BMC Cardiovascular Disorders

RESEARCH

Open Access

Association between inflammatory burden index and risk of heart failure: evidence from NHANES 2003–2017

Li-Xin Yun[1†], Wan-Zhong Huang[2†], Changjing He[3,4], Yuan Huang[2], Hua-Feng Yang[5], Qiang Su[2*], Da-Zhi Lan[6*] and Yang-Chun Liu[5*]

Abstract

Background Systemic inflammation contributes to the progression of heart failure (HF). This study aims to investigate the association between inflammatory burden index (IBI) and HF risk.

Methods In this cross-sectional study of NHANES 2003–2017, data from 19,856 participants were analyzed, including 652 participants with HF and 19,204 without HF. Participants were categorized into quartiles based on IBI levels (Q1–Q4). The risk of HF across these quartiles was assessed with adjustment for potential confounders and restricted cubic spline analyses were used to evaluate dose-response relationships.

Results Our results show that participants with HF have higher IBI levels compared to those without HF (2.66 ± 0.27 vs. 1.05 ± 0.03, $p < 0.001$). The prevalence of HF increases with higher IBI quartiles: Quartile 1 (1.2%), Quartile 2 (1.33%), Quartile 3 (2.60%), and Quartile 4 (4.37%) ($p < 0.001$). After adjusting for potential confounders, the risk of HF remained elevated across the quartiles: Quartile 2 (odds ratio [OR] = 0.72, 95% confidence interval [CI]: 0.48–1.10), Quartile 3 (OR = 1.06, 95% CI: 0.70–1.61), and Quartile 4 (OR = 1.46, 95% CI: 1.02–2.10) compared to Quartile 1. Restricted cubic spline analysis further confirmed a substantial positive-linear correlation between IBI and HF risk.

Conclusion Higher levels of IBI are related to a high risk of HF, independent of traditional risk factors. These results suggest that IBI could be a useful parameter for identifying individuals at higher risk of HF.

Clinical trial number Not applicable.

Keywords Association, Inflammatory burden index, Risk, Heart failure, NHANES

[†]Li-Xin Yun and Wan-Zhong Huang contributed equally to this work and share co-first authorship.

*Correspondence:
Qiang Su
drsuqiang@163.com
Da-Zhi Lan
15519042@qq.com
Yang-Chun Liu
dryangyang@sr.gxmu.edu.cn
[1]Department of Cardiology, The Second Affiliated Hospital of Guangxi Medical University, No. 166 Daxuedong Road, Nanning, Guangxi 530007, China
[2]Department of Cardiology, Jiangbin Hospital of Guangxi Zhuang Autonomous Region, No. 85 Hedi Road, Nanning, Guangxi 530021, China
[3]Department of Pediatric Surgery, The Affiliated Hospital of Youjiang Medical University for Nationalities, Baise, Guangxi, China
[4]Key Laboratory of Molecular Pathology for Hepatobiliary Diseases of Guangxi, Guangxi Zhuang, Guangxi, China
[5]Cardiothoracic Surgery Intensive Care Unit, The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi 530021, China
[6]School of Public Health and Management, Guangxi University of Chinese Medicine, Nanning, Guangxi 530200, China

Introduction

Heart failure (HF) is a prevalent clinical syndrome resulting from ventricular systolic and/or diastolic dysfunction [1–7]. Despite considerable progress in medical treatments and care, patients with HF continue to experience a poor prognosis and elevated risk of mortality. Estimates indicate that the mortality rate for HF patients varies from 2 to 17% during the initial hospitalization, and then rising to 17–45% within the first year of admission. Moreover, no more than 50% of HF patients survive within five years of follow up [8, 9]. Nowadays, as populations age and the frequency of cardiovascular risk factors, including hypertension [10, 11], diabetes [12], acute coronary syndromes [13] and obesity [14], the incidence of HF is rising, with an estimated 64 million individuals living with HF worldwide [15]. Considering the substantial burden of HF, characterized by elevated mortality and morbidity [16, 17], it is critical to improve risk stratification strategies of HF.

Inflammation plays a pivotal role in HF pathogenesis through mechanisms such as promoting atherosclerosis, vascular dysfunction, and myocardial injury [18–20]. Elevated inflammatory markers (e.g., interleukin (IL)-6, tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP)) have been consistently linked to HF incidence and progression [21, 22]. The inflammatory burden index (IBI) [23, 24] is a novel inflammatory index that combines multiple inflammatory markers, including CRP, neutrophils, and lymphocytes, to provide a more comprehensive information of systemic inflammatory burden. Previous studies have demonstrated that IBI [24–26] is more effective in predicting disease prognosis compared to traditional inflammatory biomarkers. However, the relationship between the IBI and the risk of HF remains unclear. In this study, we utilized data from the National Health and Nutrition Examination Survey (NHANES) 2003–2017 to investigate the relationship between IBI and the risk of HF, in order to provide better understanding of the role of inflammatory and in HF pathophysiology, and identify individuals with a high risk of HF.

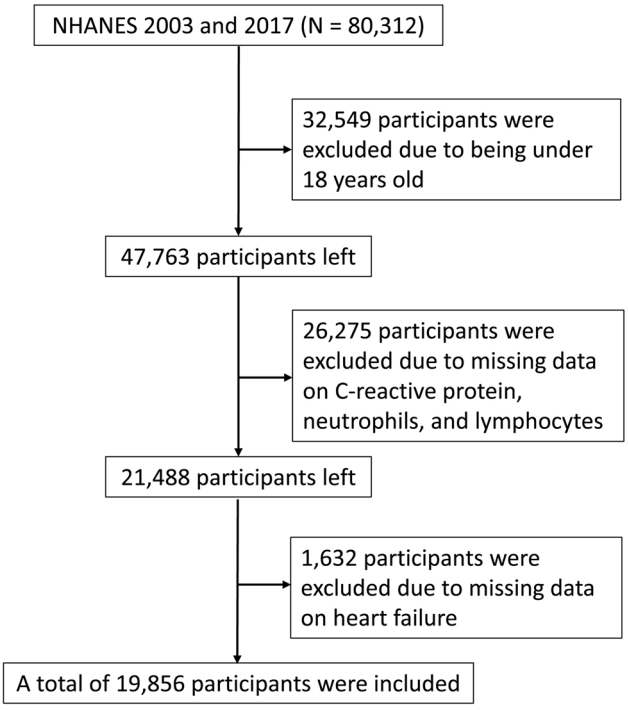

Fig. 1 Flowchart of this study

Methods

Study design and population

This cross-sectional investigation employed data derived from the NHANES gathered between the years 2003 and 2017. Briefly, NHANES (https://www.cdc.gov/nchs/nhanes/) survey utilizes a complex, multistage probability sampling methodology to procure data that accurately represents the civilian, non-institutionalized population of the U.S. For the objectives of this research, the subsequent inclusion criteria must be satisfied: participants are required to be 18 years of age or older and have data of CRP, neutrophils, and lymphocytes. Furthermore, individuals lacking information of HF were excluded from this study. The flowchart of this study is depicted in Fig. 1.

Outcome evaluation

The primary outcome of this study was the presence or absence of HF, determined based on self-reported data documented in the NHANES survey (https://wwwn.cdc.gov/Nchs/Nhanes/2017-2018/P_MCQ.htm#MCQ160b). Participants were asked, "*Has a doctor or other health professional ever told you/SP that you/s/he...had congestive heart failure?*" If the answer was "Yes," the participant was classified as having HF. Conversely, if the answer was "No," the participant was classified as not having HF. Responses of "Refused," "Don't know," or any missing data resulted in exclusion from the study.

IBI calculation

In line with earlier investigations [23, 24], the IBI for each participant was calculated by multiplying the CRP concentration with the neutrophil count, which was then divided by the lymphocyte count. This formulation can be described as IBI = CRP × neutrophil/lymphocyte.

Covariates

In this study, we considered various covariates as potential confounding variables in assessing the association between the IBI and the risk of HF. The covariates included demographic variables (age, gender, race/ethnicity); anthropometric measures (height, weight, body mass index [BMI], calculated as weight in kilograms

divided by height in meters squared, and waist circumference); socioeconomic factors (marital status, and education level); lifestyle factors (smoking status and alcohol use); biochemical and clinical variables (hemoglobin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], total bilirubin, creatinine, uric acid, triglycerides, total cholesterol, high-density lipoprotein [HDL] cholesterol, and low-density lipoprotein [LDL] cholesterol); medical history (hyperlipidemia, hypertension, coronary heart disease, stroke, and diabetes); and medication use (antidiabetic treatment, antihyperlipidemic treatment, and antihypertensive treatment).

Statistical analysis

The statistical analyses were executed utilizing RStudio (version 4.4.1) software. The complex survey design of NHANES was considered through the application of appropriate survey weights, strata, and primary sampling units. Descriptive statistics were employed to summarize the baseline characteristics of the study participants. Continuous variables were expressed as mean accompanied by standard error (SE), whereas categorical variables were delineated in terms of numbers and percentages.

Before the analysis, we employed multiple imputation [23, 27] to address the issue of missing data relating to covariates. Missing values were imputed using chained equations with a total of five imputations. The imputation model was exclusively comprised of covariates, omitting any data related to IBI and HF. Initially, we conducted a comparative analysis of IBI between individuals diagnosed with HF and those who were not. In the subsequent analysis, the participants were stratified into quartiles based on their respective IBI levels: Quartile 1 (< 0.15), Quartile 2 (0.15–0.403), Quartile 3 (0.403–1.072), and Quartile 4 (> 1.072). We then evaluated the risk of HF among these quartiles. Following this, we executed a multivariate logistic regression analysis to adjust for potential confounding factors. Considering the potential impact of demographic and lifestyle factors, biochemical profiles, comorbidities, and medication use on the conclusions of this study, three multivariable models were constructed as follows: model 1 did not adjust for any confounding variables; in model 2, we systematically integrated covariates into the analysis, which encompassed factors such as age, gender, race/ethnicity, height, weight, BMI, marital, education, smoke, alcohol user and waist circumference; in model 3, we further adjusted for additional parameters including hemoglobin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatinine, uric acid, triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol, hyperlipidemia, hypertension, coronary heart disease, stroke, diabetes, antidiabetic treatment, antihyperlipidemic treatment, and antihypertensive treatment, building upon Model 2. Results are presented using odds ratio (OR) and 95% confidence interval (CI).

Furthermore, we employed restricted cubic spline analysis to examine the dose-response relationship between IBI and HF risk, while controlling for the same covariates utilized in the model 1,2 and 3, as described previously. Furthermore, we also conducted subgroup analyses to investigate the correlation between IBI and HF across various subgroups. A two-tailed p-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of patients with and without HF

This investigation encompasses a total of 19,856 participants, with the baseline characteristics delineated in Table 1. Individuals diagnosed with HF ($n = 652$) demonstrate an advanced age and a heightened prevalence of comorbid conditions, such as coronary heart disease and diabetes, when compared with individuals without HF ($n = 19{,}204$). The mean age of HF participants is 66.25 (0.64) years, in contrast to 46.23 (0.27) years for those not experiencing HF. Within the HF cohort, the prevalence rates of diabetes and coronary heart disease were documented at 54.78% and 38.62%, respectively, whereas in the non-HF cohort, its prevalence were 18.51% and 2.57%. The mean BMI in the HF cohort was 31.28 (0.36) kg/m^2, as opposed to 28.48 (0.09) kg/m^2 in the non-HF cohort. Moreover, patients diagnosed with HF exhibited a more pronounced IBI than those without HF [2.66 (0.27) versus 1.05 (0.03), $p < 0.001$].

Baseline characteristics across IBI quartiles

Baseline characteristics stratified by IBI quartiles are delineated in Table 2. As indicated, participants categorized within the highest IBI quartile (Quartile 4) were, on average, more advanced in age and exhibited a greater BMI in comparison to individuals in the lowest quartile (Quartile 1). Furthermore, participants in Quartile 4 demonstrated a heightened prevalence of comorbidities, encompassing hyperlipidemia, coronary heart disease, stroke, and diabetes, relative to individuals in Quartile 1. In addition, individuals in Quartile 4 shows increased concentrations of uric acid, triglycerides, total cholesterol, and LDL cholesterol, while simultaneously displaying reduced levels of hemoglobin, albumin, and HDL cholesterol when compared with those in Quartile 1. Furthermore, Fig. 2 depicts the prevalence of HF throughout the four quartiles, showing a relatively low prevalence in Quartile 1 (1.20%) and a progressive increase in Quartile 2 (1.33%), Quartile 3 (2.60%), and Quartile 4 (4.37%).

Association between IBI and risk of HF

We employed three distinct models to adjust for potential confounding factors and further examine the relationship

Table 1 Baseline characteristics of patients with and without heart failure

Variables	Without heart failure	Heart failure	*P* value
N	19,204	652	
Inflammatory burden index	1.05(0.03)	2.66(0.27)	< 0.0001
Age (years)	46.23(0.27)	66.25(0.64)	< 0.0001
Height (cm)	168.97(0.11)	168.04(0.51)	0.060
Weight (kg)	81.58(0.27)	88.61(1.20)	< 0.0001
Body mass index (kg/m^2)	28.48(0.09)	31.28(0.36)	< 0.0001
Waist circumference (cm)	97.75(0.24)	108.59(0.92)	< 0.0001
Hemoglobin (g/dl)	14.41(0.04)	13.85(0.10)	< 0.0001
Alanine aminotransferase (U/L)	25.99(0.16)	23.57(0.79)	0.005
Aspartate aminotransferase (U/L)	25.76(0.14)	26.17(0.63)	0.530
Total bilirubin (mg/dl)	0.76(0.00)	0.78(0.01)	0.240
Albumin (g/dl)	4.26(0.01)	4.05(0.02)	< 0.0001
Creatinine (mg/dl)	0.89(0.00)	1.24(0.04)	< 0.0001
Uric acid (mg/dl)	5.40(0.02)	6.41(0.09)	< 0.0001
Triglyceride (mg/dl)	232.11(2.10)	219.51(7.11)	0.070
Total cholesterol (mg/dl)	198.56(0.43)	183.20(2.50)	< 0.0001
HDL cholesterol (mg/dl)	53.51(0.21)	49.12(0.72)	< 0.0001
LDL cholesterol (mg/dl)	99.19(0.46)	90.44(2.68)	0.002
Male, N (%)	9245(48.04)	381(56.49)	< 0.001
Race/ethnicity, N (%)			< 0.0001
Mexican American	3706(8.30)	60(3.15)	
Non-Hispanic Black	3675(10.65)	144(13.67)	
Non-Hispanic White	9533(70.91)	396(75.92)	
Other Race	2290(10.15)	52(7.26)	
Marital, N (%)			< 0.0001
Married	10,340(57.95)	309(52.14)	
Never married	3198(16.77)	46(6.37)	
Others	5666(25.28)	297(41.50)	
Education, N (%)			< 0.0001
Below high school	2465(6.31)	129(14.12)	
High school	7639(36.71)	299(46.40)	
Over high school	9100(56.98)	224(39.48)	
Smoke, N (%)			< 0.0001
Active	4280(23.15)	123(19.33)	
Former	4786(24.30)	289(44.66)	
Never	10,138(52.54)	240(36.01)	
Alcohol user, N (%)			< 0.0001
Active	9331(55.53)	124(21.01)	
Former	6257(28.50)	395(60.15)	
Never	3616(15.97)	133(18.84)	
Hyperlipidemia, N (%)	13,993(71.70)	558(86.39)	< 0.0001
Hypertension, N (%)	18,628(97.15)	636(96.73)	0.63
Coronary heart disease, N (%)	600(2.57)	259(38.62)	< 0.0001
Stroke, N (%)	668(2.52)	138(20.50)	< 0.0001
Diabetes, N (%)	4501(18.51)	365(54.78)	< 0.0001
Antidiabetic treatment, N (%)	1732(6.42)	211(30.01)	< 0.0001
Antihyperlipidemic treatment, N (%)	3187(14.58)	348(52.69)	< 0.0001
Antihypertensive treatment, N (%)	5395(23.86)	561(83.70)	< 0.0001

Results are presented as means accompanied by the standard error, or as numbers and percentages, as appropriate

HDL cholesterol: high-density lipoprotein HDL cholesterol; LDL cholesterol: low-density lipoprotein cholesterol

Table 2 Baseline characteristics across IBI quartiles

Variables	Quantile 1	Quantile 2	Quantile 3	Quantile 4	*P* value
N	4984	4939	4969	4964	
Inflammatory burden index	0.08(0.00)	0.26(0.00)	0.66(0.00)	3.78(0.09)	< 0.0001
Age (years)	43.02(0.29)	47.18(0.34)	48.65(0.36)	48.59(0.36)	< 0.0001
Height (cm)	170.17(0.19)	169.62(0.21)	168.53(0.23)	167.07(0.21)	< 0.0001
Weight (kg)	73.13(0.29)	80.37(0.32)	84.65(0.42)	91.07(0.51)	< 0.0001
Body mass index (kg/m^2)	25.11(0.08)	27.77(0.09)	29.67(0.13)	32.57(0.17)	< 0.0001
Waist circumference (cm)	89.10(0.25)	96.76(0.23)	101.29(0.31)	107.07(0.36)	< 0.0001
Hemoglobin (g/dl)	14.48(0.04)	14.57(0.04)	14.43(0.04)	14.05(0.04)	< 0.0001
Alanine aminotransferase (U/L)	24.31(0.25)	26.56(0.26)	27.08(0.32)	26.00(0.40)	< 0.0001
Aspartate aminotransferase (U/L)	25.45(0.21)	25.86(0.19)	26.05(0.22)	25.76(0.33)	0.100
Total bilirubin (mg/dl)	0.83(0.01)	0.78(0.01)	0.74(0.01)	0.68(0.01)	< 0.0001
Albumin (g/dl)	4.40(0.01)	4.32(0.01)	4.22(0.01)	4.04(0.01)	< 0.0001
Creatinine (mg/dl)	0.89(0.00)	0.90(0.00)	0.90(0.01)	0.89(0.01)	0.060
Uric acid (mg/dl)	5.11(0.03)	5.44(0.03)	5.56(0.03)	5.64(0.03)	< 0.0001
Triglyceride (mg/dl)	208.23(2.81)	234.12(3.43)	251.26(4.76)	237.73(3.61)	< 0.0001
Total cholesterol (mg/dl)	191.66(0.67)	199.79(0.81)	203.00(0.89)	199.42(0.81)	< 0.0001
HDL cholesterol (mg/dl)	57.46(0.31)	53.19(0.33)	51.52(0.33)	50.63(0.31)	< 0.0001
LDL cholesterol (mg/dl)	92.96(0.75)	100.44(0.78)	101.91(0.84)	101.74(0.90)	< 0.0001
Male, N (%)	2727(52.91)	2657(53.78)	2309(46.41)	1933(37.85)	< 0.0001
Race/ethnicity, N (%)					< 0.0001
Mexican American	779(7.00)	978(8.44)	996(8.44)	1013(9.08)	
Non-Hispanic Black	1053(10.89)	867(9.62)	927(10.33)	972(12.18)	
Non-Hispanic White	2456(70.07)	2467(71.28)	2504(71.91)	2502(70.95)	
Other Race	696(12.04)	627(10.66)	542(9.31)	477(7.79)	
Marital, N (%)					< 0.0001
Married	2594(57.22)	2776(59.68)	2695(59.17)	2584(54.92)	
Never married	1114(21.00)	748(15.74)	679(13.42)	703(15.21)	
Others	1276(21.78)	1415(24.58)	1595(27.42)	1677(29.87)	
Education, N (%)					< 0.0001
Below high school	520(5.24)	673(6.89)	741(7.16)	660(6.86)	
High school	1805(31.88)	1964(37.13)	2048(38.81)	2121(41.02)	
Over high school	2659(62.89)	2302(55.98)	2180(54.03)	2183(52.11)	
Smoke, N (%)					< 0.0001
Active	1021(19.91)	1073(23.22)	1134(24.11)	1175(25.74)	
Former	1140(23.23)	1271(25.38)	1323(24.54)	1341(26.24)	
Never	2823(56.86)	2595(51.40)	2512(51.35)	2448(48.02)	
Alcohol user, N (%)					< 0.0001
Active	2617(58.80)	2338(53.96)	2273(53.83)	2227(51.52)	
Former	1431(24.79)	1695(30.31)	1753(30.17)	1773(32.53)	
Never	936(16.42)	906(15.73)	943(16.00)	964(15.95)	
Hyperlipidemia, N (%)	3069(60.64)	3675(73.28)	3888(77.79)	3919(78.73)	< 0.0001
Hypertension, N (%)	4805(96.55)	4807(97.52)	4837(97.52)	4815(97.05)	0.110
Coronary heart disease, N (%)	142(2.30)	190(2.85)	258(4.37)	269(4.33)	< 0.0001
Stroke, N (%)	126(1.99)	169(2.20)	230(3.32)	281(4.54)	< 0.0001
Diabetes, N (%)	761(11.47)	1092(16.62)	1319(21.18)	1694(30.43)	< 0.0001
Antidiabetic treatment, N (%)	324(4.44)	422(5.73)	521(7.09)	676(11.42)	< 0.0001
Antihyperlipidemic treatment, N (%)	723(12.21)	940(16.28)	995(17.50)	877(16.32)	< 0.0001
Antihypertensive treatment, N (%)	998(16.03)	1407(23.93)	1655(28.41)	1896(34.86)	< 0.0001

Results are presented as means accompanied by the standard error, or as numbers and percentages, as appropriate

Quartile 1 (IBI < 0.15), Quartile 2 (IBI: 0.15–0.403), Quartile 3 (IBI: 0.403–1.072), and Quartile 4 (IBI > 1.072)

IBI: inflammatory burden index; HDL cholesterol: high-density lipoprotein HDL cholesterol; LDL cholesterol: low-density lipoprotein cholesterol

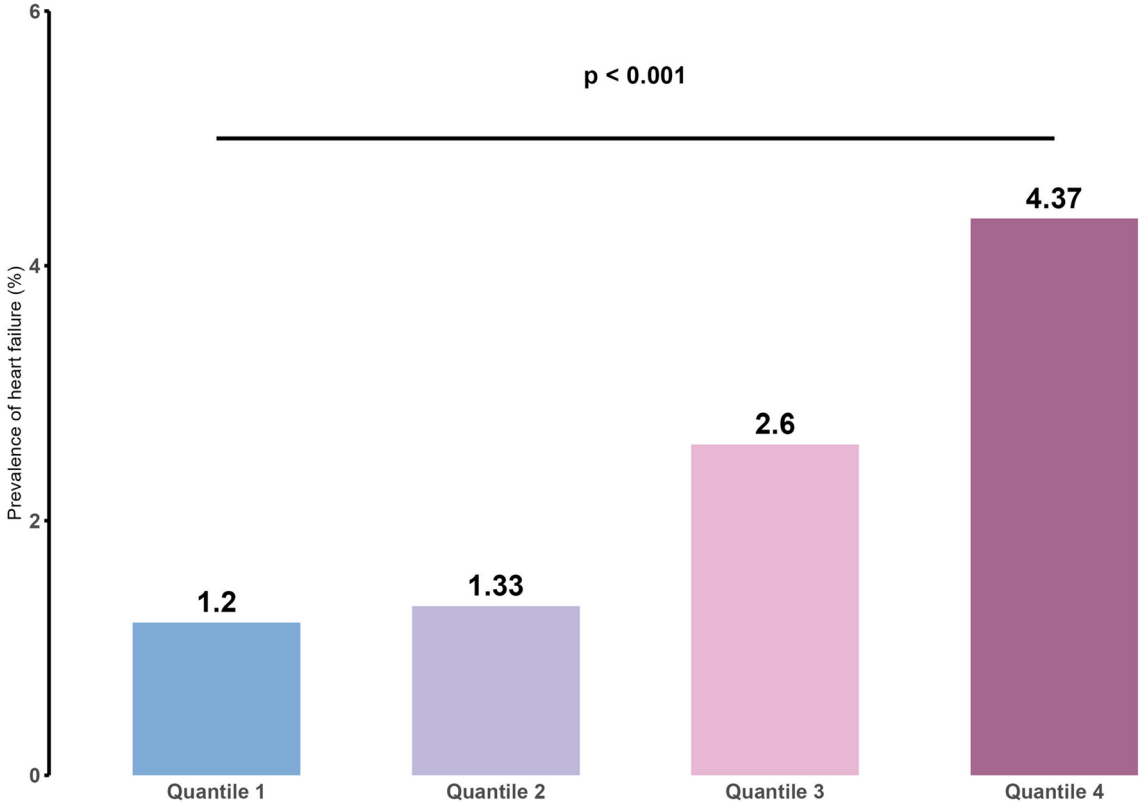

Fig. 2 The prevalence of heart failure across the four quartiles of inflammatory burden index. Quartile 1 (IBI < 0.15), Quartile 2 (IBI: 0.15–0.403), Quartile 3 (IBI: 0.403–1.072), and Quartile 4 (IBI > 1.072) IBI: inflammatory burden index

Table 3 Association between inflammatory burden index and risk of heart failure

Models	Variables	OR	95% CI	*P* value	*P* for trend
Model 1	Quantile 1	Reference	Reference		< 0.001
	Quantile 2	1.11	0.77 to 1.59	0.59	
	Quantile 3	2.19	1.57 to 3.05	< 0.0001	
	Quantile 4	3.76	2.71 to 5.20	< 0.0001	
Model 2	Quantile 1	Reference	Reference		< 0.001
	Quantile 2	0.67	0.46 to 0.98	0.04	
	Quantile 3	1.04	0.73 to 1.49	0.82	
	Quantile 4	1.57	1.12 to 2.20	0.01	
Model 3	Quantile 1	Reference	Reference		< 0.001
	Quantile 2	0.72	0.48 to 1.10	0.12	
	Quantile 3	1.06	0.70 to 1.61	0.76	
	Quantile 4	1.46	1.02 to 2.10	0.04	

Quartile 1 (IBI < 0.15), Quartile 2 (IBI: 0.15–0.403), Quartile 3 (IBI: 0.403–1.072), and Quartile 4 (IBI > 1.072)

Model 1: none was adjusted

Model 2: Age, sex, race/ethnicity, height, weight, body mass index, marital, education, smoke, alcohol user and waist circumference were adjusted;

Model 3: Age, sex, race/ethnicity, height, weight, body mass index, marital, education, smoke, alcohol user and waist circumference, hemoglobin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatinine, uric acid, triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol, hyperlipidemia, hypertension, coronary heart disease, stroke, diabetes, antidiabetic treatment, antihyperlipidemic treatment, and antihypertensive treatment were adjusted

IBI: inflammatory burden index; HDL cholesterol: high-density lipoprotein HDL cholesterol; LDL cholesterol: low-density lipoprotein cholesterol

between IBI and HF risk, as described in Table 3. In the unadjusted model (model 1), we observed that, compared to Quartile 1, the risk of HF was significantly higher in Quartiles 3 (OR = 2.19, 95% CI: 1.57 to 3.05, $p < 0.001$), and 4 (OR = 3.76, 95% CI: 2.71 to 5.20, $p < 0.001$). After adjusting for age, gender, race/ethnicity, height, weight, BMI, marital status, education, smoking status, alcohol use, and waist circumference, we still found that elevated IBI was associated with a higher risk of HF (model 2, p for trend < 0.001). In model 3, which adjusted for all potential confounders, including age, gender, race/ethnicity, height, weight, BMI, marital status, education, smoking status, alcohol use, waist circumference, hemoglobin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatinine, uric acid, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, hyperlipidemia, hypertension, coronary heart disease, stroke, diabetes, antidiabetic treatment, antihyperlipidemic treatment, and antihypertensive treatment, we persistently observed a higher risk of HF in Quartile 4 compared to Quartile 1 (OR = 1.46, 95% CI: 1.02 to 2.10, $p = 0.04$). Additionally, we consistently observed a significant p for trend across models 1, 2, and 3.

Restricted cubic spline analysis

In order to further evaluate the dose-response association between IBI and the risk of HF, we conducted a restricted cubic spline analysis while controlling for the same confounding variables employed in models 1, 2, and 3. The findings of the analysis revealed a positive-linear correlation between IBI and HF risk, regardless of whether no adjustments, partial adjustments, or comprehensive adjustments were made for confounding variables, as illustrated in Fig. 3.

Subgroup analysis

To examine the correlation between IBI and the risk of HF across various subgroups, we conducted a subgroup analysis. Figure 4 elucidates that the association between IBI and the likelihood of HF persisted as significant across the majority of subgroups, including gender, race/ethnicity, marital status, educational level, smoking behaviors, alcohol usage, hyperlipidemia, coronary artery disease, cerebrovascular incidents, and diabetes mellitus. Nevertheless, the association was attenuated in never-married individuals and those without cerebrovascular or treatment histories.

Discussion

Key findings

To our knowledge, this investigation is the first attempt to examine the correlation between IBI and the risk of HF within a substantial sample cohort. The findings of this study indicated a significant relationship between elevated IBI levels and an increased risk of HF. Participants diagnosed with HF exhibited markedly higher levels of IBI, with the prevalence of HF rising across IBI quartiles, ranging from 1.20% in Quartile 1 to 4.37% in Quartile 4 (p for trend < 0.001). This association persisted even after controlling for confounding variables, yielding an OR of 1.46 (95% CI: 1.02 to 2.10, $p = 0.04$) for Quartile 4 in comparison to Quartile 1. Moreover, restricted cubic spline analysis demonstrated a considerable positive-linear association between IBI and the risk of HF. Additionally, subgroup analyses revealed a consistent association across various demographic categories and comorbid conditions, although certain subgroups manifested non-significant outcomes.

Relationship between inflammation and HF

A persistent inflammatory reaction is a crucial characteristic of HF [28, 29], and it is related to both the severity and prognosis of HF. In 1990, Levine et al. [30]. detected a possible link between HF and inflammation. They found that individuals with chronic HF had higher levels of TNF than healthy people of the same age (115 ± 25 U/mL vs. 9 ± 3 U/mL, $p < 0.001$). Also, higher levels of TNF were linked to more advanced HF, which suggests that high levels of TNF are a marker of HF severity. Following this, many studies have shown that the inflammatory reaction

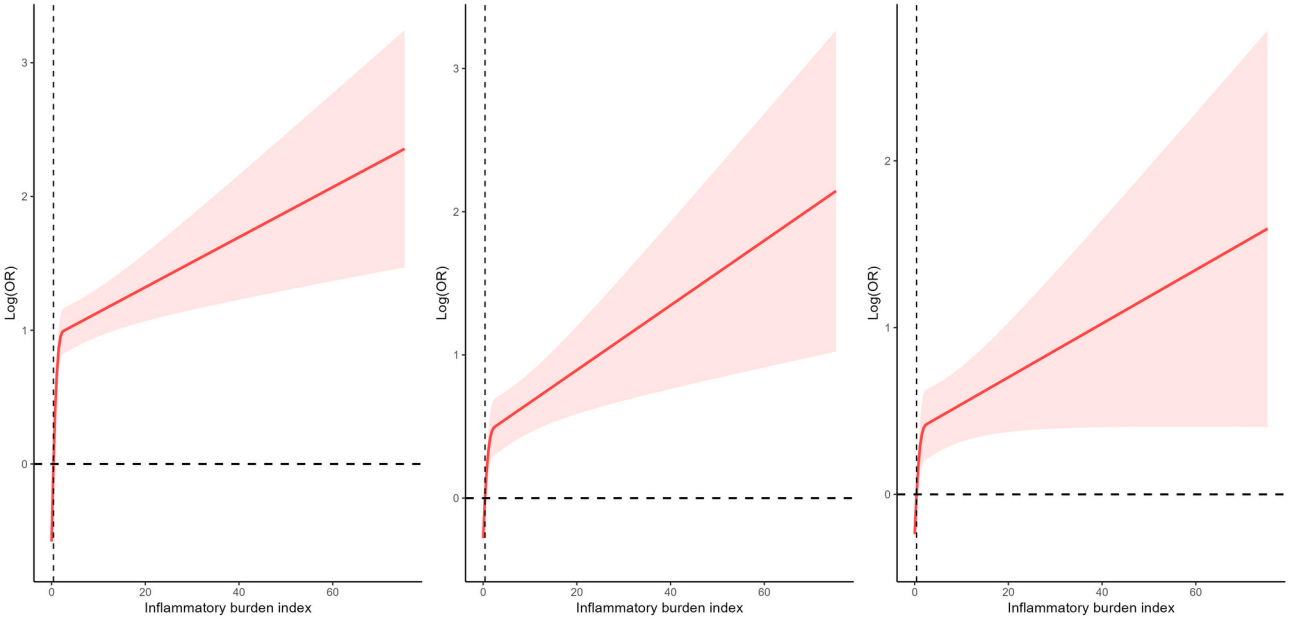

Fig. 3 Restricted cubic spline analysis of inflammatory burden index and risk of heart failure None was adjusted in the left panel; Age, gender, race/ethnicity, height, weight, BMI, marital status, education, smoking status, alcohol use, and waist circumference were adjusted in the middle panel; Age, gender, race/ethnicity, height, weight, BMI, marital status, education, smoking status, alcohol use, waist circumference, hemoglobin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatinine, uric acid, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, hyperlipidemia, hypertension, coronary heart disease, stroke, diabetes, antidiabetic treatment, antihyperlipidemic treatment, and antihypertensive treatment were adjusted in the right panel HDL cholesterol: high-density lipoprotein HDL cholesterol; LDL cholesterol: low-density lipoprotein cholesterol

Subgroup	Quantile 1	Quantile 2	Quantile 3	Quantile 4	p for trend	p for interaction
Gender						0.116
Male	Ref	0.875 (0.561,1.367)	2.426 (1.556,3.782)	4.196 (2.845,6.189)	<0.0001	
Female	Ref	1.531 (0.881,2.660)	2.041 (1.272,3.275)	3.933 (2.289,6.759)	<0.0001	
Race/ethnicity						0.609
Non-Hispanic White	Ref	1.089 (0.682,1.739)	2.186 (1.412,3.387)	3.828 (2.584,5.672)	<0.0001	
Non-Hispanic Black	Ref	1.594 (0.898,2.829)	2.136 (1.132,4.030)	3.576 (1.938,6.598)	<0.0001	
Mexican American	Ref	2.551 (0.856, 7.604)	2.871 (1.210, 6.815)	6.476 (2.555,16.418)	<0.001	
Other Race	Ref	0.497 (0.132,1.862)	2.401 (0.760,7.579)	3.117 (1.248,7.788)	0.003	
Marital						0.704
Married	Ref	0.982 (0.589,1.639)	1.974 (1.286,3.029)	3.735 (2.406,5.797)	<0.0001	
Others	Ref	1.290 (0.790,2.106)	2.410 (1.493,3.890)	3.561 (2.266,5.596)	<0.0001	
Never married	Ref	0.735 (0.249,2.171)	1.099 (0.397,3.042)	2.319 (0.892,6.025)	0.096	
Education						0.874
High school	Ref	0.977 (0.548,1.743)	2.244 (1.400,3.594)	3.576 (2.216,5.773)	<0.0001	
Over high school	Ref	1.094 (0.696,1.720)	2.034 (1.278,3.237)	3.353 (2.161,5.203)	<0.0001	
Below high school	Ref	1.156 (0.455,2.937)	1.602 (0.751,3.416)	3.854 (1.496,9.933)	0.002	
Smoke						0.719
Never	Ref	0.984 (0.583,1.658)	1.624 (0.973,2.711)	3.036 (1.869,4.931)	<0.0001	
Active	Ref	1.298 (0.461, 3.650)	2.140 (0.955, 4.795)	4.258 (1.759,10.304)	<0.001	
Former	Ref	1.119 (0.560,2.238)	2.852 (1.619,5.024)	4.143 (2.432,7.058)	<0.0001	
Alcohol user						0.698
Former	Ref	1.053 (0.610,1.816)	2.079 (1.246,3.469)	3.275 (2.141,5.009)	<0.0001	
Active	Ref	1.250 (0.669,2.335)	1.714 (0.877,3.350)	3.474 (1.777,6.791)	<0.001	
Never	Ref	0.618 (0.258,1.479)	2.181 (1.033,4.601)	3.535 (1.784,7.004)	<0.0001	
Hyperlipidemia						< 0.001
No	Ref	1.849 (0.573, 5.965)	7.569 (2.652,21.604)	13.206 (4.520,38.588)	<0.0001	
Yes	Ref	0.901 (0.612,1.327)	1.558 (1.106,2.196)	2.654 (1.884,3.738)	<0.0001	
Coronary heart disease						0.151
No	Ref	1.245 (0.810,1.914)	1.924 (1.250,2.960)	4.057 (2.652,6.206)	<0.0001	
Yes	Ref	0.677 (0.341,1.345)	1.522 (0.894,2.591)	2.130 (1.214,3.734)	<0.001	
Stroke						0.027
No	Ref	1.123 (0.732,1.722)	2.239 (1.504,3.332)	3.991 (2.694,5.914)	<0.0001	
Yes	Ref	0.944 (0.406,2.195)	1.299 (0.673,2.507)	1.463 (0.709,3.018)	0.159	
Diabetes mellitus						0.739
No	Ref	1.045 (0.651,1.680)	2.024 (1.358,3.017)	2.626 (1.711,4.032)	<0.0001	
Yes	Ref	0.883 (0.516,1.513)	1.509 (0.864,2.636)	2.426 (1.438,4.095)	<0.0001	
Antidiabetic treatment						0.042
No	Ref	0.475 (0.110,2.047)	1.462 (0.528,4.051)	1.713(0.455,6.451)	0.304	
Yes	Ref	0.886 (0.440,1.785)	1.302 (0.734,2.309)	2.751(1.541,4.910)	<0.0001	
Antihyperlipidemic treatment						0.038
No	Ref	0.475(0.110,2.047)	1.462 (0.528,4.051)	1.713 (0.455,6.451)	0.304	
Yes	Ref	0.745(0.461,1.204)	1.374 (0.951,1.986)	2.554 (1.621,4.023)	<0.0001	
Antihypertensive treatment						0.098
No	Ref	0.475(0.110,2.047)	1.462 (0.528,4.051)	1.713 (0.455,6.451)	0.304	
Yes	Ref	0.819(0.544,1.233)	1.471 (1.021,2.119)	2.284 (1.597,3.267)	<0.0001	

Fig. 4 The relationship between inflammatory burden index and risk of heart failure in different subgroups Quartile 1 (IBI < 0.15), Quartile 2 (IBI: 0.15–0.403), Quartile 3 (IBI: 0.403–1.072), and Quartile 4 (IBI > 1.072) IBI: inflammatory burden index

continues to cause cardiac dysfunction and the worsening of HF. In a rat model, Bozkurt et al. [31]. found that TNF-αleads to left ventricular disfunction and remodeling. In addition, Torre-Amione et al. [32] found that failing hearts express higher concentrations of TNF-α. They further observed that levels of TNF-αand IL-6 were also considerably higher in HF patients compared to controls [33]. Moreover, higher levels of these inflammatory factors were linked to worsening heart function, showing that inflammation are essential in the pathophysiology of HF. In addition, the use of anti-inflammatory drugs has substantially improved the prognosis of HF patients, including reductions in hospitalization for HF and HF-related mortality [34]. In alignment with prior literature [30–32], the present investigation similarly recognizes IBI as exhibiting a strong correlation with HF. This association demonstrates a positive linear relationship, indicating that higher concentrations of IBI are associated with an increased risk of HF.

Clinical implications

It is well-established that inflammation plays a significant role in myocardial injury and remodeling [20, 35, 36], potentially initiating or aggravating cardiac function. The

integration of IBI, which encompasses CRP, neutrophil and lymphocyte—biomarkers indicative of both acute inflammatory responses and the equilibrium of immune cell activities—may yield a more comprehensive assessment of inflammatory status compared to the evaluation of either biomarker in isolation. Furthermore, the strong correlation noted across diverse subgroups, such as gender, race, and the presence of comorbidities, further supports the prospective utility of IBI as a suitable biomarker to access the risk of HF. From a clinical perspective, these revelations could facilitate the stratification of patients according to inflammation-related risk factors, thereby informing more individualized strategies for monitoring and treatment. For example, individuals exhibiting elevated IBI levels may be prioritized for intensive lifestyle modifications [37–39] or pharmacological interventions [34, 40] aimed at mitigating inflammatory load and then reduce the risk of HF. In addition, as IBI requires only routine lab parameters, it could serve as a cost-effective screening tool in primary care settings. The simplicity and accessibility of IBI make it an attractive option for widespread use, as it would not require specialized equipment or extensive patient testing. By utilizing existing laboratory data, primary care providers could easily identify individuals at elevated risk for heart failure, facilitating earlier interventions and potentially reducing hospitalizations.

Potential limitations

Although the evidence of the present investigation is supported by a substantial sample size and representative data, several limitations warrant consideration. First, the cross-sectional design of the study inhibits the ability to determine a causal relationship between IBI and HF. Therefore, longitudinal investigations or mendelian randomization analysis are essential to further validate the causal association. Second, although our adjustments for various confounding variables, residual confounding stemming from unmeasured or inaccurately defined factors may potentially affect the observed associations. Third, the assessment of CRP and NLR at a single time point may insufficiently capture the complexity in inflammatory levels that could arise from transient health conditions or therapeutic interventions. Finally, another limitation of this study is the reliance on self-reported data for HF diagnosis, which may introduce potential bias.

Conclusion

In summary, this study demonstrates that elevated IBI correlates with an increased susceptibility to HF. These results support the role of systemic inflammation in the pathophysiological mechanisms underlying HF, underscoring the prospective utility of IBI as a prognostic indicator for the identification of individuals at high risk of HF. Given that HF persistently represents a predominant contributor to morbidity and mortality, the incorporation of innovative biomarkers such as IBI may serve a pivotal function in facilitating early detection and preventive measures, ultimately enhancing clinical outcomes.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04781-x.

Supplementary Material 1

Acknowledgements

None.

Author contributions

Li-Xin Yun, Wan-Zhong Huang, Qiang Su, Da-Zhi Lan and Yang-Chun Liu participated in the conception and designed the study. Li-Xin Yun, Wan-Zhong Huang, Changjing He, Yuan Huang, Hua-Feng Yang, Yang-Chun Liu, Da-Zhi Lan and Qiang Su were responsible for research design, data analysis, writing of first drafts. Li-Xin Yun, Wan-Zhong Huang, Changjing He, Yuan Huang, Hua-Feng Yang, Yang-Chun Liu and Qiang Su wrote the manuscript. Yang-Chun Liu, Da-Zhi Lan and Qiang Su revised the whole writing process. All authors have read and approved the final manuscript.

Funding

National Natural Science Foundation of China (No.82300376) and the Joint Project on Regional High-Incidence Diseases Research of Guangxi Natural Science Foundation (No.2024GXNSFBA010082).

Data availability

All of the data used in this study is accessible from the NHANES database (https://www.cdc.gov/nchs/nhanes/).

Declarations

Ethics approval and consent to participate

The protocols of NHANES were approved by the institutional review board of the National Center for Health Statistics, CDC (https://www.cdc.gov/nchs/nhanes/irba98.htm). NHANES has obtained written informed consent from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 7 December 2024 / Accepted: 18 April 2025
Published online: 24 April 2025

References

1. Morris DA, Gailani M, Pérez AV, Blaschke F, Dietz R, Haverkamp W, et al. Left atrial systolic and diastolic dysfunction in heart failure with normal left ventricular ejection fraction. J Am Soc Echocardiogr. 2011;24:651–62.
2. Badano LP, Albanese MC, De Biaggio P, Rozbowsky P, Miani D, Fresco C, et al. Prevalence, clinical characteristics, quality of life, and prognosis of patients with congestive heart failure and isolated left ventricular diastolic dysfunction. J Am Soc Echocardiogr. 2004;17:253–61.
3. Liu Z, Huang Y, Yang Y, Li W, Ju W, Zhang F, et al. Analysis and prediction of research hotspots and trends in heart failure research. J Transl Int Med. 2024;12:263–73.

4. Liu Z, Huang Y, Li H, Li W, Zhang F, Ouyang W, et al. A generalized deep learning model for heart failure diagnosis using dynamic and static ultrasound. J Transl Int Med. 2023;11:138–44.
5. Crespo-Leiro MG, Metra M, Lund LH, Milicic D, Costanzo MR, Filippatos G, et al. Advanced heart failure: a position statement of the heart failure association of the European society of cardiology. Eur J Heart Fail. 2018;20:1505–35.
6. Hu SS. Heart failure in China: epidemiology and current management. J Geriatr Cardiol. 2024;21:631–41.
7. Wei J, Du J. Mechanisms of sodium-glucose cotransporter 2 inhibitors in heart failure. Cardiovasc Innovations Appl. 2023;8:987.
8. Dick SA, Epelman S. Chronic heart failure and inflammation: what do we really know?? Circ Res. 2016;119:159–76.
9. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu S, et al. Heart failure: preventing disease and death worldwide. ESC Heart Fail. 2014;1:4–25.
10. Slivnick J, Lampert BC. Hypertension and heart failure. Heart Fail Clin. 2019;15:531–41.
11. Yan Y, Han Y, Liu B, Du J, Wang J, Jing X et al. Optimal blood pressure control target for older patients with hypertension: A systematic review and Meta-Analysis. Cardiovasc Innovations Appl. 2023;7. 979.
12. Lehrke M, Marx N. Diabetes mellitus and heart failure. Am J Cardiol. 2017;120:S37–47.
13. Cesaro A, Acerbo V, Scialla F, Scherillo G, De Michele G, Panico D et al. Role of lipoprotein (a) in cardiovascular diseases and premature acute coronary syndromes (RELACS Study): impact of Lipoprotein (a) levels on the premature coronary event and the severity of coronary artery disease. Nutr Metabolism Cardiovasc Dis. 2024:103843.
14. Alpert MA, Lavie CJ, Agrawal H, Aggarwal KB, Kumar SA. Obesity and heart failure: epidemiology, pathophysiology, clinical manifestations, and management. Translational Res. 2014;164:345–56.
15. Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats AJS. Global burden of heart failure: a comprehensive and updated review of epidemiology. Cardiovasc Res. 2023;118:3272–87.
16. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB, et al. Predictors of mortality and morbidity in patients with chronic heart failure. Eur Heart J. 2006;27:65–75.
17. Angermann CE, Störk S, Gelbrich G, Faller H, Jahns R, Frantz S et al. Mode of action and effects of standardized collaborative disease management on mortality and morbidity in patients with systolic heart failure: the Interdisciplinary Network for Heart Failure (INH) study. Circulation: Heart Failure. 2012;5:25–35.
18. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002;105:1135–43.
19. Sprague AH, Khalil RA. Inflammatory cytokines in vascular dysfunction and vascular disease. Biochem Pharmacol. 2009;78:539–52.
20. Frangogiannis NG. The inflammatory response in myocardial injury, repair, and remodelling. Nat Reviews Cardiol. 2014;11:255–65.
21. Albar Z, Albakri M, Hajjari J, Karnib M, Janus SE, Al-Kindi SG. Inflammatory markers and risk of heart failure with reduced to preserved ejection fraction. Am J Cardiol. 2022;167:68–75.
22. Sánchez-Lázaro IJ, Almenar L, Reganon E, Vila V, Martínez-Dolz L, Martínez-Sales V, et al. Inflammatory markers in stable heart failure and their relationship with functional class. Int J Cardiol. 2008;129:388–93.
23. He C, Wu D, Wei X, Li Y, Liao Y, Yang D. Association between inflammatory burden index and all-cause mortality in the general population aged over 45 years: data from NHANES 2005–2017. Nutr Metab Cardiovasc Dis. 2024;34:64–74.
24. Xie H, Ruan G, Ge Y, Zhang Q, Zhang H, Lin S, et al. Inflammatory burden as a prognostic biomarker for cancer. Clin Nutr. 2022;41:1236–43.
25. Xie H, Ruan G, Wei L, Deng L, Zhang Q, Ge Y, et al. The inflammatory burden index is a superior systemic inflammation biomarker for the prognosis of non-small cell lung cancer. J Cachexia Sarcopenia Muscle. 2023;14:869–78.
26. Yu F, Peng J. Association between inflammatory burden index and cardiovascular disease in adult Americans: evidence from NHANES 2005–2010. Heliyon. 2024;10:e38273.
27. Ho P-R, Koendgen H, Campbell N, Haddock B, Richman S, Chang I. Risk of natalizumab-associated progressive multifocal leukoencephalopathy in patients with multiple sclerosis: a retrospective analysis of data from four clinical studies. Lancet Neurol. 2017;16:925–33.
28. Gullestad L, Ueland T, Vinge LE, Finsen A, Yndestad A, Aukrust P. Inflammatory cytokines in heart failure: mediators and markers. Cardiology. 2012;122:23–35.
29. Shirazi LF, Bissett J, Romeo F, Mehta JL. Role of inflammation in heart failure. Curr Atheroscler Rep. 2017;19:1–9.
30. Levine B, Kalman J, Mayer L, Fillit HM, Packer M. Elevated Circulating levels of tumor necrosis factor in severe chronic heart failure. N Engl J Med. 1990;323:236–41.
31. Bozkurt B, Kribbs SB, Clubb FJ Jr., Didenko MLH, Hornsby VV. Pathophysiologically relevant concentrations of tumor necrosis factor-alpha promote progressive left ventricular dysfunction and remodeling in rats. Circulation. 1998;97:1382–91.
32. Torre-Amione G, Kapadia S, Lee J, Durand JB, Bies RD, Young JB, et al. Tumor necrosis factor-alpha and tumor necrosis factor receptors in the failing human heart. Circulation. 1996;93:704–11.
33. Torre-Amione G, Kapadia S, Benedict C, Oral H, Young JB, Mann DL. Proinflammatory cytokine levels in patients with depressed left ventricular ejection fraction: a report from the studies of left ventricular dysfunction (SOLVD). J Am Coll Cardiol. 1996;27:1201–6.
34. Everett BM, Cornel JH, Lainscak M, Anker SD, Abbate A, Thuren T, et al. Anti-Inflammatory therapy with Canakinumab for the prevention of hospitalization for heart failure. Circulation. 2019;139:1289–99.
35. Saxena A, Russo I, Frangogiannis NG. Inflammation as a therapeutic target in myocardial infarction: learning from past failures to Meet future challenges. Translational Res. 2016;167:152–66.
36. Suleiman M, Khatib R, Agmon Y, Mahamid R, Boulos M, Kapeliovich M, et al. Early inflammation and risk of long-term development of heart failure and mortality in survivors of acute myocardial infarction: predictive role of C-reactive protein. J Am Coll Cardiol. 2006;47:962–8.
37. Kalantar-Zadeh K, Anker SD, Horwich TB, Fonarow GC. Nutritional and anti-inflammatory interventions in chronic heart failure. Am J Cardiol. 2008;101:S89–103.
38. Gielen S, Adams V, Möbius-Winkler S, Linke A, Erbs S, Yu J, et al. Anti-inflammatory effects of exercise training in the skeletal muscle of patients with chronic heart failure. J Am Coll Cardiol. 2003;42:861–8.
39. Kaluza J, Levitan EB, Michaëlsson K, Wolk A. Anti-inflammatory diet and risk of heart failure: two prospective cohort studies. Eur J Heart Fail. 2020;22:676–82.
40. Zhang Z, Chen F, Wan J, Liu X. Potential traditional Chinese medicines with anti-inflammation in the prevention of heart failure following myocardial infarction. Chin Med. 2023;18:28.

Publisher's note