

Diagnostic Value of a Novel Junctional Cardiometabolic Index (NJCI) for Identifying Reduced Left Ventricular Ejection Fraction in Chinese Patients with Heart Failure: A Retrospective Observational Study

Shiraz Rafiq

rshiraz59@icloud.com

Fifth Affiliated Hospital of Xinjiang Medical University

Jannat Atajanova

Fifth Affiliated Hospital of Xinjiang Medical University

He PengYi

Fifth Affiliated Hospital of Xinjiang Medical University

Research Article

Keywords: Heart failure, Reduced left ventricular ejection fraction, Novel Junctional Cardiometabolic Index (NJCI), NT-proBNP, Cardiometabolic biomarkers, Diagnostic performance, Risk stratification

Posted Date: August 18th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10033555/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Identification of a patient's reduced left ventricular ejection fraction (LVEF) is critical for determining their risk and treatment strategy when they are diagnosed with heart failure. Nonetheless, traditional clinical and imaging markers may be unable to account for all the multifactorial processes involved in heart dysfunction. The aim of this study was to assess the diagnostic performance of a new biomarker called Novel Junctional Cardiometabolic Index (NJCI) in detecting reduced LVEF in comparison with NT-proBNP.

Methods

This retrospective cohort consisting of 338 patients suffering from heart failure was included in this study, who further categorized into those having a reduced left ventricular ejection fraction (LVEF < 45%) and those with preserved LVEF (LVEF ≥ 45%). The NJCI was assessed by $\ln(\text{total bilirubin}) \times \ln(\text{D-dimer})/\text{albumin}$, combining the role of hepatic function, coagulation, and nutritional-inflammatory systems to form a composite score. The diagnostic utility of NJCI was compared with NT-proBNP, using ROC curve analysis and binary logistic regression analysis.

Results

In total, there were 338 patients with heart failure analyzed, which were divided into groups of reduced LVEF (< 45%) and preserved LVEF (≥ 45%), according to echocardiography data. It was found out that patients with reduced LVEF had significantly elevated NJCI than those with preserved LVEF ($p < 0.001$). The ROC analysis showed that NJCI had excellent discrimination potential for the identification of patients with reduced LVEF (AUC = 0.903, 95% CI: 0.871–0.934), compared with NT-proBNP, which had a significantly lower diagnostic efficiency (AUC = 0.773, 95% CI: 0.723–0.823). For the cutoff value, calculated using Youden's index, 0.383, NJCI demonstrated high sensitivity (98.7%) and acceptable specificity (41.0%) for diagnosing of the target pathology. Binary logistic regression analysis proved NJCI to be an independent predictor of reduced LVEF even after adjusting for NT-proBNP (odds ratio = 5.95, 95% CI: 4.04–8.76, $p < 0.001$). The model obtained was highly explanatory and informative (Nagelkerke $R^2 = 0.572$, classification accuracy = 81.4%).

Conclusion

The NJCI has been found to have better diagnostic accuracy than NT-proBNP in identifying low LVEF and could be considered an appropriate biomarker that can be used for risk stratification among HF patients.

1. Introduction

Heart failure is one of the major causes of morbidity and mortality from cardiovascular disease around the world and still exerts an enormous cost in terms of clinical care and economics despite developments in current treatment approaches[1]. In addition, individuals who experience heart failure after a myocardial infarction constitute one of the highest risk groups. It is important for LV systolic dysfunction to be recognized early on since LVEF is one of the most important factors influencing the prognosis and management of heart failure patients[2].

The transthoracic echocardiography examination continues to represent the gold standard in imaging-based LVEF measurement; yet, frequent use might be associated with such drawbacks as dependence on the operator, variability between observers, and lack of accessibility in different health care settings[3]. These constraints are believed to foster increased interest in the development of inexpensive, easy-to-use, and universal biomarkers that can facilitate early detection and risk stratification in patients susceptible to ventricular dysfunction[4]. Among currently recognized biomarkers, NT-proBNP is recommended for the diagnosis and prognostic prediction of heart failure, given its high sensitivity to ventricular loading and myocardial wall stress[5]. However, the test accuracy is not entirely specific due to the influence of different clinical and physiological parameters on the level of NT-proBNP such as age, renal dysfunction, obesity, and hemodynamics changes[6].

Heart failure is now widely regarded as a systemic syndrome, which involves complicated interactions between myocardial abnormalities and multi-organ abnormalities of physiopathology [7]. Specifically, hepatic congestion, systemic inflammation, coagulation disturbance, and malnutrition are very common problems seen in patients with heart failure of severe degrees and are associated with the severity and prognosis of the disease [8]. Therefore, biological markers representing the above different pathways of physiological abnormalities including bilirubin as an indicator for liver abnormality, D-dimer as a representation for hypercoagulability state, and albumin for nutrition and inflammation have individually shown correlations with severity and prognosis of heart failure [9]. However, due to the nature of heart failure, which includes many factors, the use of single biomarker cannot accurately diagnose the heart failure. The combination of several domains of physiopathological abnormalities can form a single composite marker that can provide a more precise diagnosis than any single biomarker [10].

In this regard, a novel composite biomarker, Novel Junctional Cardiometabolic Index (NJCI) was developed, which comprises the combination of hepatic dysfunction, activation of coagulation, and nutritional inflammatory state into one parameter. Although there is growing interest in using multimarker approaches for assessing cardiovascular disease, no research work till date has studied a composite index incorporating all three biological systems for detection of reduced LVEF in patients with heart failure. The purpose of this research work was to assess the role of Novel Junctional Cardiometabolic Index (NJCI) in detecting reduced LVEF in patients with heart failure compared with NT-proBNP.

2. Methods

2.1 Study Design and Population

This was a retrospective observational study conducted at a tertiary teaching hospital between 2024 and 2025. Diagnosis of heart failure was made on the basis of ESC (European Society of Cardiology) guidelines 2021 which gave guidance on the diagnosis and management of both chronic and acute heart failures[11]. Participants with complete data on clinic, laboratory, and echocardiography were included in the study. Participants were categorized depending on their left ventricular ejection fraction (LVEF) either as a group with reduced LVEF (< 45%) or a group with preserved LVEF (≥ 45%).

2.2 Data Collection

Demographic characteristics, laboratory findings, and echocardiographic parameters were extracted from electronic medical records. Laboratory variables included NT-proBNP, total bilirubin, D-dimer, albumin, renal function indices, lipid profile, and hematological parameters. Blood samples were collected during hospitalization and analyzed using standard laboratory procedures.

2.3 Echocardiographic Assessment

Transthoracic echocardiography was performed by experienced cardiologists according to current echocardiographic recommendations. LVEF was assessed using the modified Simpson biplane method and used to classify patients into reduced LVEF (< 45%) and preserved LVEF (≥ 45%) groups [12].

2.4 NJCI Calculation

The Novel Junctional Cardiometabolic Index (NJCI) was calculated using the following formula:

$$\text{NJCI} = \frac{\ln(\text{Total Bilirubin}) \times \ln(\text{D-dimer})}{\text{Albumin}}$$

This index was developed to integrate markers of hepatic dysfunction, coagulation activation, and nutritional-inflammatory status into a single composite biomarker.

2.5 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 31.0.2.0(126) (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality and are presented as mean ± standard deviation or median (interquartile range), as appropriate. Comparisons between groups were performed using the independent-samples t-test or Mann-Whitney U test. Categorical variables are expressed as frequencies and percentages and were compared using the chi-square test.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of NJCI and NT-proBNP for identifying reduced LVEF. Areas under the curve (AUCs) with 95% confidence intervals (CIs) were calculated, and the optimal cutoff value was determined using

Youden's index. Binary logistic regression analysis was used to identify independent predictors of reduced LVEF. Odds ratios (ORs) and 95% CIs were reported. A two-sided p-value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline Characteristics

Patients with reduced LVEF had significantly higher NT-proBNP, bilirubin, and D-dimer levels and lower albumin levels compared with preserved LVEF patients ($p < 0.001$).

The distribution of NJCI according to LVEF category is presented in Fig. 1. Patients with reduced LVEF exhibited significantly higher NJCI values than those with preserved LVEF.

3.2 ROC Analysis

The diagnostic performance of the NJCI was evaluated using receiver operating characteristic (ROC) curve analysis. As shown in Fig. 2&3, the ROC curve demonstrated a pronounced deviation from the reference line, indicating good discriminatory ability.

The area under the curve (AUC) was 0.903 (95% confidence interval [CI]: 0.871–0.934), with a standard error of 0.016. The asymptotic significance was $p < 0.001$ ($p < 0.001$ (null hypothesis: true area = 0.5), confirming that NJCI has statistically significant diagnostic accuracy.

These results indicate that NJCI has **excellent diagnostic performance** (AUC > 0.9), with a lower bound of the 95% CI above 0.87, supporting its potential utility as a reliable diagnostic test.

NJCI demonstrated excellent diagnostic performance:

AUC = 0.903 \ (95% \ CI: \ 0.871–0.934)

3.3 Logistic Regression

NJCI was an independent predictor of reduced LVEF:

OR = 5.948 \ (95% \ CI: \ 4.040–8.756, \ $p < 0.001$)

Model performance:

Nagelkerke R^2 = 0.572

Overall accuracy = 81.4%

The results of the univariable logistic regression analysis are illustrated in Fig. 4.

4. Discussion

The current retrospective observational study was conducted to assess the diagnostic accuracy of Novel Junctional Cardiometabolic Index (NJCI), a novel composite biomarker comprising total bilirubin, D-dimer, and albumin. In this regard, the main finding from the current research is the very high discriminative power of NJCI in relation to reduced LVEF, with AUC of 0.903 compared to NT-proBNP with AUC of 0.773. Moreover, NJCI remained independently associated with reduced LVEF in multivariable analysis, meaning that it provides additional information about diagnosis beyond that provided by single biomarkers. HF is nowadays seen not only as a cardiac dysfunction syndrome but also a systemic disorder with complex interactions of many physiological processes, such as cardiac dysfunction, venous congestion, inflammation, disorders of coagulation, and metabolism [13]. Thus, a multimarker strategy that reflects multifactorial disease mechanism may be better in assessing the disease than using biomarkers individually [14]. Indeed, several studies have shown that multimarker strategy can improve the diagnostic and prognostic outcomes in cardiovascular diseases by capturing various aspects of disease biology [15].

Justification for NJCI is based on the combined use of three laboratory measures that represent different, yet related pathophysiological processes occurring during the development of heart failure. High bilirubin concentration has increasingly gained acceptance as an indicator of liver congestion or impaired liver perfusion owing to high pressure within the right side of the circulation and systemic venous congestion [16]. High bilirubin concentrations were found to be associated with higher heart failure severity, poor hemodynamics, and unfavorable prognosis [17]. Increased concentrations of D-dimer are a sign of the activation of the coagulation and fibrinolytic system that is usually seen in heart failure patients due to endothelial damage, systemic inflammation, stasis of blood circulation, and neurohormonal activation [18]. Increased D-dimer concentrations were linked to mortality, thromboembolic complications, and advanced disease stage in acute and chronic heart failure patients [19]. Albumin is a well-known indicator of malnutrition and systemic inflammation and was shown to be associated with poor cardiovascular outcomes [20]. The development of hypoalbuminemia among HF patients is due to several factors such as chronic inflammation, impaired liver function, bowel edema, and malnutrition, contributing to worsening of the condition and poor outcomes [21]. Several studies showed the significant correlation between serum albumin concentration and mortality and hospitalization rates in patients with heart failure [22]. Although the level of NT-proBNP remains the main indicator for diagnosis and risk stratification of HF, there are several factors that could affect its results, such as patient age, renal dysfunction, obesity, and hemodynamics [23]. As a result, NT-proBNP cannot adequately represent the multi-systemic manifestations of heart failure [24]. In our study, NJCI was more accurate than NT-proBNP for HF diagnosis, indicating that combining several features of HF pathology is beneficial for better diagnostics. Furthermore, the relationship between NJCI and NT-proBNP across different LVEF categories is illustrated in Fig. 5. Patients with reduced LVEF generally exhibited higher NJCI values across a broad range of NT-proBNP concentrations, supporting the complementary diagnostic information provided by NJCI.

The high level of diagnostic efficacy exhibited by NJCI can, therefore, be attributed to its capacity to incorporate various important pathophysiological processes involved in heart failure. While single biomarkers represent only one biological process, NJCI incorporates venous congestion, thrombo-inflammation, and metabolism-nutrition processes all into one index. The combination of different biological processes may help capture the systemic complexity of heart failure, which explains the higher accuracy with which it detects patients with impaired LVEF. The proposed biological pathways linking elevated NJCI values to impaired cardiac systolic function are summarized in Fig. 6. By integrating biomarkers of hepatic congestion, coagulation activation, and nutritional-inflammatory status, NJCI may provide a comprehensive reflection of the multisystem pathophysiological alterations associated with heart failure and reduced LVEF.

5. Limitations

However, there are several limitations associated with the current study that must be mentioned. Firstly, the current study represents a single-center trial with relatively small sample size consisting of 338 participants. The second important limitation related to the study under discussion is that all the patients included in this research represented Chinese population. As a result, the applicability of the conclusions obtained within the scope of the current study among different ethnical groups or geographical regions cannot be guaranteed. Thirdly, a cross-sectional study design implies that no cause-and-effect relationship between NJCI and reduced left ventricular ejection fraction can be established. In contrast to prospective cohort designs, the current study was based on one-time measurements conducted among participants. This prevented the authors from evaluating prognostic utility of NJCI in terms of predicting future adverse clinical events.

Finally, although NJCI displayed an impressive level of accuracy in the detection of low LVEF, there could still have been some degree of confounding by uncontrolled clinical factors in this study. Further large multicentered and prospective research with extended follow-up is required to confirm the usefulness of NJCI in the clinical setting and its potential prognostic implications. Despite these shortcomings, NJCI showed a good discriminative capacity and can be considered an easily obtainable biomarker for patients with reduced LVEF in routine clinical practice.

6. Conclusion

In summary, the Novel Junctional Cardiometabolic Index (NJCI), derived from readily available laboratory markers such as total bilirubin, D-dimer, and albumin, exhibited excellent diagnostic accuracy for detecting reduced left ventricular ejection fraction in patients suffering from heart failure. NJCI possessed superior discriminatory power than NT-proBNP and was an independent predictor of reduced LVEF in the presence of various confounding variables. Due to the inclusion of several pathophysiologic factors that contribute to the development of heart failure, such as hepatic congestion, inflammation, and activation of the coagulation cascade, NJCI might be able to give a more holistic view on the development of heart failure than individual biomarkers. With its simplicity and outstanding diagnostic

power, NJCI might be useful as an additional test to identify patients with reduced cardiac ejection fraction. Further multicenter prospective investigations are needed for validation purposes.

Abbreviations

HF

Heart Failure

LVEF

Left Ventricular Ejection Fraction

NJCI

Novel Junctional Cardiometabolic Index

NT-proBNP

N-terminal pro-B-type natriuretic peptide

ROC

Receiver Operating Characteristic

AUC

Area Under the Curve

CI

Confidence Interval

OR

Odds Ratio

ESC

European Society of Cardiology

BMI

Body Mass Index

eGFR

Estimated Glomerular Filtration Rate

LDL

Low-Density Lipoprotein

WBC

White Blood Cell

IQR

Interquartile Range

SD

Standard Deviation

Declarations

Ethics approval and consent to participate

This retrospective observational study was conducted in accordance with the Declaration of Helsinki and relevant national regulations. The study protocol was reviewed and approved by the Ethics Committee of The Fifth Affiliated Hospital of Xinjiang Medical University (approval number: XYDWFLSK-2025-280). All patient data were anonymized prior to analysis. Due to the retrospective nature of the study, the Ethics Committee waived the requirement for informed consent from individual participants.

Consent for publication

Not applicable. This manuscript does not contain any individual person's data in any form (including individual details, images, or videos).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contributions

Shiraz Rafiq: Conceptualization, Data curation, Formal analysis,Methodology, Investigation,Writing original draft

Jannat Atajanova: Data curation, Validation, Writing review & editing

He PengYi: Conceptualization, Supervision, Writing review & editing

Acknowledgements

Not applicable.

Declaration of Generative AI and AI-assisted Technologies in the Manuscript Preparation Process

During the preparation of this work, the author(s) used ChatGPT to create/modify Figure 6. After using this tool, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the published article.

References

1. Khan MS, Shahid I, Bennis A, Rakisheva A, Metra M, Butler J. Global epidemiology of heart failure. *Nat Rev Cardiol*. 2024;21(10):717–734. 10.1038/s41569-024-01046-6. Epub 2024 Jun 26. PMID: 38926611.
2. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW, ACC/AHA Joint Committee Members. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(18):e895-e1032. doi: 10.1161/CIR.0000000000001063. Epub 2022 Apr 1. Erratum in: *Circulation*. 2022;145(18):e1033. doi: 10.1161/CIR.0000000000001073. Erratum in: *Circulation*. 2022;146(13):e185. doi: 10.1161/CIR.0000000000001097. Erratum in: *Circulation*. 2023;147(14):e674. 10.1161/CIR.0000000000001142. PMID: 35363499.
3. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, Horton K, Ogunyankin KO, Palma RA, Velazquez EJ. Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2019;32(1):1–64. doi: 10.1016/j.echo.2018.06.004. Epub 2018 Oct 1. PMID: 30282592.
4. Alzaabi MA, Abdelsalam A, Alhammadi M, Bani Hani H, Almheiri A, Al Matrooshi N, Al Zaman K. Evaluating Biomarkers as Tools for Early Detection and Prognosis of Heart Failure: A Comprehensive Review. *Card Fail Rev*. 2024;10:e06. 10.15420/cfr.2023.24. . PMID: 38915376; PMCID: PMC11194781.
5. Javed N, El-Far M, Vittorio TJ. Clinical markers in heart failure: a narrative review. *J Int Med Res*. 2024;52(5):3000605241254330. 10.1177/03000605241254330. . PMID: 38779976; PMCID: PMC11119339.
6. Jhund PS. Use of NT-proBNP for the screening, diagnosis and risk-stratification of left ventricular dysfunction. *Diabetes Obes Metab*. 2025;27(Suppl 8):7–14. 10.1111/dom.16388. . Epub 2025 Apr 9. PMID: 40205856; PMCID: PMC12400483.
7. Boulet J, Sridhar VS, Bouabdallaoui N, Tardif JC, White M. Inflammation in heart failure: pathophysiology and therapeutic strategies. *Inflamm Res*. 2024;73(5):709–23. 10.1007/s00011-023-01845-6. . Epub 2024 Mar 28. PMID: 38546848; PMCID: PMC11058911.
8. Mocan D, Jipa R, Jipa DA, Lala RI, Rasinar FC, Groza I, Sabau R, Sulea Bratu D, Balta DF, Cioban ST, Puschita M. Unveiling the Systemic Impact of Congestion in Heart Failure: A Narrative Review of Multisystem Pathophysiology and Clinical Implications. *J Cardiovasc Dev Dis*. 2025;12(4):124. 10.3390/jcdd12040124. . PMID: 40278183; PMCID: PMC12028304.
9. Singh G, Bamba H, Inban P, Chandrasekaran SH, Priyatha V, John J, Prajiwal P. The role of biomarkers in the prognosis and risk stratification in heart failure: A systematic review. *Dis Mon*. 2024;70(10):101782. 10.1016/j.disamonth.2024.101782. . Epub 2024 Jul 2. PMID: 38955639.

10. Meijers WC, Bayes-Genis A, Mebazaa A, Bauersachs J, Cleland JGF, Coats AJS, Januzzi JL, Maisel AS, McDonald K, Mueller T, Richards AM, Seferovic P, Mueller C, de Boer RA. Circulating heart failure biomarkers beyond natriuretic peptides: review from the Biomarker Study Group of the Heart Failure Association (HFA), European Society of Cardiology (ESC). *Eur J Heart Fail.* 2021;23(10):1610–32. 10.1002/ejhf.2346. . Epub 2021 Oct 10. PMID: 34498368; PMCID: PMC9292239.
11. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A, ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42(36):3599–3726. 10.1093/eurheartj/ehab368. Erratum in: *Eur Heart J.* 2021;42(48):4901. doi: 10.1093/eurheartj/ehab670. PMID: 34447992.
12. Taub CC, Stainback RF, Abraham T, Forsha D, Garcia-Sayan E, Hill JC, Hung J, Mitchell C, Rigolin VH, Sachdev V, Sengupta PP, Sorrell VL, Strom J. Guidelines for the Standardization of Adult Echocardiography Reporting: Recommendations From the American Society of Echocardiography. *J Am Soc Echocardiogr.* 2025;38(9):735–774. 10.1016/j.echo.2025.06.001. PMID: 40912865.
13. Ponikowska B, Fudim M, Iwanek G, Zymlński R, Biegus J. Harnessing the lymphatic system. *Heart Fail Rev.* 2025;30(4):673–83. 10.1007/s10741-024-10449-z. . Epub 2024 Oct 15. PMID: 39402329; PMCID: PMC12165986.
14. Kovenskiy A, Mukhatayev Z, Sailybayeva A, Bekbossynova M, Kushugulova A. Diagnostic and prognostic value of circulating biomarkers in heart failure. *Front Cardiovasc Med.* 2025;12:1633164. 10.3389/fcvm.2025.1633164. . PMID: 41070093; PMCID: PMC12504382.
15. Netala VR, Hou T, Wang Y, Zhang Z, Teertam SK. Cardiovascular Biomarkers: Tools for Precision Diagnosis and Prognosis. *Int J Mol Sci.* 2025;26(7):3218. 10.3390/ijms26073218. . PMID: 40244022; PMCID: PMC11989402.
16. Aspromonte N, Fumarulo I, Petrucci L, Biferali B, Liguori A, Gasbarrini A, Massetti M, Miele L. The Liver in Heart Failure: From Biomarkers to Clinical Risk. *Int J Mol Sci.* 2023;24(21):15665. 10.3390/ijms242115665. . PMID: 37958649; PMCID: PMC10649397.
17. Jurkiewicz M, Szczurek-Wasilewicz W, Skrzypek M, Krych S, Gąsior M, Szyguła-Jurkiewicz B. Albumin-Bilirubin (ALBI) Score Predicts Long-Term Survival in Elderly Patients with Decompensated Heart Failure. *J Clin Med.* 2025;14(3):808. 10.3390/jcm14030808. . PMID: 39941479; PMCID: PMC11818102.
18. Halim C, Teruna BP, Harahap IR, Fernando ET, Nugroho LBC. Coagulation biomarkers as prognostic indicators in heart failure: A systematic review and meta-analysis of 14,773 patients. *Glob Cardiol Sci Pract.* 2025;2025(4):e202541. 10.21542/gcsp.2025.41. . PMID: 41978707; PMCID: PMC13070239.
19. Huang L, Liang L, Tian P, Zhao L, Chen Y, Huang Y, Zhou Q, Zhai M, Zhang Y, Ambrosio G, Zhang J. D-dimer and outcomes in hospitalized heart failure patients across the ejection fraction phenotypes.

- ESC Heart Fail. 2022;9(5):3060–70. Epub 2022 Jun 23. PMID: 35747927; PMCID: PMC9715882.
20. Jiang J, Miao P, Xin G. Prognostic value of albumin-based indices for mortality after heart failure: a systematic review and meta-analysis. *BMC Cardiovasc Disord.* 2024;24(1):570. 10.1186/s12872-024-04244-9. . PMID: 39420315; PMCID: PMC11484320.
21. Ghazal M, Khalife WI. Hypoalbuminemia in heart failure: pathophysiology, clinical implications, and management strategies. *Heart Fail Rev.* 2025;30(6):1407–14. 10.1007/s10741-025-10558-3. . Epub 2025 Sep 6. PMID: 40913686.
22. Barbiero R, Baccillieri M, Santagata D, Biancucci M, Pennella B, Tangianu F, Nicolini E, Maresca AM, Dentali F, Bonaventura A. Lower albumin levels are associated with 1-year mortality in older patients hospitalized for acute heart failure: THE ALBIMED-HF study. *Intern Emerg Med.* 2025;20(3):805–16. 10.1007/s11739-025-03882-x. . Epub 2025 Feb 13. PMID: 39948326.
23. Ibrahim NE, Januzzi JL Jr.. NT-proBNP Concentrations in the Community: Elevation, Deficiency, and Everything in Between. *JACC Heart Fail.* 2024;12(1):64–6. 10.1016/j.jchf.2023.08.014. . Epub 2023 Sep 20. PMID: 37737761.
24. White A, Huang S, Agrawal V, Bachmann KN, Brittain EL, Dixon DD, Dupuis L, Garner E, Schlendorf K, Wang TJ, Gupta DK. Body Mass Index, Left Ventricular Wall Stress, and NT-proBNP in Elderly Adults. *JACC Adv.* 2026;5(2):102564. Epub 2026 Jan 21. PMID: 41570791; PMCID: PMC12859251.

Tables

Table 1

Data are presented as mean $\pm$ SD for normally distributed variables and median (IQR) for non-normally distributed variables.

Characteristic	EF $\geq$ 45% (n = 189)	EF < 45% (n = 149)	p-value
Demographics			
Age, years	60.0 $\pm$ 13.0	65.0 $\pm$ 15.0	0.001
Male sex, n (%)	158 (83.6)	112 (75.2)	0.05
BMI, kg/m ²	26.4 $\pm$ 4.6	25.0 $\pm$ 5.9	0.017
Cardiac Biomarker			
NT-proBNP, pg/mL	511 (134–1,729)	3,586 (1,463–8,822)	< 0.001
BDA Index Components			
Total bilirubin, μ mol/L	15.5 (12.2–20.7)	20.2 (17.7–27.9)	< 0.001
D-dimer, ng/mL	152 (103–264)	353 (228–686)	< 0.001
Albumin, g/L	38.6 (36.4–40.5)	33.8 (31.3–36.4)	< 0.001
Renal Function			
Creatinine, μ mol/L	72.9 (63.6–86.0)	88.9 (78.1–112.7)	0.008
eGFR, mL/min/1.73m ²	92.8 (75.5–103.0)	74.8 (52.2–88.9)	< 0.001
Metabolic and Hematologic			
LDL cholesterol, mmol/L	2.59 (2.09–3.22)	2.03 (1.56–2.64)	< 0.001
Hemoglobin, g/L	142 (130–153)	137 (117–149)	0.003
WBC count, $\times 10^3/\mu$ L	9.2 (7.3–12.0)	7.6 (5.9–8.9)	0.003
Novel Index			
NJCI index	0.36 (0.30–0.43)	0.53 (0.47–0.61)	< 0.001

BMI: body mass index; NT-proBNP: N-terminal pro-B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; LDL: low-density lipoprotein; WBC: white blood cell; NJCI: bilirubin–D-dimer–albumin index.

NJCI = LN(total bilirubin [μ mol/L]) $\times$ LN(D-dimer [ng/mL]) / albumin [g/L].

Table 2
Univariate Binary Logistic Regression Analysis for Predictors of Reduced Ejection Fraction
(EF < 45%)

Variable	B	SE	Wald χ^2	OR (95% CI)	p-value
NJCI (per 0.1-unit increase)	1.783	0.197	81.67	5.95 (4.04–8.76)	< 0.001
Ln D-dimer (per 1 Ln-unit)	1.338	0.175	58.35	3.81 (2.70–5.37)	< 0.001
Ln NT-proBNP (per 1 Ln-unit)	0.615	0.080	59.58	1.85 (1.58–2.16)	< 0.001
Total bilirubin (per 1 $\mu\text{mol/L}$)	0.090	0.016	32.63	1.09 (1.06–1.13)	< 0.001
Creatinine (per 10 $\mu\text{mol/L}$)	0.043	0.018	5.72	1.04 (1.01–1.08)	0.017
Age (per 1 year)	0.026	0.008	10.20	1.03 (1.01–1.04)	0.001
Hemoglobin (per 1 g/L)	−0.014	0.005	8.40	0.99 (0.98–1.00)	0.004
WBC (per 1 $\times 10^3/\mu\text{L}$)	−0.097	0.033	8.81	0.91 (0.85–0.97)	0.003
BMI (per 1 kg/m^2)	−0.058	0.024	5.70	0.94 (0.90–0.99)	0.017
GFR (per 1 mL/min/1.73m^2)	−0.026	0.005	29.31	0.97 (0.97–0.98)	< 0.001
LDL (per 1 mmol/L)	−0.560	0.134	17.35	0.57 (0.44–0.74)	< 0.001
Albumin (per 1 g/L)	−0.336	0.040	70.68	0.71 (0.66–0.77)	< 0.001
Male sex (vs. Female)	−0.521	0.273	3.64	0.59 (0.35–1.01)	0.05

B: unstandardized regression coefficient; SE: standard error; OR: odds ratio; CI: confidence interval; NJCI: Novel Junctional Cardiometabolic Index; Ln: natural logarithm; NT-proBNP: N-terminal pro-B-type natriuretic peptide; WBC: white blood cell; BMI: body mass index; GFR: glomerular filtration rate; LDL: low-density lipoprotein.

Variables are ordered by descending OR magnitude

Figures

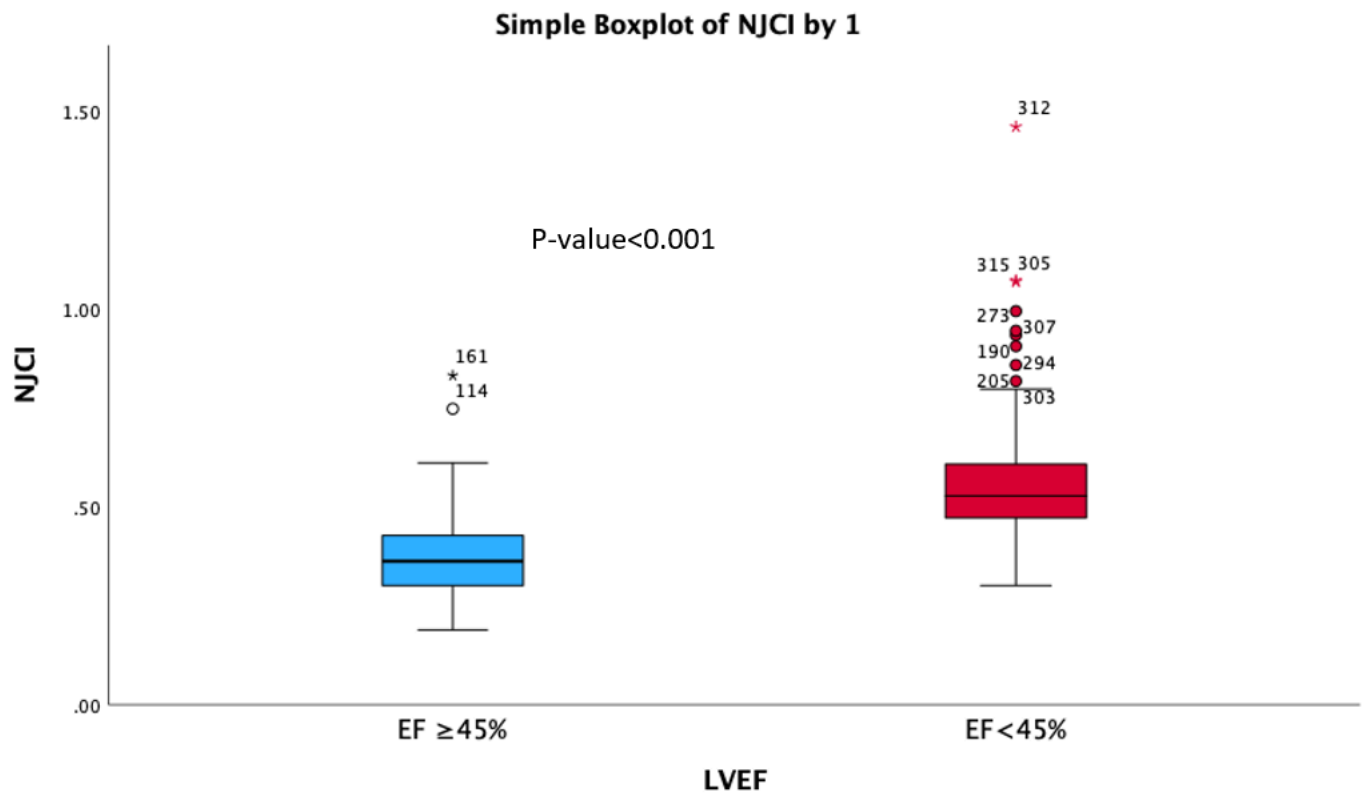


Figure 1

Distribution of NJCI according to left ventricular ejection fraction (LVEF) category.

Boxplots compare NJCI values between patients with LVEF $\geq 45\%$ and those with LVEF $< 45\%$. The central line within each box represents the median, while the box boundaries indicate the interquartile range (IQR). Whiskers represent the range of non-outlying observations, and circles indicate outliers. Patients with LVEF $< 45\%$ exhibited significantly higher NJCI values compared with those with LVEF $\geq 45\%$ ($p < 0.001$).

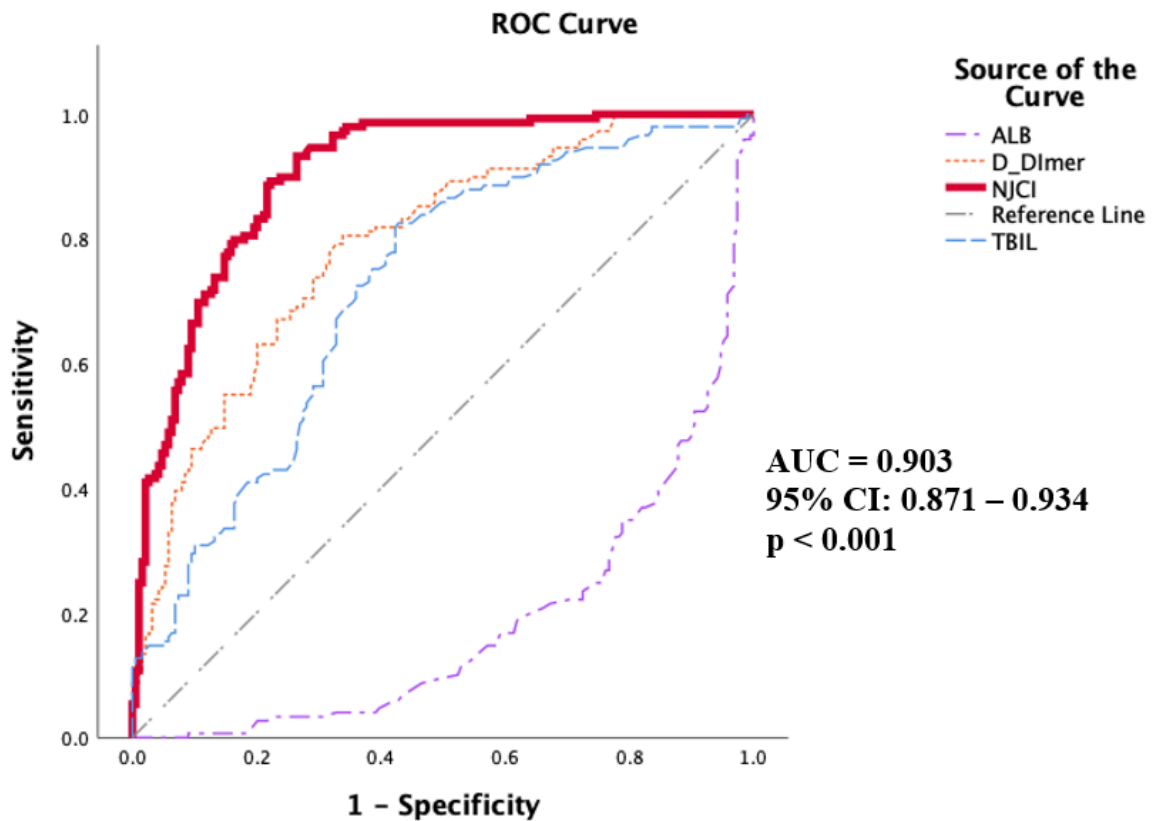


Figure 2

Receiver Operating Characteristic (ROC) Curves of NJCI and Its Individual Components for Identifying Reduced Left Ventricular Ejection Fraction

Receiver operating characteristic (ROC) curve of the NJCI for identifying reduced left ventricular ejection fraction (EF <45%). The area under the curve (AUC) is 0.903 (95% confidence interval: 0.871–0.934; p < 0.001). The dashed diagonal line represents a non-discriminating test (AUC = 0.5). NJCI = Novel Junctional Cardiometabolic Index

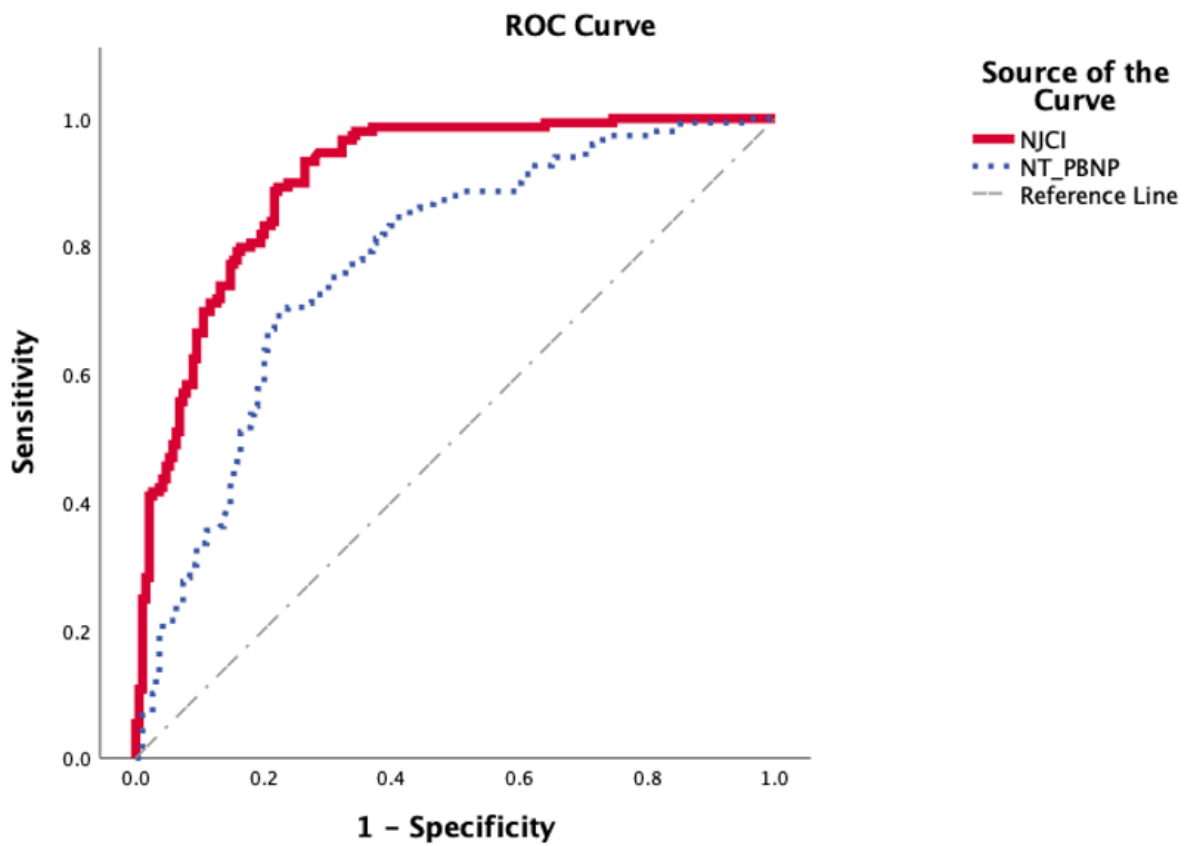


Figure 3

Receiver Operating Characteristic (ROC) Curves of NJCI and NT-proBNP for Identifying Reduced Left Ventricular Ejection Fraction in Patients with Heart Failure

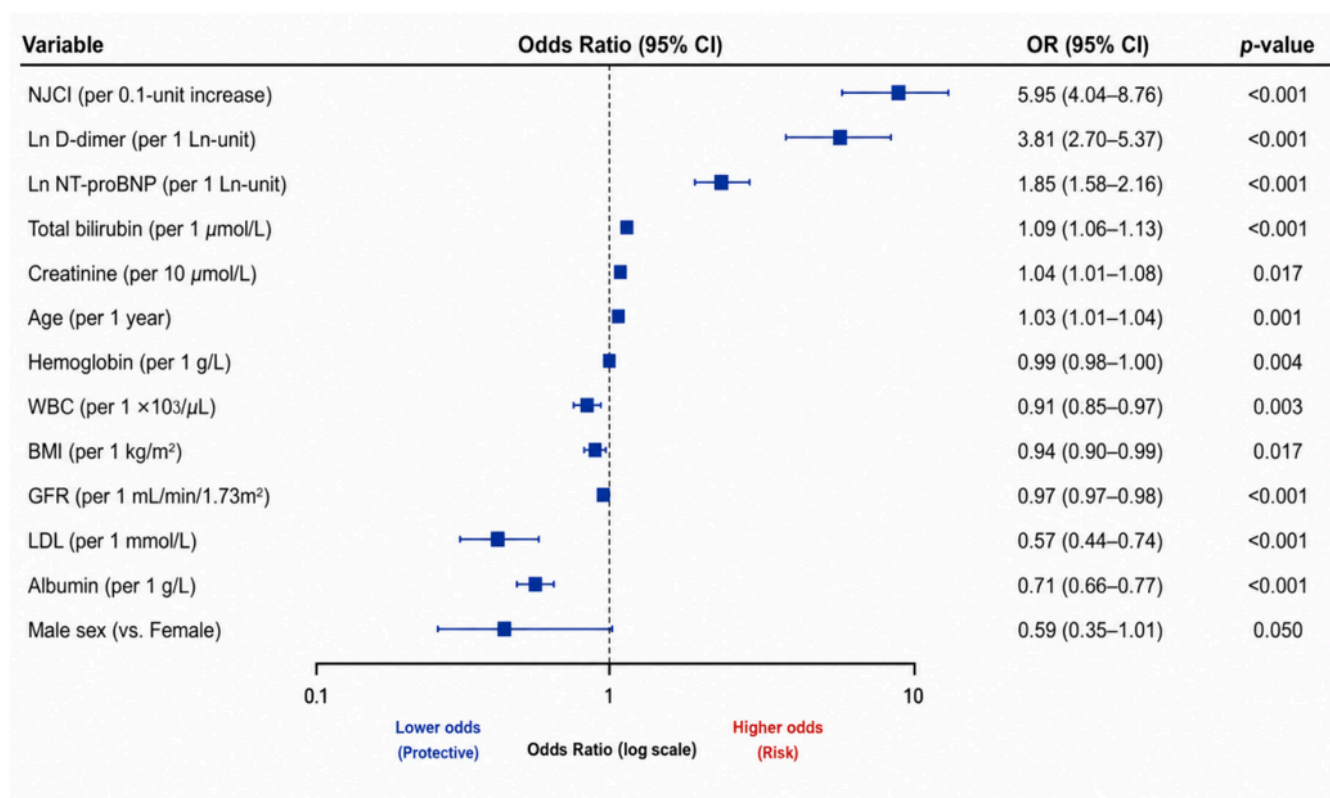


Figure 4

Forest plot of univariable logistic regression analysis for factors associated with reduced left ventricular ejection fraction (LVEF <45%)

Squares represent odds ratios (ORs), and horizontal lines indicate 95% confidence intervals (CIs). The vertical dashed line corresponds to an OR of 1.0, indicating no association with reduced LVEF. Variables located to the right of the reference line are associated with increased odds of reduced LVEF, whereas variables located to the left are associated with decreased odds. NJCI demonstrated the strongest association with reduced LVEF among all evaluated predictors (OR 5.95, 95% CI 4.04–8.76, $p < 0.001$).

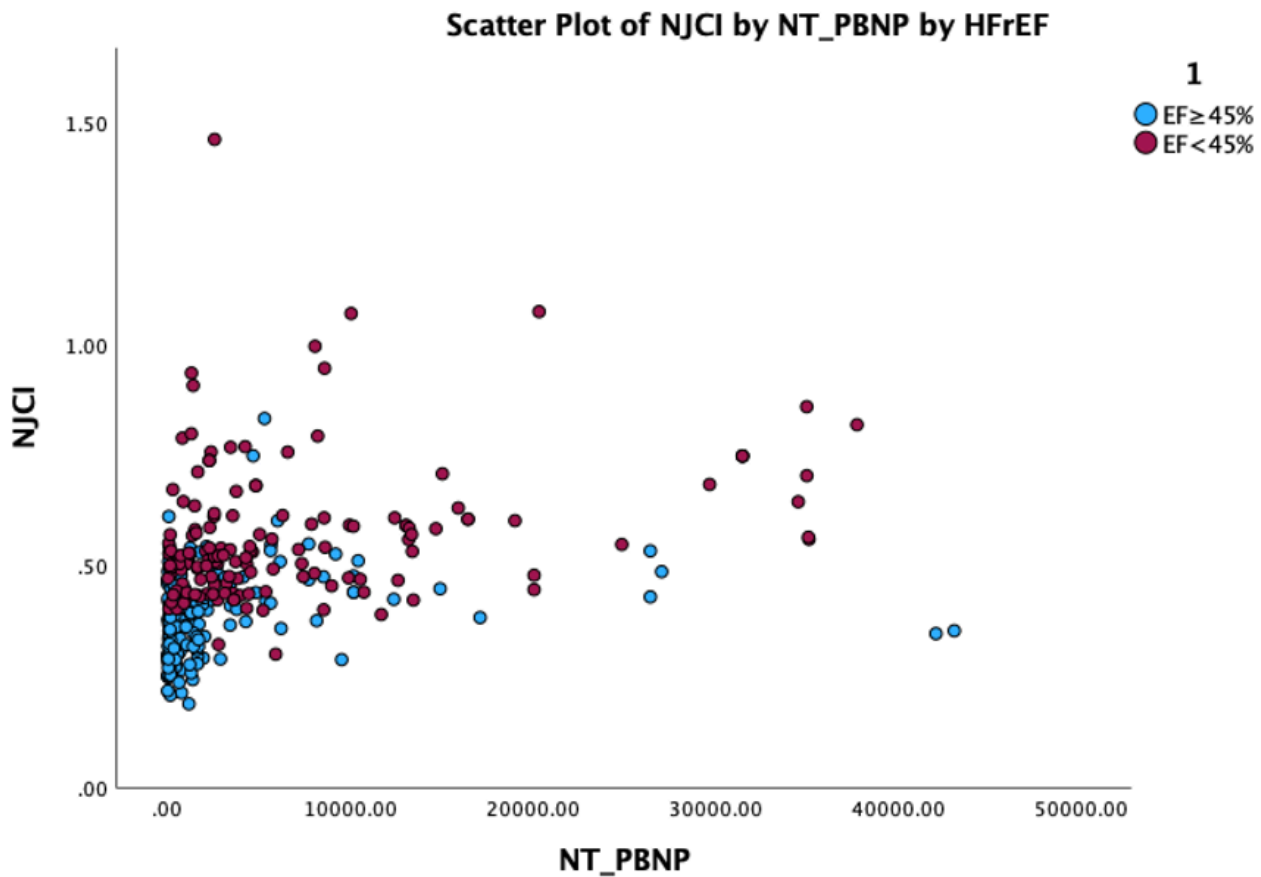


Figure 5

Scatter plot showing the relationship between NJCI and NT-proBNP according to left ventricular ejection fraction (LVEF) category.

Each point represents an individual patient. Blue circles indicate patients with LVEF $\geq 45\%$, whereas red circles indicate patients with LVEF $< 45\%$. Patients with reduced LVEF tended to exhibit higher NJCI values across a broad range of NT-proBNP concentrations. A positive clustering of higher NJCI values was observed among patients with elevated NT-proBNP levels, suggesting a potential association between increased systemic congestion/inflammation and impaired left ventricular systolic function.

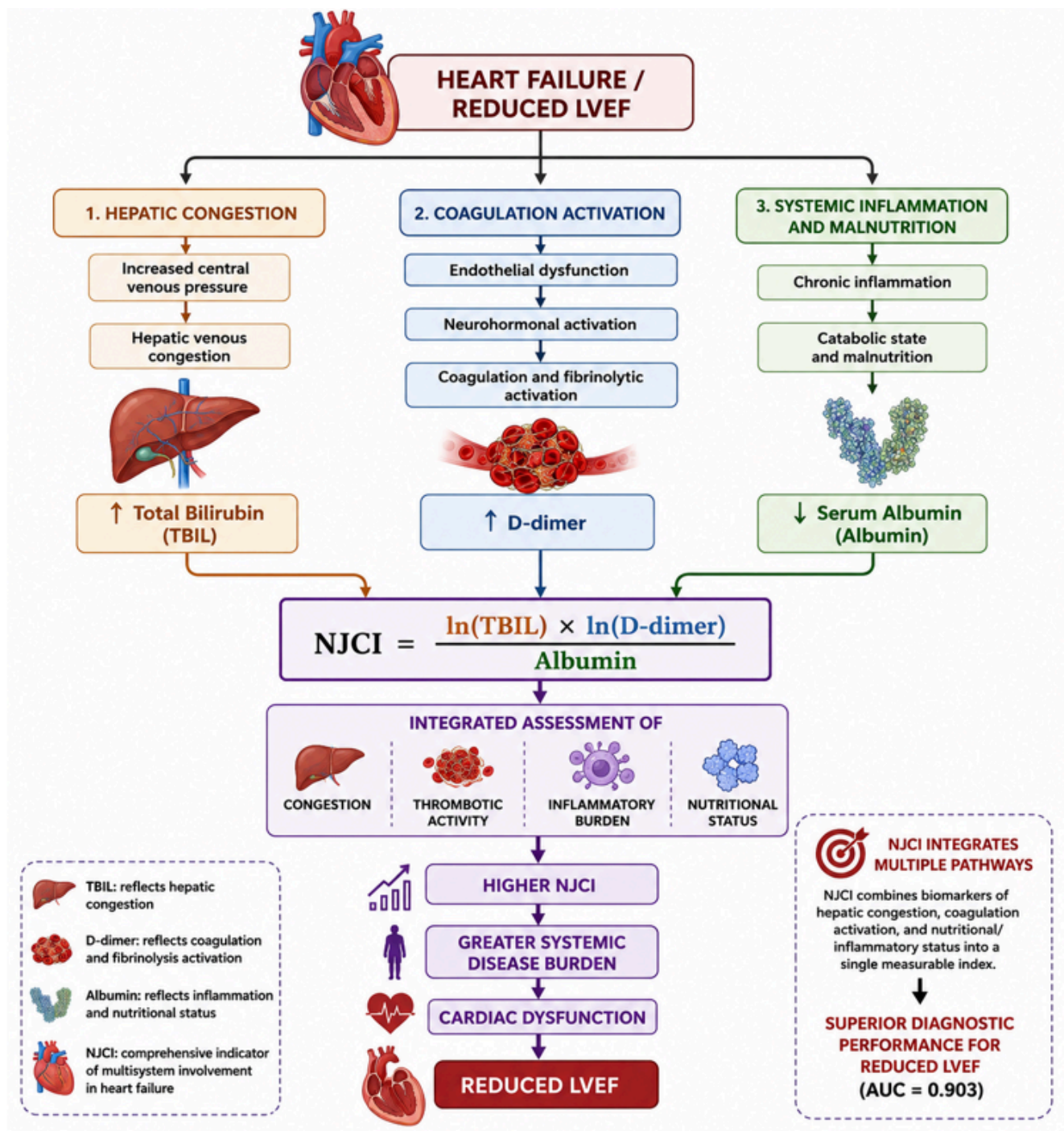


Figure 6

Proposed pathophysiological mechanisms linking NJCI to reduced left ventricular ejection fraction (LVEF).

Heart failure is associated with hepatic congestion, systemic inflammation, and activation of coagulation pathways. Hepatic congestion results in elevated total bilirubin levels, whereas systemic inflammation contributes to reduced serum albumin concentrations. Simultaneously, activation of coagulation and fibrinolytic pathways leads to increased D-dimer levels. NJCI integrates these three pathophysiological domains through the formula $\ln(\text{total bilirubin}) \times \ln(\text{D-dimer}) / \text{albumin}$. Elevated NJCI

values may therefore reflect the combined burden of congestion, inflammation, and thrombogenic activity, which are associated with worsening cardiac function and reduced LVEF.