





The Diagnostic and Progressive Value of Serum GSDMD in Patients with Heart Failure: A Retrospective Study

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Objective: This study analyzes the value of serum Gasdermin D (GSDMD) as a novel biomarker for the early diagnosis and disease progression of heart failure.

Methods: We conducted a retrospective analysis of clinical data and laboratory results to compare the GSDMD levels among the heart failure group, other cardiac disease group, and healthy control group. We investigate the correlation between GD and other indicators, as well as the independent risk factors for heart failure. Receiver operating characteristic (ROC) curve analysis was conducted to compare the diagnostic value of serum GSDMD, N-terminal pro-B-type natriuretic peptide (NT-ProBNP), ejection fraction (EF) in patients.

Results: There were statistically significant differences in serum GSDMD, EF and other laboratory tests among the three groups ($P < 0.05$). Among heart failure patients with different cardiac function classifications, the serum levels of NT-ProBNP, GSDMD increased with the increase in cardiac function classification. Serum GSDMD was correlated with all indicators ($P < 0.05$) in subjects. Serum GSDMD and NT-ProBNP were independent risk factors while EF was an independent protective factor for heart failure. The AUCs of serum GSDMD, NT ProBNP, and EF for diagnosing heart failure were 0.819, 0.970, and 0.831, respectively, while the AUC of their combined diagnosis of heart failure was 0.986.

Conclusion: This study suggests that Serum GSDMD, as a novel sensitive biomarker, has the potential for early diagnosis and disease progression assessment of heart failure.

Keywords: heart failure, serum GSDMD, diagnostic value

Introduction

Heart failure (HF) is a clinical syndrome caused by structural or functional abnormalities of the heart that impaired the filling or ejection capacity of the ventricles, posing a serious threat to human health. It represents the final stage of most heart diseases and has become one of the major public health issues globally.¹⁻³ Studies indicate that there are approximately 64 million heart failure patients worldwide, while there are about 330 million individuals suffering from cardiovascular diseases in China. The prevalence of heart failure in those over 35 years old is estimated at 1.3% (1.2% in females and 1.4% in males), with an estimated 8.9 million heart failure patients in China.^{4,5} It is projected that the total percentage of the heart failure population will rise from 2.4% in 2012 to 3.0% in 2030.⁶ With the development of social economy, the acceleration of urbanization, population aging, and the increase of chronic diseases such as coronary heart disease, hypertension, and diabetes, the prevalence of heart failure continues to rise. Due to the atypical early clinical symptoms of heart failure and the influence of various factors, early diagnosis is often prone to misdiagnosis. Under the current circumstances, the difficulty in early diagnosis of heart failure still exists and remains urgent.

Clinical auxiliary diagnostic tools for heart failure include electrocardiogram, echocardiographic ejection fraction (EF), and biomarkers. The sensitivity of echocardiographic EF for the early diagnosis of heart failure is relatively low.⁷

Common biomarkers used for the diagnosis and monitoring of heart failure include brain natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-ProBNP), which are part of the guideline-recommended laboratory evaluation.¹ Although the benefits of biomarkers in the management of patients with heart failure are widely recognized, certain limitations still remain. BNP has a short half-life and is unstable *ex vivo*, making it prone to yielding inaccurate test results. NT-proBNP is cleared by the kidneys and is therefore susceptible to alterations in renal function. In the era of precision medicine, the etiological characterization of heart failure become both feasible and meaningful for understanding underlying diseases, predicting their natural progression, tailoring personalized treatment strategies, and identifying and designing new therapeutic target trials. Biomarkers and proteomic profiles will play a crucial role in aiding the diagnosis and treatment of the disease. Consequently, there is a need for new biomarkers to guide the early diagnosis, prognosis, and development of treatment strategies for heart failure.

Pyroptosis is a form of inflammatory programmed cell death that is dependent on the activation of cysteine proteases and triggered by inflammasomes, leading to the lytic death of cells through gasdermins (GSDMs) family proteins.⁸ The human GSDM family consists of six members: GSDMA, GSDMB, GSDMC, GSDMD, GSDME (DNFA5), and PJVK (DFNB59), all of which participate in pyroptosis under different contextual conditions.⁹ When cells were subjected to specific stimuli, these activation factors were triggered, initiating a cascade of responses. Caspase-1, as a protease, can activate interleukin-1 β (IL-1 β), interleukin-18 (IL-18), and GSDMD, converting these downstream molecules into their mature forms. In this process, Gasdermin D is the executor of cell death.^{10,11} In recent years, an increasing number of studies has highlighted the crucial role of pyroptosis in the occurrence and progression of cardiovascular diseases, with the pyroptosis of cardiomyocytes and vascular endothelial cells considered one of the important mechanisms underlying cardiovascular disease development.^{12,13} Pyroptosis of cardiomyocytes can lead to significant diseases such as myocardial infarction and heart failure.¹⁴ Based on the above, pyroptosis may already occur in the early stages of heart failure, and serum GSDMD expression may be elevated above normal levels, which is more valuable than EF for the diagnosis of heart failure. Serum GSDMD is unrelated to renal metabolism, which may make it superior to NT-proBNP.

The objective of this study is to explore the relationship between serum GSDMD and heart failure in depth, analyze the correlation between serum GSDMD levels and disease severity, and assess its role as an independent risk factor for the onset of heart failure. Additionally, the study aims to evaluate the diagnostic value of serum GSDMD for heart failure, providing a theoretical foundation for early screening.

Material and Methods

Study Population

Group 1, Recruitment of Patients. 228 patients were recruited from the registry of Hebei General Hospital including 118 patients with heart failure; The 118 patients included 74 males and 44 females, with an age of (69.40 \pm 14.86) years; Group 2, Records of another 100 patients with cardiovascular disease were also examined for comparison that comprising 61 males and 39 females, with an age of (65.26 \pm 13.67) years; Group 3, Apart from above two groups, 100 apparently healthy individuals were also included as control group that including 54 males and 46 females, with an age of (67.76 \pm 16.93) years.

Diagnostic Criteria: 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.²

Inclusion criteria: (1) Age \geq 18 years; (2) Heart failure patients who met the diagnostic criteria; (3) Patients with other cardiac diseases did not meet the diagnostic criteria for heart failure.

Exclusion criteria: (1) Individuals with heart diseases complicated by acute or chronic infections; (2) Individuals with heart diseases complicated by malignant tumors, mental disorders or autoimmune diseases; (3) Individuals with heart diseases complicated by severe liver dysfunction, or kidney dysfunction; (4) Recent use of immunosuppressants or corticosteroid treatment; (5) Repeated registration of the same patient.

Collection of Data

Clinical basic information was collected from case record form, including gender, age, medical history, and medication status. Echocardiographic parameters included left ventricular ejection fraction (EF). Patients were divided into three groups based on the American College of Cardiology heart function classification: functional classes I/II, III, and IV.

All subjects fasted for more than 8 hours and had 5 mL of non-anticoagulated venous blood drawn. The blood was centrifuged at 1000×g for 10 minutes for analysis. Laboratory blood indicators included NT-ProBNP, myoglobin (MYO), lactate dehydrogenase (LDH), creatine kinase-MB (CK-MB), creatine kinase (CK) and hydroxybutyrate dehydrogenase (HBDH). The NT-ProBNP was detected using the Roche cobas 8000 automated biochemical analyzer and its corresponding testing reagents. MYO, LDH, CK-MB, CK, HBDH were conducted using the Beckman AU5800 automated biochemical analyzer and its associated reagents.

Detection of Serum GSDMD

The levels of GSDMD in serum were detected using a chemiluminescence method (BEIJING MDTK BIOLOGY TECHNOLOGY CO. LTD), strictly following the instructions provided in the reagent kit.

Statistical Analysis

Data analysis and graphing were performed using SPSS 26.0 software and GraphPad Prism 8.0. Normally distributed measurement data were expressed as mean ± standard deviation (x±s), and comparisons among three groups were performed using one-way ANOVA. For measurement data that did not conform to a normal distribution, results were expressed as median (P25, P75), and the non-parametric Kruskal–Wallis test was used for comparisons among groups. Correlation analysis was performed using Spearman analysis to evaluate the correlation between serum GSDMD and other indicators. The diagnostic value of individual indicators was assessed using ROC curve analysis. For multiple indicators combined in diagnosis, they were included as independent variables in binary logistic regression to obtain the regression equation and combined predictive probability, followed by ROC curve analysis to evaluate their diagnostic value. P < 0.05 was considered statistically significant.

Results

Comparison of Clinical Data Among the Three Groups

When comparing the heart failure group, other cardiac disease group, and healthy control group, there were no differences in gender and age among the three groups (P > 0.05, Table 1). However, there were significant differences in GSDMD, NT-ProBNP, MYO, LDH, CK-MB, CK, HBDH and EF among the three groups (P < 0.05, Table 1). Specifically, the serum levels of GSDMD, NT-ProBNP, MYO, LDH, CK-MB and CK in the healthy control group were significantly lower than those in the other cardiac disease group (P < 0.05, Table 1 and Figure 1a–g). The serum levels of GSDMD, NT-ProBNP, MYO, LDH, CK-MB, CK and HBDH in the healthy control group were also significantly lower than those in the heart failure group, while the EF was higher in the healthy control group compared to the heart failure group, with statistical significance (P < 0.05, Table 1 and Figure 1a–h). The serum levels of GSDMD, NT-ProBNP, MYO, LDH and HBDH in the other cardiac disease group were significantly lower than those in the heart failure group,

Table 1 Comparison of Clinical Data Among the Three Groups

Projects	Healthy Control Group	Other Cardiac Disease Group	Heart Failure Group	P
Gender(Male/Female)	54/46	61/39	74/44	0.397
Age(year)	67.76±16.93	65.26±13.67	69.40±14.86	0.063
GSDMD(pg/mL)	5.12 (3.0,7.17)	55 (30.51,76.6) [△]	67.0 (43.07,99.87) ^{*#}	0.000
NT-ProBNP(pg/mL)	73.55 (25.65,118.75)	134.5 (60.0,414.75) [△]	2295.0 (1085.3,5937.5) ^{*#}	0.000
MYO(ng/mL)	26.0 (21.0,36.0)	32.5 (27.0,44.0) [△]	53.0 (37.0,104.25) ^{*#}	0.000
LDH(U/L)	160.1 (146.9,184.95)	176.55 (149.5,205.23) [△]	196.0 (163.78,268.38) ^{*#}	0.000
CK-MB(U/L)	10.5 (7.53,13.5)	14.5 (11.83,16.63) [△]	13.5 (11.18,17.4) [#]	0.000
CK(U/L)	62.25 (47.53,90.83)	85.6 (60.35,123.83) [△]	73.1 (48.68,157.9) [#]	0.000
HBDH(U/L)	111.6 (95.83, 129.05)	115.35 (102.75,136.5)	135.25 (112.23,178.45) ^{*#}	0.000
EF(%)	62.0 (59.0,66.0)	63.5 (60.25, 66.0)	46.5 (39.75,59.0) ^{*#}	0.000

Notes: *Indicated comparison between the heart failure group and the other cardiac disease group had a statistically difference; # indicated comparison between the heart failure group and the healthy control group had a statistically difference; [△]Indicated comparison between the other cardiac disease group and the healthy control group had a statistically difference.

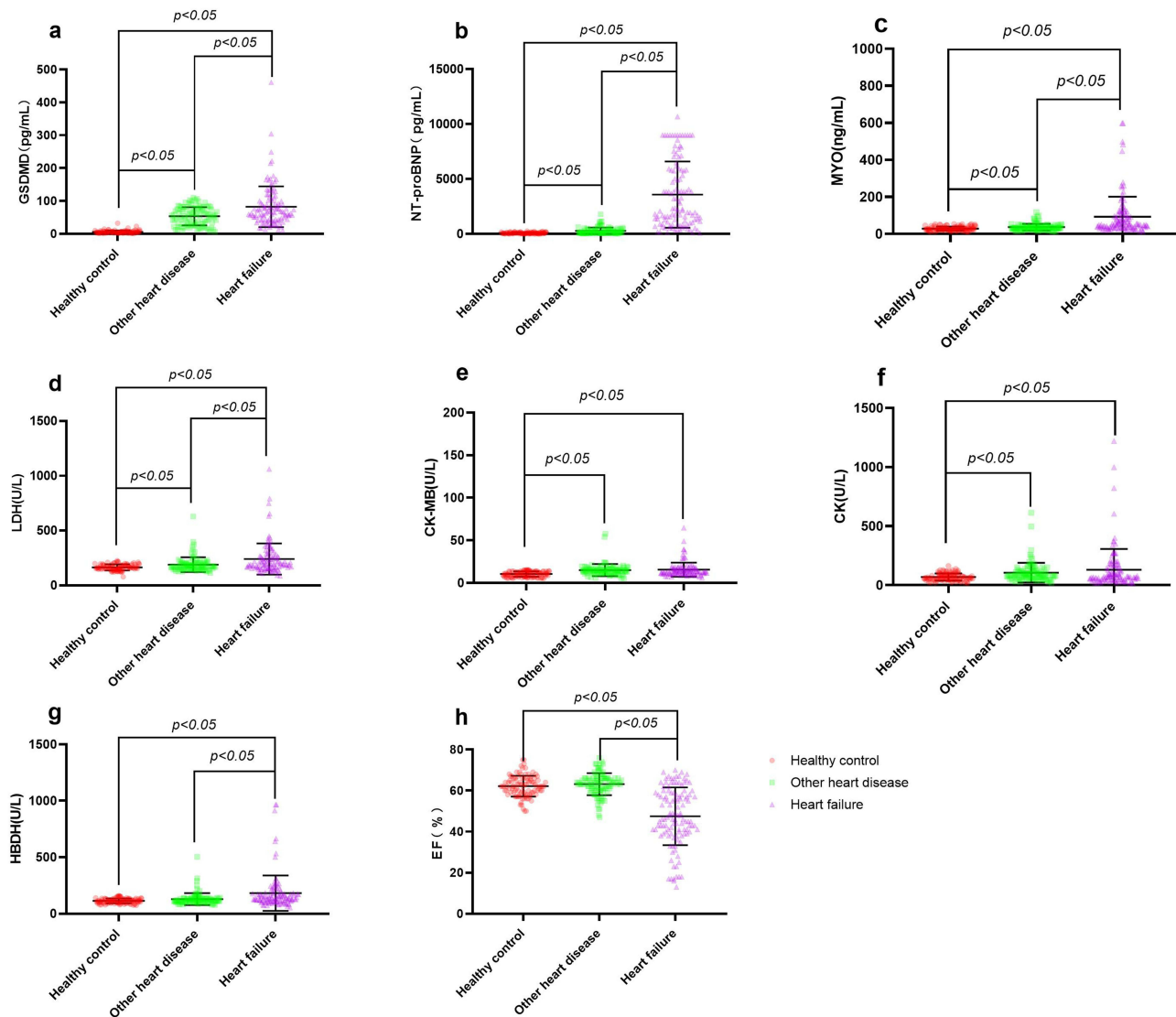


Figure 1 Serum levels of GSDMD (a), NT-ProBNP (b), MYO (c), LDH (d), CK-MB(e), CK (f), HBDH(g) and EF (h) in Healthy control group, Other cardiac disease group and Heart failure group.

while the EF was higher in the other cardiac disease group compared to the heart failure group, with statistical significance ($P < 0.05$, Table 1, Figure 1a–d, g and h).

Comparison of Clinical Data Among Different Heart Function Classifications in the Heart Failure Group

There were significant differences in serum GSDMD, NT-ProBNP, MYO, LDH and CK-MB among the three groups of heart failure patients with different cardiac function classification ($P < 0.05$, Table 2 and Figure 2a–e). The levels of GSDMD and NT-ProBNP increased with the increase of functional grade. There were differences in serum GSDMD between each two groups ($P < 0.05$, Table 2 and Figure 2a). However, there were no differences in gender, age, EF, HBDH and CK among the different heart function classifications ($P > 0.05$, Table 2).

Correlation Analysis Between Serum GSDMD and Other Indicators

According to Spearman correlation analysis, the serum GSDMD levels in all patients showed a significant positive correlation with NT-ProBNP, MYO, LDH, CK-MB, CK and HBDH ($P < 0.05$, Table 3 and Figure 3a–f). Conversely, serum GSDMD levels showed a negative correlation with EF ($P < 0.05$, Table 3 and Figure 3g).

Table 2 Comparison of Clinical Data Among Different Heart Function Classifications

Projects	Cardiac Function Class I/II	Cardiac Function Class III	Cardiac Function Class IV	P
Gender(Male/Female)	18/5	19/18	37/21	0.667
Age(year)	67.48±12.99	69.30±16.05	70.22±14.95	0.606
GSDMD(pg/mL)	41.49 (28.37, 56.23)	64.56 (49.71,76.90)*	89.07 (54.43,132.87) ^{#Δ}	0.000
NT-ProBNP(pg/mL)	898.0 (527.0,1744.0)	2309.0 (1190.5,5794.0)*	3855.5 (1721.25,7947.25) [#]	0.000
MYO(ng/mL)	42.0 (32.0,57.0)	50.0 (34.0,77.0)	73.5 (40.5,168.75) [#]	0.008
LDH(U/L)	188.3 (152.5,204.6)	188.2 (157.2,248.4)	224.1 (167.08,345.83) ^{#Δ}	0.039
CK-MB(U/L)	12.1 (11.4,15.2)	12.3 (10.5,15.85)	14.15 (11.78,18.83) ^Δ	0.030
CK(U/L)	68.1 (53.7,86.3)	68.1 (44.45,103.85)	94.2 (48.58,207.88)	0.099
HBDH(U/L)	123.3 (106.6,163.1)	133.8 (116.1,156.1)	154.35 (112.23,223.23)	0.091
EF(%)	46.0 (40.0,64.0)	53.0 (41.0,60.0)	45.5 (37.5,57.0)	0.306

Notes: *Indicated comparison between Cardiac function class I/II and Cardiac function class III had a statistically difference; #Indicated comparison between Cardiac function class I/II and Cardiac function class IV had a statistically difference; ΔIndicated comparison between Cardiac function class III and Cardiac function class IV had a statistically difference.

Logistic Regression Analysis of Serum GSDMD

A binary logistic regression analysis was conducted with the occurrence of heart failure as the dependent variable and GSDMD, NT-ProBNP, MYO, LDH, CK, HBDH and EF as independent variables. Univariate logistic regression showed

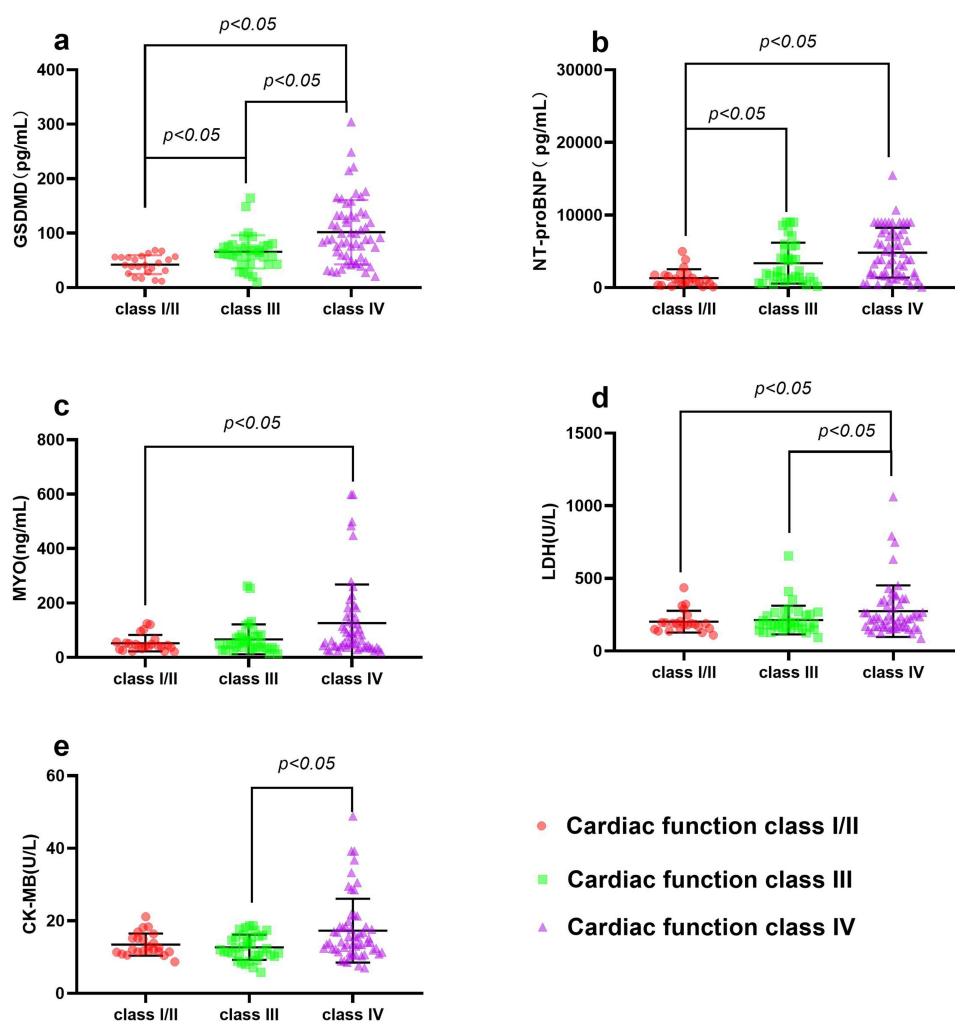


Figure 2 Serum levels of GSDMD (a), NT-ProBNP (b), MYO(c), LDH (d) and CK-MB (e) in Cardiac function class I/II, Cardiac function class III and Cardiac function class IV.

Table 3 Correlation Between Serum GSDMD and Other Indicators

Projects	r	P
Gender(Male/Female)	-0.094	0.095
Age(year)	-0.023	0.683
NT-ProBNP	0.581	0.000
MYO(ng/mL)	0.323	0.000
LDH(U/L)	0.241	0.000
CK-MB(U/L)	0.306	0.000
CK(U/L)	0.132	0.018
HBDH(U/L)	0.178	0.001
EF(%)	-0.295	0.000

that all the observed indexes were independent influencing factors;Multivariate logistic regression showed that serum GSDMD and NT-ProBNP were independent risk factors for heart failure, and EF was an independent protective factor for heart failure (P <0.05, Table 4).

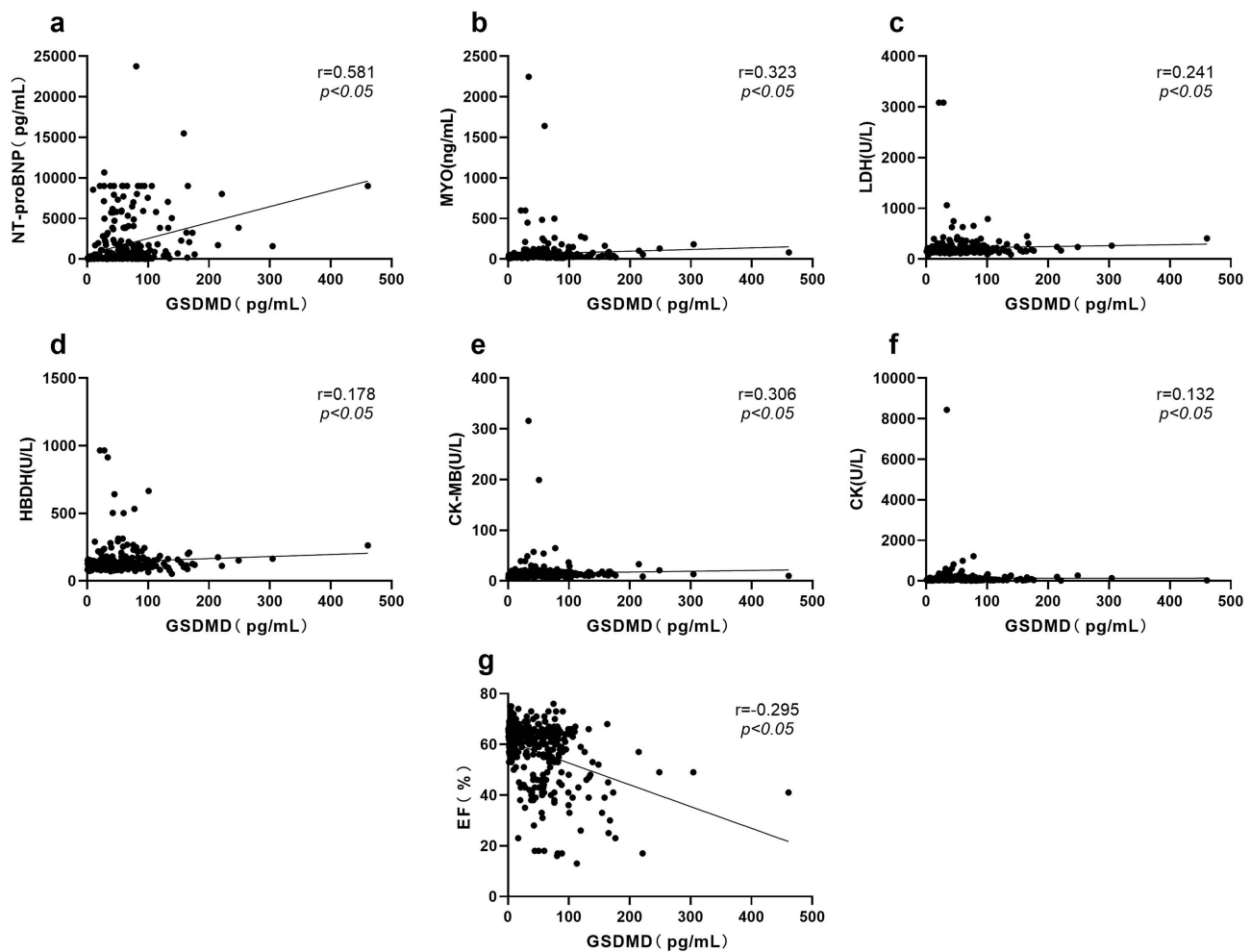


Figure 3 Correlation Between Serum GSDMD and NT-proBNP (a), MYO (b), LDH(c), HBDH (d), CK-MB (e), CK(f), EF (g).

Table 4 Logistic Regression Analysis of Serum GSDMD and Other Indicators in Heart Failure

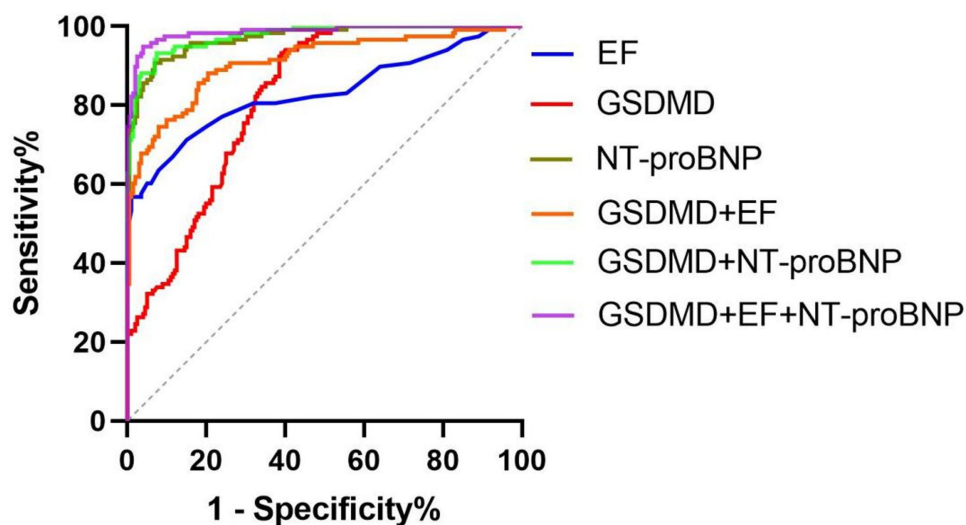
Independent Variable	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
GSDMD	1.034 (1.025–1.042)	0.000	1.027 (1.009–1.045)	0.003
NT-ProBNP	1.005 (1.003–1.006)	0.000	1.004 (1.002–1.006)	0.000
MYO	1.05 (1.035–1.066)	0.000	1.022 (0.994–1.051)	0.131
LDH	1.01 (1.006–1.014)	0.000	0.988 (0.966–1.011)	0.313
CK	1.004 (1.001–1.004)	0.007	1.002 (0.995–1.009)	0.530
HBDH	1.013 (1.007–1.019)	0.000	1.008 (0.974–1.043)	0.653
EF	0.835 (0.800–0.871)	0.000	0.836 (0.774–0.903)	0.000

Table 5 Comparison of the Diagnostic Value of Serum GSDMD, NT-ProBNP, and EF for Heart Failure

Project	AUC	P	95%CI	Critical Value	Sensitivity	Specificity	Youden's Index
GSDMD	0.819	0.000	0.775–0.863	25.685	93.2	61.0	0.542
NT-ProBNP	0.970	0.000	0.954–0.987	526.5	90.7	93.0	0.837
EF	0.831	0.000	0.778–0.883	57.5	71.2	85.0	0.562
GSDMD+NT-ProBNP	0.976	0.000	0.961–0.990		93.2	92.5	0.857
GSDMD+EF	0.909	0.000	0.874–0.945		88.1	79.5	0.676
Combined detection	0.986	0.000	0.975–0.997		94.9	96	0.909

Diagnostic Value of Serum GSDMD, NT-ProBNP, and Ejection Fraction in Heart Failure Patients

The predictive performance of serum GSDMD, NT-ProBNP, and ejection fraction for heart failure patients was compared using ROC curves. A binary logistic regression analysis was applied to obtain the combined prediction probabilities, and ROC curves were plotted. The AUC, critical values, sensitivity, and specificity for serum GSDMD, NT-ProBNP, and EF in the diagnosis of heart failure were 0.819, 25.685 pg/mL, 93.2%, 61%; 0.970, 526.5 pg/mL, 90.7%, 93%; and 0.831, 57.5%, 71.2%, 85%, respectively; The AUC, sensitivity, and specificity for the combination of serum GSDMD and NT-ProBNP, the combination of serum GSDMD and EF, and the combination of all three were 0.976, 93.2%, 92.5%; 0.909, 88.1%, 79.5%; and 0.986, 94.9%, 96%, respectively (Table 5 and Figure 4).

**Figure 4** Comparison of the Diagnostic Value of Serum GSDMD, NT-ProBNP, and EF for Heart Failure.

Discussion

The etiology of heart failure is complex and diverse, potentially resulting from coronary artery disease, hypertension, cardiomyopathy, valvular heart disease, congenital heart disease, arrhythmias, pericardial disease, myocarditis, pulmonary hypertension, and cardiotoxic substances including alcohol.¹⁵ Heart failure represents the end stage of various cardiac diseases, and early detection and timely treatment can alleviate suffering and improve patient survival rates. Left ventricular EF is usually measured by echocardiography and serves as the basis for diagnosis, treatment selection, and monitoring in patients with heart failure. Echocardiography has a relatively low sensitivity for detecting early-stage heart failure, with high detection rates achieved only in more advanced cases.⁷ Consistent with the results of this study, the EF in the healthy control group (62.18±5.06) showed no statistically significant difference compared to the EF in other cardiac disease groups (63.5 (60.25, 66.0)). However, both groups exhibited statistically significant differences when compared to the EF in the heart failure group (46.5 (39.75, 59.0)). The differences in EF among various heart function classifications in the heart failure group did not reach statistical significance. Therefore, there are certain limitations to EF regarding the early diagnosis of heart failure and the severity of heart function classification.

Studies have shown that inflammatory responses play a crucial role in the progression of heart failure. In cardiovascular diseases, pyroptosis as a cellular pathway that contributes to myocardial damage, thereby accelerating the expansion of necrotic areas in the myocardium, leading to a rapid decline in cardiac function, which may trigger severe arrhythmias and the progression of heart failure.^{16,17} Therefore, preventing or reducing the process of pyroptosis in the myocardium is of great significance for preserving cardiac function and improving patient prognosis.¹⁸ The mechanisms of pyroptosis include intracellular protein aggregation, mitochondrial dysfunction, and changes in cell membrane permeability, leading to the release of pro-inflammatory factors and the initiation of inflammatory responses. These processes are vital for the body's immune regulation and response to external injury.^{19,20} The pyroptosis pathway includes three types: the classical Caspase-1-dependent pathway, the non-classical Caspase-11/4/5-dependent pathway, and other forms of pyroptosis pathways. The classical and non-classical pyroptotic pathways are not entirely independent; both rely on the cleavage of GSDMD and can transition from non-classical to classical pyroptosis. GSDMD is the true executor of pyroptosis.^{21–24} Therefore, the detection of GSDMD expression can reflect the extent of pyroptosis in patients with heart failure, indicating the overall inflammatory response and providing broader insights for the study of heart failure.

In this study, serum levels of GSDMD, NT-ProBNP, LDH and MYO progressively increased from the healthy control group to the other cardiac disease group and then to the heart failure group, with statistically significant differences observed between each pair of groups. Research has shown that myocardial injury and pyroptosis can cause increased release of LDH into the bloodstream.²⁵ Studies internationally have shown that pyroptosis indeed occurs in heart failure, as evidenced by elevated serum LDH levels in model mice, alongside increased expression of pyroptosis-related proteins such as NLRP3, ASC, caspase-1, IL-18, IL-1 β and GSDMD,²⁶ which is consistent with our study's conclusions. Currently, there are no clinical studies on the correlation of this marker with the progression of heart failure. To further investigate whether these serological markers are associated with the severity of the disease in heart failure patients, we classified the patients into three groups based on their cardiac function classification. There were no differences in EF, HBDH and CK among the three groups. The serum levels of LDH was lower in groups I/II and III compared to group IV. The serum level of MYO in group I/II and CK-MB in group III were lower than those in group IV. Serum levels of GSDMD and NT-ProBNP increased with the severity of heart failure. The trend of NT-ProBNP changes is consistent with the findings of Vignesh Mariappan et al.²⁷ This study found that serum GSDMD levels increase with the severity of heart failure. Therefore, monitoring GSDMD levels in heart failure patients may also assist in assessing disease progression and treatment efficacy.

This study indicated that GSDMD levels in heart failure patients showed a moderate positive correlation with NT-ProBNP. Serum levels of GSDMD and NT-ProBNP were independent risk factors in heart failure. EF was independent protective factor in heart failure. Serum GSDMD played an important role in the occurrence, progression, and prognosis of heart failure; however, there are no reports in China on the diagnostic value of GSDMD for heart failure. The ROC curve has now become a widely used comprehensive evaluation method in clinical diagnosis and population screening research which is plotted with the true positive rate (TPR) on the y-axis and the false positive rate (FPR) on the x-axis. It reflects the relationship between sensitivity and specificity under different threshold conditions. At the same time, the diagnostic efficiency of a test can be evaluated by calculating the area under the ROC curve (AUC). Through ROC curve analysis, we compared the diagnostic

efficacy of serum NT-ProBNP, EF, and GSDMD in heart failure patients, which indicated that NT-ProBNP and EF had high predictive value for heart failure, with AUCs of 0.970 and 0.831, respectively, consistent with findings from Rawaz D Tawfeeq et al.²⁸ Serum GSDMD also demonstrated good predictive value for heart failure and exhibited diagnostic efficacy comparable to that of EF, with an AUC of 0.819, sensitivity of 93.2%, and specificity of 61%.

Serum biomarkers are commonly used tools for diagnosing and predicting heart failure. Due to the varying specificity of different biomarkers and their diverse implications in heart failure (such as inflammation, injury, and fibrosis), relying on a single biomarker for assessment often leads to a biased understanding. Clinically, it is necessary to enhance diagnostic, risk stratification, and prognostic evaluation through the combined monitoring of multiple biomarkers. The sensitivity, specificity, and AUC of serum GSDMD combined with NT-ProBNP were 93.2%, 92.5%, and 0.976, respectively, all higher than the diagnostic efficacy of single biomarker measurements. The combination of serum GSDMD and EF yielded sensitivity, specificity, and AUC values of 88.1%, 79.5%, and 0.909, significantly surpassing the diagnostic efficacy of EF alone. The combined testing of serum GSDMD, NT-ProBNP, and EF resulted in sensitivity, specificity, and AUC values of 94.9%, 96%, and 0.986, respectively, indicating that the diagnostic efficacy of this triple combination surpassed individual or dual measurements, further enhancing diagnostic value in heart failure patients.

It is noteworthy that serum GSDMD levels are elevated in the early stages of heart failure, and compared to EF, it holds potential value for early diagnosis. Clinically, serum GSDMD can be used to screen for the risk of heart failure onset in high-risk populations with impaired cardiac function. In the heart failure prediction model established in this study, the serum GSDMD threshold is 25.685 pg/mL, and levels exceeding this threshold are associated with a higher risk of developing heart failure. This study found that serum GSDMD levels increase with the severity of heart failure. Therefore, monitoring GSDMD levels in heart failure patients may also assist in assessing disease progression and treatment efficacy. In addition, the combination of serum GSDMD with NT-ProBNP and EF demonstrated improved predictive power and clinical application value for assisting in the diagnosis of heart failure.

The current study has limitations. Due to the retrospective nature of the study, some other clinical variables, including behavioral characteristics and the causes of heart failure, are not analysed and discussed, which may potentially limit the finding. However, research on GSDMD in heart failure is still in its early stages, and further large-scale clinical studies are needed to validate its diagnostic value and clinical applicability. In addition, there is a need to develop more accurate, rapid, and convenient detection methods to enhance its application in clinical practice.

Conclusion

In summary, serum GSDMD levels are elevated in both other cardiac disease patients and heart failure patients, with levels in heart failure patients being higher than those in patients with other cardiac diseases prior to heart failure. With the aggravation of cardiac function classification, the expression of GSDMD in serum will increase. These results also indicate the extent of disease progression, which helps clinicians provide better treatment. Serum GSDMD shows good diagnostic value for heart failure, and its combination with NT-ProBNP and EF further enhances predictive value for heart failure, potentially serving as a novel biomarker for the diagnosis and monitoring of heart failure treatment.

Data Sharing Statement

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

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki, received approval from the Ethics Committee of Hebei General Hospital [Approval Number: 2024(268)], and all participants provided informed consent.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors have no potential conflicts of interest for this work.

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