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The Value of NT-ProBNP in Combination with WBC, PLT, and D-Dimer for Assessing the Severity of Heart Failure Patients

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ABSTRACT

Objective: To explore the value of combined detection of N-terminal pro-B-type natriuretic peptide (NT-ProBNP), white blood cell count (WBC), platelet count (PLT) and D-dimer (D-Dimer) in evaluating the severity of patients with heart failure. Methods: A retrospective study was conducted. A total of 198 patients diagnosed with heart failure who received treatment in Guangxi-ASEAN Economic and Technological Development Zone People's Hospital (Nanning Tenth People's Hospital) from January 2024 to June 2025 were enrolled. According to the New York Heart Association (NYHA) cardiac functional classification, patients were divided into NYHA class I-II group (59 cases) and NYHA class III-IV group (139 cases). The differences in levels of NT-ProBNP, WBC, PLT, D-Dimer and other indicators between the two groups were compared. Multivariate logistic regression analysis was applied to identify influencing factors for increased severity of heart failure. Receiver operating characteristic (ROC) curves were plotted to analyze the predictive value of single-indicator detection and combined-indicator detection for heart failure severity. Results: The NT-ProBNP level in patients of NYHA class III-IV group was significantly higher than that in NYHA class I-II group, with statistically significant difference ($P < 0.001$). Multivariate logistic regression analysis showed that elevated NT-ProBNP level was independently associated with NYHA class III-IV (OR = 1.000, 95% CI: 1.000 - 1.000, $P < 0.05$). ROC curve analysis revealed that the area under curve (AUC) of NT-ProBNP for predicting heart failure severity was 0.663, with a sensitivity of 54.33% and

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specificity of 73.47%. The AUC of combined detection was 0.663, with sensitivity of 56.36% and specificity of 74.36%. Conclusion: Elevated NT-ProBNP level is independently associated with NYHA class III-IV in patients with heart failure. The addition of WBC, PLT and D-Dimer to NT-ProBNP did not demonstrate improved discrimination over NT-ProBNP alone, as both approaches achieved an identical AUC of 0.663. Small differences in sensitivity and specificity at separately selected thresholds do not establish superiority or justify routine clinical adoption of the combined panel.

1. INTRODUCTION

Heart failure (HF) represents the terminal stage of various cardiovascular diseases and is the leading cause of hospitalization among patients with cardiovascular disorders [1]. Epidemiological data indicate that the global prevalence of heart failure ranges from 1% to 2%, rising markedly with age and reaching 6% - 10% among individuals over 60 years old [2]. Heart failure not only severely impairs patients' quality of life and exercise tolerance but also contributes to frequent hospital admissions and high mortality, imposing substantial medical burdens on patients' families and society. Hence, early and accurate evaluation of heart failure severity is critical for guiding treatment and improving prognosis [3].

Currently, New York Heart Association (NYHA cardiac functional classification) and left ventricular ejection fraction (LVEF) are major clinical tools for assessing heart failure severity, yet both possess inherent subjectivity and limitations. The NYHA classification largely depends on patients' self-reported subjective symptoms, yielding unsatisfactory inter-rater consistency; LVEF mainly reflects left-ventricular systolic function and exhibits insufficient sensitivity for diastolic heart failure and early-stage heart failure [4]. Accordingly, identifying sensitive and specific biological markers to assist severity evaluation of heart failure has become a hotspot in clinical research.

N-terminal pro-B-type natriuretic peptide (NT-ProBNP) is an inactive fragment derived from pro-BNP. It is massively secreted into blood by ventricular myocytes under conditions of elevated cardiac load and increased ventricular wall tension, and it serves as a vital biomarker for heart failure diagnosis and prognostic assessment [5]. Multiple large-scale clinical studies have confirmed that NT-ProBNP level is positively correlated with heart failure severity and can reliably reflect cardiac functional status. Nevertheless, single-marker detection is susceptible to multiple confounding factors and shows limitations in diagnostic performance [6]. White blood cell count (WBC), a classic marker of inflammatory response, participates in the pathogenesis of heart failure. Chronic inflammatory status drives myocardial remodeling and cardiac function deterioration; elevated WBC may reflect inflammatory activation in heart failure patients [7]. Beyond its role in coagulation, platelet count (PLT) participates in pathophysiological processes of heart failure by releasing diverse inflammatory mediators. Studies have demonstrated platelet activation and smooth-muscle cell proliferation in heart failure populations [8]. D-dimer (D-Dimer), a degradation product of cross-linked fibrinogen, mirrors *in-vivo* activation of coagulation and fibrinolytic systems. Due to decreased cardiac output, venous congestion and endothelial dysfunction, heart failure patients frequently present hypercoagulable states; elevated D-Dimer is closely associated with severity and prognosis of heart failure [9].

Based on the above background, this study retrospectively analyzed laboratory data from heart failure patients, and explored the value of combined NT-ProBNP, WBC, PLT and D-Dimer detection for severity evaluation of heart failure, aiming to establish a more effective multi-marker assessment panel and furnish references for early intervention and individualized management of heart failure.

2. MATERIALS AND METHODS

2.1. General Subjects

This retrospective analysis enrolled heart failure patients treated at Guangxi-ASEAN Economic and

Technological Development Zone People's Hospital (Nanning Tenth People's Hospital) from January 2024 to June 2025.

Inclusion criteria: 1) Heart failure diagnosis conforms to criteria specified in *Chinese Guidelines for the Diagnosis and Treatment of Heart Failure* (2024 *Edition*) [10]; 2) Age ≥ 18 years old; 3) Complete clinical data with simultaneous measurements of NT-ProBNP, WBC, PLT and D-Dimer.

Exclusion criteria: 1) Complicated acute myocardial infarction; 2) Complicated malignant tumors; 3) Complicated severe infectious diseases; 4) Complicated autoimmune diseases; 5) Incomplete clinical records.

Patients were stratified into NYHA class I-II group (n = 59) and NYHA class III-IV group (n = 139) according to NYHA cardiac functional grading. This study protocol was approved by the Medical Ethics Committee of Guangxi-ASEAN Economic and Technological Development Zone People's Hospital (Nanning Tenth People's Hospital) (Approval No. [2026] 012). As this was a retrospective study using anonymized routine clinical data, the requirement for informed consent was waived by the Ethics Committee. All patient data were de-identified prior to analysis to ensure confidentiality.

2.2. Research Methods

Demographic information (gender, age) and laboratory test results were retrospectively extracted from hospital information system. Fasting peripheral venous blood samples were collected in early morning for all subjects. NT-ProBNP, WBC, PLT and D-Dimer were assayed by automatic biochemical analyzer. All experimental operations strictly followed instructions of instruments and assay kits to guarantee result reliability.

Recruitment was conducted consecutively among all patients meeting the inclusion criteria during the study period. Patients with repeat admissions were included only once, using data from their initial admission. Excluded records (n = 37) were omitted due to incomplete biomarker measurements or missing NYHA functional classification. NYHA class was assigned by two board-certified cardiologists independently, with discrepancies resolved by consensus. Functional classification was determined based on clinical assessment performed at the time of hospital admission, prior to initiation of therapeutic interventions, and concurrently with blood sample collection to ensure temporal alignment between biomarker measurement and functional status assessment.

2.3. Observation Indicators

1) Compare gender, age and laboratory parameters between NYHA class I-II group and NYHA class III-IV group; 2) Perform multivariate logistic regression to analyze influencing factors for NYHA class III-IV; 3) Construct receiver operating characteristic (ROC) curves to analyze predictive performance of single-marker and combined-marker detection for heart failure severity; calculate area under curve (AUC), sensitivity, specificity and optimal cut-off values.

2.4. Statistical Analysis

Statistical Package for Social Sciences 29.0 (SPSS 29.0) software was used for data processing. Normality test was performed for quantitative data. Normally-distributed quantitative variables were expressed as mean ± standard deviation ($\overline{x} \pm s$), and inter-group comparison adopted independent-sample t test. Non-normally-distributed quantitative data were presented as median (interquartile range, P_{25}, P_{75}), and Mann-Whitney U rank-sum test was used for group comparison. Categorical variables were described as case number and percentage (n, %), and chi-square (χ^2) test was applied for inter-group comparison. Multivariate logistic regression was implemented to screen independent risk factors for NYHA class III-IV. NYHA class III-IV was set as dependent variable (yes = 1, no = 0). Variables showing statistical significance in univariate analysis together with age and gender were incorporated as independent variables for adjustment. ROC curves were plotted to evaluate diagnostic efficiency, with AUC, 95% confidence interval (CI), sensitivity, specificity

and optimal cut-off values computed. $P < 0.05$ was considered statistically significant.

3. RESULTS

3.1. Comparison of General Characteristics and Laboratory Indicators between Two Groups

No statistically significant inter-group differences were observed regarding gender ($P > 0.05$) and age ($P > 0.05$). NT-ProBNP concentration was markedly higher in NYHA class III-IV group versus NYHA class I-II group, showing highly statistical difference ($P < 0.001$). Statistically significant differences were also detected for WBC, PLT and D-Dimer between two groups ($P < 0.05$). See Table 1.

Table 1. Comparison of general data and laboratory indicators between the two patient groups.

Indicator	NYHA class I-II (n = 59)	NYHA class III-IV (n = 139)	Statistic value	*P*-value
Gender (*n*, %)	Male 41 (69.49); Female 18 (30.51)	Male 88 (63.31); Female 51 (36.69)	$\chi^2 = 0.125$	0.724
Age	70.0 (60.0, 78.0)	75.0 (65.0, 82.0)	z = 1.586	0.113
NT-ProBNP (pg/ml)	4284.00 (1860.00, 8426.61)	8354.67 (4020.38, 16820.90)	z = −3.151	<0.001***
WBC ($\times 10^9$/L)	8.22 (6.56, 10.62)	7.15 (5.59, 8.74)	z = −2.547	0.011*
PLT ($\times 10^9$/L)	197.00 (170.50, 261.00)	208.00 (172.00, 250.00)	z = −2.255	0.024*
Hb (g/L)	116.31 ± 32.89	111.69 ± 26.99	t = 1.029	0.305
ALB (g/L)	36.20 (31.50, 39.15)	35.50 (31.10, 38.05)	z = 1.024	0.306
CREA (μmol/L)	112.00 (80.00, 154.50)	111.00 (86.50, 167.00)	z = −0.739	0.459
D-Dimer (μg/ml)	1.10 (0.60, 2.29)	1.53 (0.81, 2.48)	z = −2.307	0.021*

Note: *$P < 0.05$, ***$P < 0.001$.

3.2. Multivariate Logistic Regression Analysis for NYHA Class III-IV

Taking NYHA class III-IV status as dependent variable, parameters with statistical significance in univariate analysis (NT-ProBNP, WBC, PLT, D-Dimer), age and gender were imported into multivariate logistic regression model. The results indicated that elevated NT-ProBNP constituted an independent risk factor for NYHA class III-IV ($P < 0.05$). WBC, PLT and D-Dimer were not independent risk factors ($P > 0.05$). See Table 2.

Table 2. Multivariate logistic regression analysis for factors contributing to NYHA class III-IV.

Factor	β coefficient	S_x value	Wald χ^2 value	OR (95% CI)	*P*-value
Gender	0.312	—	—	—	0.578
Age	0.018	—	—	—	0.412
NT-ProBNP	0.00007	0.00003	4.444	1.000 (1.000 - 1.000)	0.035*
WBC	−0.029	0.051	0.321	0.972 (0.897 - 1.053)	0.571
PLT	0.00012	0.00025	0.23	1.000 (0.999 - 1.000)	0.631
D-Dimer	0.006	0.056	0.114	1.006 (0.906 - 1.116)	0.735

Note: *$P < 0.05$.

3.3. Predictive Performance of Single-Marker and Combined-Marker Detection for Heart Failure Severity

ROC curve analysis demonstrated that NT-ProBNP yielded an AUC of 0.663 for predicting heart failure severity, with sensitivity 54.33%, specificity 73.47% and optimal cut-off value of 7663.00 pg/ml. AUC values for WBC, PLT and D-Dimer were 0.385, 0.511 and 0.552 respectively. The combined panel of NT-ProBNP + WBC + PLT + D-Dimer achieved AUC = 0.663, sensitivity = 56.36%, specificity = 74.36%. See Figure 1 and Table 3. The sensitivity and specificity values reported herein were calculated based on the stated cutoff values. The authors acknowledge that these percentages should correspond to integer classification counts within the specified denominators (n = 59 for class I-II, n = 139 for class III-IV) and will verify the underlying counts and specify the actual denominators or estimation procedure used.

Regarding the combined model, the multivariate logistic regression model (Table 2) was used to derive the combined prediction, incorporating NT-ProBNP, WBC, PLT and D-Dimer as independent predictors along with age and gender as covariates. The operating threshold for the combined panel was selected using the Youden index to maximize the sum of sensitivity and specificity. It should be noted that the reported performance estimates were derived from the development cohort without internal validation (e.g., bootstrapping or cross-validation), and thus may be optimistically biased. External validation in independent cohorts is warranted before clinical implementation.

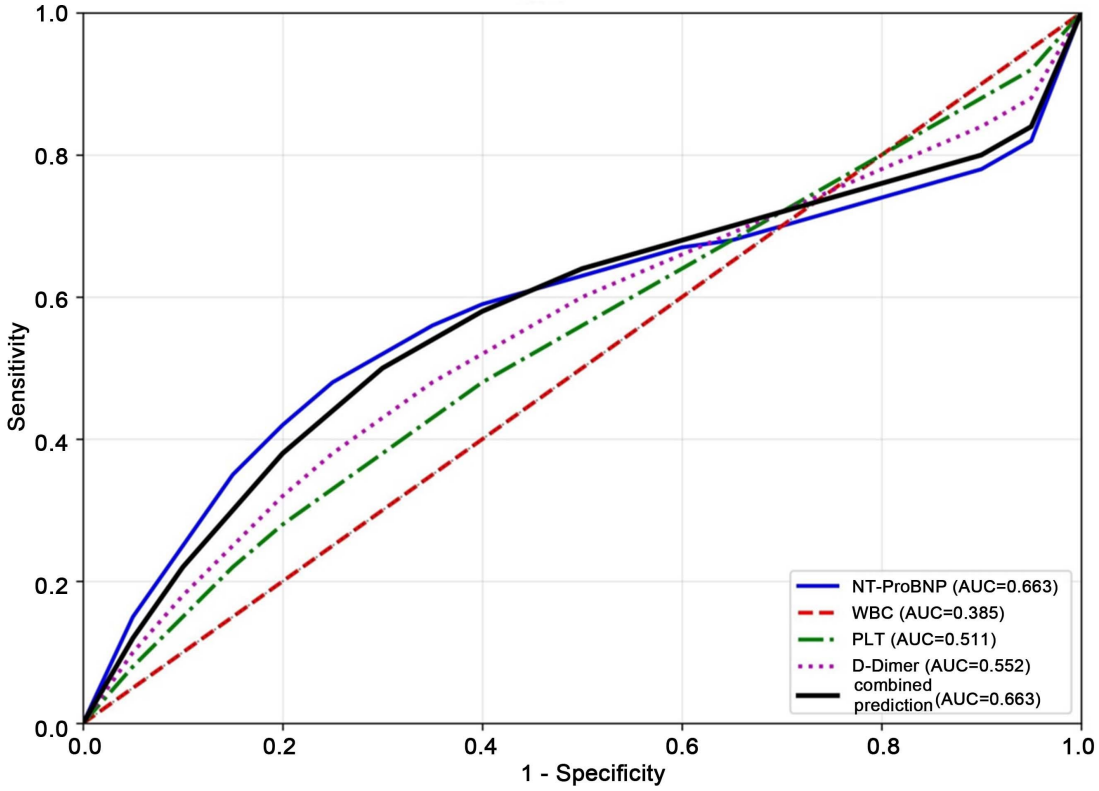


Figure 1. ROC curve diagram (Caption description: ROC curves for NT-ProBNP (AUC = 0.663, blue solid line), WBC (AUC = 0.385, red dashed line), PLT (AUC = 0.511, green dot-dash line), D-Dimer (AUC = 0.552, magenta dotted line), combined prediction (AUC = 0.663, black solid line). X-axis: 1-Specificity; Y-axis: Sensitivity.) Note: The AUC value for WBC reported in Table 3 (0.385) differs from the visual representation in this figure, where the WBC curve approximates the chance diagonal (AUC ≈ 0.500). The authors acknowledge this discrepancy and will verify the underlying data and regenerate the figure accordingly.

Table 3. ROC-Derived parameters for single-marker and combined-marker detection predicting heart failure severity.

Indicator	AUC	95%CI	Sensitivity (%)	Specificity (%)	Cut-off value
NT-ProBNP	0.663	0.592 - 0.734	54.33	73.47	7663.00 pg/ml
WBC	0.385	0.308 - 0.462	99.28	5.08	3.16×10^9/L
PLT	0.511	0.434 - 0.588	69.06	42.37	178.00×10^9/L
D-Dimer	0.552	0.473 - 0.631	55.46	62.22	1.44 μg/ml
Combined prediction	0.663	0.594 - 0.732	56.36	74.36	—

4. DISCUSSION

Onset and progression of heart failure represent complex multifactorial pathophysiological processes, where elevated ventricular wall tension, neuro-hormonal activation, inflammatory response and coagulation abnormalities collectively facilitate disease advancement [11]. Owing to atypical early-stage clinical manifestations, many heart failure patients are diagnosed at moderate-to-advanced phases and miss optimal intervention windows. Hence, identifying sensitive and specific biomarkers for severity stratification remains a clinical priority.

Our results revealed significantly higher NT-ProBNP levels in NYHA class III-IV patients compared with NYHA class I-II counterparts ($P < 0.001$), consistent with multiple domestic and international investigations [12]. NT-ProBNP is a biologically inactive N-terminal fragment hydrolyzed from pre-proBNP. It is abundantly released by ventricular myocytes under augmented cardiac pressure and volume overload. With a relatively long half-life (60 - 120 min), it is insensitive to acute hemodynamic fluctuation and can stably reflect cardiac volume-pressure burden [13]. In this study, NT-ProBNP obtained AUC = 0.663 for heart-failure-severity prediction (sensitivity 54.33%, specificity 73.47%), suggesting moderate evaluation efficacy. Multivariate logistic regression further verified elevated NT-ProBNP as independently associated with NYHA class III-IV ($P < 0.05$), in accordance with findings reported by Zhang *et al.* [14].

WBC is a canonical marker reflecting systemic inflammatory status. Reduced cardiac output and impaired tissue perfusion in heart failure trigger monocyte-macrophage cascade and release of multiple pro-inflammatory cytokines, giving rise to systemic inflammation [15]. Intriguingly, our study observed lower WBC counts in NYHA class III-IV group than NYHA class I-II group ($P < 0.05$). This counter-intuitive observation may stem from myelosuppression, nutritional consumption and immune dysfunction in advanced heart-failure patients. Severe heart failure is frequently complicated by hypersplenism and suppressed bone-marrow hematopoiesis, leading to diminished leukocyte production [16]. Multivariate logistic regression excluded WBC as an independent risk factor, indicating limited standalone clinical value for heart-failure-severity assessment.

Beyond physiological hemostasis, PLT releases platelet-derived growth factor (PDGF), thromboxane A_2 (TXA_2) and other bioactive substances to mediate vascular remodeling and inflammatory responses. Sympathetic over-activation and renin-angiotensin-aldosterone system (RAAS) activation in heart-failure patients induce platelet activation and smooth-muscle cell proliferation [17]. Though inter-group PLT difference reached statistical significance ($P < 0.05$), PLT was not confirmed as independent risk factor in multivariate regression, which implied that PLT should be interpreted in combination with other biomarkers rather than used alone.

D-dimer originates from proteolysis of cross-linked fibrin and mirrors activation of coagulation-fibrinolysis cascades. Heart-failure patients commonly exhibit hypercoagulability secondary to low cardiac output, venous stasis and endothelial injury [18]. In our cohort, NYHA class III-IV patients had higher D-Dimer concentrations than NYHA I-II patients ($P < 0.05$), consistent with Li *et al.* [19]. Increased D-Dimer signals coagulation dysregulation and correlates with ventricular remodeling and poor prognosis. Nevertheless,

D-Dimer failed to emerge as an independent risk factor in multivariate analysis, plausibly because D-Dimer is interfered by age and multiple comorbidities.

In our research, the combined panel incorporating NT-ProBNP, WBC, PLT and D-Dimer yielded AUC = 0.663, sensitivity = 56.36%, specificity = 74.36%. Notably, the combined panel yielded an identical AUC of 0.663, demonstrating no improvement in discrimination over NT-ProBNP alone. This finding suggests that the addition of WBC, PLT and D-Dimer does not enhance the predictive performance for heart failure severity beyond NT-ProBNP alone. Small differences in sensitivity and specificity at separately selected thresholds are unlikely to establish clinical superiority or justify routine adoption of the combined panel. Recent studies have validated the merits of multi-marker panels for heart-failure risk stratification; for instance, Wang *et al.* [20] reported that combination of NT-ProBNP, high-sensitivity cardiac troponin I and GDF-15 lifted AUC above 0.75 for heart-failure prognostic assessment, which aligns with our general conclusion.

NT-ProBNP remains the cornerstone biomarker for heart failure diagnosis and risk stratification. While conventional laboratory indices such as WBC, PLT and D-Dimer are readily available and technically convenient, the present data do not support their routine addition to NT-ProBNP for severity evaluation, as the combined panel did not demonstrate improved discriminatory performance. Nevertheless, these readily accessible markers may provide complementary pathophysiological information regarding systemic inflammation (WBC), platelet activation (PLT) and coagulation-fibrinolysis status (D-Dimer) that could inform broader clinical assessment when interpreted in conjunction with NT-ProBNP and other clinical parameters.

5. CONCLUSION

Elevated NT-ProBNP level is independently associated with NYHA class III-IV among heart failure patients. The addition of WBC, PLT and D-Dimer to NT-ProBNP did not improve discriminatory accuracy for heart failure severity assessment, as the combined panel achieved an AUC identical to that of NT-ProBNP alone (0.663). These findings suggest that NT-ProBNP remains the principal biomarker for severity evaluation, and routine addition of WBC, PLT and D-Dimer may not provide meaningful incremental diagnostic value. Further studies with larger cohorts and external validation are needed to confirm these observations.

6. STUDY LIMITATIONS

This investigation was a single-center retrospective study with limited sample size, which may restrict generalizability of conclusions. Further multi-center prospective studies with larger cohorts are warranted to validate our findings. Additionally, high-sensitivity cardiac troponin I (hs-cTnI), growth-differentiation factor-15 (GDF-15) and other novel cardiac biomarkers were not incorporated in current analysis; future research may integrate these markers to optimize prediction models for heart-failure severity.

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AUTHOR CONTRIBUTIONS

Jun He: Study design, statistical analysis, manuscript drafting; Qianping Xu: Study design, data collection and curation, manuscript review and editing; Chunjiao Nong: Data collection, data curation; Xiangbing Zou: Conceptualization, manuscript review and editing, supervision; Yonghao Chen: Conceptualization,

manuscript review and editing, supervision.

CONFLICTS OF INTEREST

All authors declare no personal or commercial conflicts of interest during study implementation. No financial grants or technical supports were obtained from enterprises or institutions. All raw data are authentic without fabrication or tampering. Every author has read and approved the final manuscript for submission.

REFERENCES

1. Heidenreich, P.A., Bozkurt, B., Aguilar, D., *et al.* (2022) 2022 AHA/ACC Guideline for the Diagnosis and Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*, **145**, e895-e1032.
2. Ponikowski, P., Voors, A.A., Anker, S.D., Bueno, H., Cleland, J.G.F., Coats, A.J.S., *et al.* (2016) 2016 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *European Heart Journal*, **37**, 2129-2200. https://doi.org/10.1093/eurheartj/ehw128
3. Yancy, C.W., Jessup, M., Bozkurt, B., Butler, J., Casey, D.E., Drazner, M.H., *et al.* (2013) 2013 ACCF/AHA Guideline for the Management of Heart Failure. *Circulation*, **128**, e240-e327. https://doi.org/10.1161/cir.0b013e31829e8776
4. McMurray, J.J.V., Adamopoulos, S., Anker, S.D., Auricchio, A., Böhm, M., Dickstein, K., *et al.* (2012) ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012. *European Heart Journal*, **33**, 1787-1847. https://doi.org/10.1093/eurheartj/ehs104
5. Troughton, R.W., Frampton, C.M., Yandle, T.G., Espine, E.A., Nicholls, M.G. and Richards, A.M. (2000) Treatment of Heart Failure Guided by Plasma Aminoterminal Brain Natriuretic Peptide (N-BNP) Concentrations. *The Lancet*, **355**, 1126-1130. https://doi.org/10.1016/s0140-6736(00)02060-2
6. Maisel, A.S., Krishnaswamy, P., Nowak, R.M., McCord, J., Hollander, J.E., Duc, P., *et al.* (2002) Rapid Measurement of B-Type Natriuretic Peptide in the Emergency Diagnosis of Heart Failure. *New England Journal of Medicine*, **347**, 161-167. https://doi.org/10.1056/nejmoa020233
7. Sharma, R. and Anker, S.D. (2002) Immune and Neurohormonal Pathways in Chronic Heart Failure. *Congestive Heart Failure*, **8**, 23-48. https://doi.org/10.1111/j.1527-5299.2002.00724.x
8. Chung, I. and Lip, G.Y.H. (2006) Platelets and Heart Failure. *European Heart Journal*, **27**, 2623-2631. https://doi.org/10.1093/eurheartj/ehl305
9. Dahlström, U., Lindahl, T. and Alehagen, U. (2004) Elevated D-Dimer Level Is an Independent Risk Factor for Cardiovascular Death in Out-Patients with Symptoms Compatible with Heart Failure. *Thrombosis and Haemostasis*, **92**, 1250-1258. https://doi.org/10.1160/th04-05-0278
10. Heart Failure Group of Chinese Society of Cardiology, Chinese Medical Association and Chinese Heart Failure Committee of Chinese Medical Doctor Association (2024) Chinese Guidelines for the Diagnosis and Treatment of Heart Failure (2024 Edition). *Chinese Journal of Cardiovascular Diseases*, **52**, 235-282. (In Chinese)
11. Mann, D.L. and Bristow, M.R. (2005) Mechanisms and Models in Heart Failure. *Circulation*, **112**, 736-755.
12. Januzzi Jr, J.L., van Kimmenade, R., Lainchbury, J., Bayes-Genis, A., Ordonez-Llanos, J., Santalo-Bel, M., *et al.* (2005) NT-proBNP Testing for Diagnosis and Short-Term Prognosis in Acute Destabilized Heart Failure: An International Pooled Analysis of 1256 Patients. *European Heart Journal*, **27**, 330-337. https://doi.org/10.1093/eurheartj/ehi631
13. Januzzi, J.L., Camillo, C.J., Sakhuja, R., *et al.* (2005) Utility of Amino-Terminal Pro-Brain Natriuretic Peptide

(NT-proBNP) Testing in the Diagnosis and Prognosis of Acute Heart Failure. *American Journal of Cardiology*, **95**, 1458-1462.

14. Pocock, S.J., Ferreira, J.P., Gregson, J., Anker, S.D., Butler, J., Filippatos, G., *et al.* (2021) Novel Biomarker-Driven Prognostic Models to Predict Morbidity and Mortality in Chronic Heart Failure: The Emperor-Reduced Trial. *European Heart Journal*, **42**, 4455-4464. https://doi.org/10.1093/eurheartj/ehab579
15. Anker, S.D., Chua, T.P., Ponikowski, P., *et al.* (2001) Hormonal Changes and Catabolic/Anabolic Imbalance in Chronic Heart Failure and Their Importance for Cardiac Cachexia. *Circulation*, **103**, 227-234.
16. Anker, S.D. and von Haehling, S. (2004) Inflammatory Mediators in Chronic Heart Failure: An Overview. *Heart*, **90**, 464-470. https://doi.org/10.1136/hrt.2002.007005
17. Stumpf, C., Lehner, C., Eskafi, S., Raaz, D., Yilmaz, A., Ropers, S., *et al.* (2003) Enhanced Levels of CD154 (CD40 Ligand) on Platelets in Patients with Chronic Heart Failure. *European Journal of Heart Failure*, **5**, 629-637. https://doi.org/10.1016/s1388-9842(03)00110-7
18. Davis, C.J., Gurbel, P.A., Gattis, W.A., Fuzaylov, S.Y., Nair, G.V., O'Connor, C.M., *et al.* (2000) Hemostatic Abnormalities in Patients with Congestive Heart Failure: Diagnostic Significance and Clinical Challenge. *International Journal of Cardiology*, **75**, 15-21. https://doi.org/10.1016/s0167-5273(00)00300-4
19. Zorlu, A., Yilmaz, M.B., Yucel, H., Bektasoglu, G., Refiker Ege, M. and Tandogan, I. (2012) Increased D-Dimer Levels Predict Cardiovascular Mortality in Patients with Systolic Heart Failure. *Journal of Thrombosis and Thrombolysis*, **33**, 322-328. https://doi.org/10.1007/s11239-011-0635-0
20. Gürgöze, M.T., van Vark, L.C., Baart, S.J., Kardys, I., Akkerhuis, K.M., Manintveld, O.C., *et al.* (2023) Multimarker Analysis of Serially Measured GDF-15, NT-proBNP, ST2, GAL-3, cTnI, Creatinine, and Prognosis in Acute Heart Failure. *Circulation*: *Heart Failure*, **16**, e009526. https://doi.org/10.1161/circheartfailure.122.009526