.71)	0.80 (0.75–0.84)	0.48 (0.35–0.61)
NLR	0.57 (0.49–0.66)	0.85 (0.81–0.89)	0.31 (0.19–0.43)
CRP	0.59 (0.50–0.68)	0.87 (0.84–0.91)	0.34 (0.22–0.47)
TyG	0.62 (0.54–0.71)	0.64 (0.59–0.70)	0.59 (0.46–0.71)
Combined model	0.79 (0.72–0.85)	0.72 (0.61–0.84)	0.78 (0.73–0.83)

AUC, area under the ROC curve.

patients with heart failure, and the results of this study are consistent with these observations [24,25]. Beyond inflammation, the TyG index—a validated surrogate marker of insulin resistance—captures metabolic dysregulation that drives heart failure progression through multiple interconnected mechanisms: shifting myocardial substrate utilization, enhancing oxidative stress, promoting mitochondrial dysfunction and cardiomyocyte apoptosis, and compromising microvascular perfusion [26–28]. The results of Jia *et al.*'s [29] study suggest that TyG is positively correlated with all-cause mortality in hospitalized patients with heart failure, which is similar to the results of this study. Notably, inflammation and metabolic abnormalities engage in bidirectional crosstalk: pro-inflammatory cytokines induce insulin resistance, while insulin resistance perpetuates a pro-inflammatory state [30]. This vicious cycle may explain why our combined model, incorporating inflammatory (NLR, CRP) and metabolic (TyG) markers, outperformed any individual indicator, as it more comprehensively captures the systemic burden of the disease.

NLR and CRP both showed independent associations with prognosis in the multivariate model, further supporting the significant association of chronic low-grade inflammation in the progression and adverse outcomes of heart failure. As a classic acute-phase reactive protein, elevated CRP levels not only reflect the systemic inflammatory state but are also closely related to the degree of myocardial injury, ventricular remodeling, and endothelial dysfunction. In addition to inflammatory factors, metabolic abnormalities also play an important role in the occurrence and progression of heart failure. The TyG index is considered a reliable surrogate marker of insulin resistance, and its elevation suggests potential disturbances in glucose and lipid metabolism. Insulin resistance can exacerbate the progression of heart failure through various mechanisms, including promoting myocardial energy metabolism disorders, enhancing oxidative stress response, inducing myocardial cell apoptosis, and accelerating ventricular remodeling. This study found that an elevated TyG index is an independent predictor of adverse prognosis in patients with heart failure. This further confirms the prognostic value of TyG in patients with heart failure.

In this study, NLR, CRP, and TyG index were all retained as independent risk factors in the multivariate model. Inflammation and metabolic abnormalities in patients with heart failure did not exist independently, but worked together to exert predictive efficacy. The results suggest that the combined model may capture patients' risk across different pathological dimensions, which could potentially enhance risk stratification. The multivariate model constructed in this study is based on routine clinical examination items, offering the advantages of accessibility, low cost, and high reproducibility. Especially in primary care or resource-limited medical environments, risk stratification can be achieved using hematological and basic biochemical indicators, which helps to identify high-risk patients early and inform follow-up and management strategies.

Interestingly, although the NYHA functional class is a well-established indicator of heart failure severity, no significant difference in NYHA distribution was observed between the event and non-event groups in our study. Several factors may explain this finding. First, NYHA clas-

sification is inherently subjective and may be influenced by physician assessment and patient perception, leading to potential inter-observer variability. Second, in hospitalized patients, NYHA class at admission may reflect acute decompensation rather than baseline disease severity and may inadequately capture the long-term prognostic trajectory. Third, the relatively small sample size and the predominance of patients with NYHA class III–IV in both groups (accounting for approximately 85% of the cohort) may have limited the ability to detect differences across functional classes. Finally, our findings suggest that objective biomarkers such as NLR, CRP, and TyG may provide complementary prognostic information beyond conventional clinical assessment, highlighting the potential value of integrating molecular markers into risk stratification strategies.

Of course, this study also has several limitations. First, this study was a single-center retrospective design with a relatively limited sample size. The study participants were all hospitalized patients with heart failure, which may introduce selection bias. The applicability of these findings to outpatient or community populations requires further validation. Second, inflammatory and metabolic markers were assessed based on a single test result at admission. It should be noted that this cohort included both patients with acute decompensated heart failure and those with chronic heart failure. In acutely decompensated patients, biomarkers measured within 24 hours of admission may partially reflect an acute stress response rather than the underlying chronic inflammatory or metabolic status, potentially introducing clinical heterogeneity. Future studies with larger sample sizes should perform stratified analyses of acute and chronic heart failure populations to clarify whether the prognostic value of these markers differs across these clinical contexts. Third, although confounding factors were controlled as much as possible in the multivariate analysis, the potential influence of unmeasured variables on the results could not be completely ruled out. Furthermore, this study did not conduct further subgroup analyses based on ejection fraction type or etiology of heart failure. Future research could explore different subtypes in larger samples.

Conclusions

In summary, this study demonstrates that integrating inflammation burden (reflected by NLR and CRP) into metabolic imbalance (reflected by the TyG index) provides incremental prognostic value beyond traditional risk factors in patients with heart failure. The combined model, constructed from routine laboratory parameters, offers a simple, inexpensive, and readily accessible tool for early risk stratification, particularly applicable in primary care or resource-limited settings where advanced cardiac assessments may not be available. These findings underscore the importance of viewing heart failure as a systemic disorder driven by the interplay between inflammation and metabolic dysregulation, and suggest that interventions targeting both pathways simultaneously may hold therapeutic benefit. Future multicenter prospective studies are warranted to validate these findings across diverse populations, establish optimal intervention thresholds, and explore whether integrating these biomarkers into clinical decision-making can improve outcomes for patients with heart failure.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

YQL and XQW designed the research study. YQL and HYL performed the research. XQW and LPW analyzed the data. XQW and LPW drafted the article. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Xianju People's Hospital (Ethics Approval No.: 2026-06) and carried out following the principles expressed in the Declaration of Helsinki. Given the retrospective design of this study, which relied solely on previous medical records and did not involve any interventions, the Ethics Committee has approved a waiver of written informed consent. All data were anonymized during the analysis to ensure patient confidentiality.

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Conflict of Interest

The authors declare no conflict of interest.

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