Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Diagnostic Utility of Pentraxin 3 Expression in Septic Cardiomyopathy: Findings from a Prospective Observational Study

Na Cui[1,2,*], Xiao-Wei Lv[2,*], Teng-Hao Shao[2], Zhan-Biao Yu[2], Zhi Chen[2], Tao Sun[2], Tie-Min Li[2], Jin-Wen Zhang[2], Zhen-Jie Hu[1]

[1]Department of Critical Care Medicine, The Fourth Affiliated Hospital of Hebei Medical University, Shijiazhuang, 050010, People's Republic of China; [2]Department of Critical Care Medicine, Affiliated Hospital of Hebei University, Baoding, 071000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Zhen-Jie Hu, Department of Critical Care Medicine, The Fourth Affiliated Hospital of Hebei Medical University, No. 12, Jiankang Road, Shijiazhuang, 050010, People's Republic of China, Tel +86 13933856908, Email 46400533@hebmu.edu.cn

Objective: The aim of this study is to investigate the expression levels of Pentraxin 3, PTX3 in patients with septic cardiomyopathy, SCM and evaluate its diagnostic potential for predicting SCM.

Methods: A prospective observational study was conducted involving 122 patients diagnosed with septic shock between February 2023 and August 2024. Demographic and clinical data, along with plasma PTX3 concentrations were recorded. Participants were categorized into two groups based on the presence of SCM. PTX3 concentrations and their dynamic changes were compared between the groups. The correlations between PTX3 concentrations and other clinical indicators were analyzed, and the influencing factors associated with SCM development were assessed. The predictive performance of PTX3 for SCM was evaluated using receiver operating characteristic, ROC curves.

Results: SCM was identified in 24.6% of the participants. Plasma PTX3 concentrations at admission and on day 3 were significantly higher in the SCM group compared to the non-SCM group, $p < 0.001$. However, no significant differences were observed on day 7, $p > 0.05$. PTX3 concentrations decreased over time in both groups. Plasma PTX3 concentrations were correlated with procalcitonin, lactate, myoglobin, troponin I, the elevated levels of troponin I on day 2 compared to admission, Sequential Organ Failure Assessment score, Acute Physiology and Chronic Health Evaluation II score, and intensive care unit length of stay. Elevated plasma PTX3 concentrations were identified as an independent risk factor for SCM development. The area under the ROC curve for PTX3 in predicting SCM was 0.784, $p < 0.001$, with a cutoff value of 20.82 ng/mL, sensitivity of 0.767, and specificity of 0.707.

Conclusion: Plasma PTX3 concentrations are markedly elevated in patients with SCM, indicating that PTX3 may serve as a reliable biomarker for the early diagnosis of SCM.

Keywords: diagnosis, PTX3, sepsis, septic cardiomyopathy, septic shock

Introduction

Sepsis is characterized by immune dysregulation resulting from infection, which can lead to life-threatening organ dysfunction.[1] The mortality rate associated with sepsis ranges from 32.5% to 55%, posing a significant global health challenge.[2,3] Annually, an estimated 47 to 50 million cases of sepsis occur worldwide, with the heart being among the most commonly affected organs. Septic cardiomyopathy, SCM is a reversible cardiac dysfunction associated with sepsis.[4] The onset of SCM is associated with severe cardiac dysfunction, which exacerbates the mortality risk in individuals with sepsis.[5]

The understanding of SCM remains limited, and the condition is often misdiagnosed or overlooked in clinical settings. Common clinical markers, including troponin, creatine kinase MB, CK-MB, myoglobin, MYO, and B-type natriuretic peptides, are frequently influenced by non-SCM-related factors, thereby limiting their specificity and diagnostic value in SCM.[6]

Received: 14 January 2025
Accepted: 16 April 2025
Published: 7 May 2025

Advancements in critical care echocardiography have enhanced diagnostic capabilities for SCM, with several indicators of ventricular function showing correlations with patient prognosis.[7] However, the clinical utility of echocardiography is constrained by its operational complexity and the subjectivity of its assessments. Consequently, there is an urgent need to identify effective and specific biomarkers for SCM. Such biomarkers could facilitate early diagnosis and intervention, thereby improving the prognosis and outcomes for individuals with sepsis.

Pentraxin 3, PTX3, a key acute-phase protein, has emerged as a critical biomarker in sepsis. Previous studies have explored its diagnostic significance in sepsis and septic shock, highlighting its potential as an early diagnostic and prognostic biomarker for these conditions.[8] A Meta-analysis demonstrated that PTX3 levels were significantly higher in non-survivors of sepsis than in survivors, and elevated PTX3 increased the risk of death by 2.09-fold, with an area under the curve predicting mortality of 0.73, which is superior to traditional inflammatory markers, eg, CRP, PCT.[9] Another Meta-analysis showed that PTX3 levels were significantly elevated in septic neonates compared to healthy neonates, and the difference was especially significant in the early sepsis subgroup.[10] Moreover, PTX3 is a locally acting inflammatory mediator that is found in elevated concentrations within damaged myocardial tissue. Bioinformatics analysis have identified *PTX3* as a key gene involved in the pathogenesis of SCM, with findings suggesting its primary role in exerting anti-inflammatory effects. These characteristics indicate that PTX3 may serve as a promising prognostic and therapeutic target in the clinical management of SCM.[11]

Despite these insights, evidence regarding the expression patterns and specific role of PTX3 in patients with SCM remains limited. The present study aims to investigate the expression of PTX3 in patients with SCM, investigate its correlation with traditional clinical indicators, and evaluate its diagnostic utility for early SCM detection. By establishing PTX3 as an effective biomarker, the findings aim to support early diagnostic and therapeutic strategies, thereby contributing to reduced mortality in SCM.

Information and Methods

Study Participants and Grouping

This study consecutively enrolled 154 individuals diagnosed with septic shock who were admitted to the Department of Intensive Care Medicine, Affiliated Hospital of Hebei University, between February 2023 and August 2024. However, 32 individuals were excluded due to acute myocardial infarction or incomplete data, leaving 122 individuals to participate in the study. The study participants were categorized into two groups based on the presence of SCM: the SCM group and the non-SCM group.

Inclusion Criteria

(1) Diagnosis meeting the Sepsis-3.0 criteria for sepsis shock,[2] defined as the presence or suspected infection. The Sequential Organ failure score, SOFA increased by ≥2 points from baseline. After adequate fluid resuscitation, vasoactive drugs are still required to maintain mean arterial pressure ≥65mmHg. Blood lactate level ≥2mmol/L. (2) age ≥ 18 years.

Exclusion Criteria

(1) Patients with organic heart disease such as ischemic cardiomyopathy, myocardial infarction, congenital heart disease, infective endocarditis, and myocarditis; (2) pregnancy; (3) presence of malignant tumors; (4) patients receiving immunosuppressive therapy; (5) hospitalization duration < 24 hours; (6) lack of informed consent or refusal of active treatment by the individual or their family members; (7) incomplete clinical data.

Ethical Approval

This study was approved by the Ethics Committee of the Affiliated Hospital of Hebei University, Approval No. HDFYLL-KY -2023-167. All participants voluntarily provided written informed consent for inclusion in the clinical research.

Research Methods

Collection of General Data

Clinical data were recorded for all participants, including demographic variables, gender, age, medical history, presence of coronary heart disease and diabetes, and mean arterial pressure, MAP at admission. All enrolled patients received

appropriate fluid resuscitation, anti-infection treatment, and, when necessary, vasoactive medications and organ support, in accordance with sepsis guidelines, upon admission. The SOFA score and Acute Physiology and Chronic Health Evaluation II, APACHE II score were assessed within the first 24 hours of admission.

Transthoracic Echocardiography

Daily color Doppler echocardiography was performed during hospitalization using the Crius TE9 ultrasound system, China equipped with an L14-6s probe, frequency 2–4 MHz. Left ventricular ejection fraction, LVEF and left ventricular end-diastolic volume, LVEDV and ventricular wall motion were assessed. LVEF was measured using M-mode ultrasound: in parasternal long-axis views, the LV end-diastolic and end-systolic internal diameters were measured using an M-mode ultrasound cursor line passing vertically through the basal segment of the LV, at the level of the mitral tendon cords and LVEF was calculated by the formula LVEF was calculated using the Simpson biplane method: in apical four-chamber and two-chamber views, the LV endocardial contours were manually sketched, and the software automatically The software automatically calculated the volume. Characteristics for SCM included LVEF < 50% or a reduction exceeding 10% from baseline, left ventricular dilation, and reversible recovery within 7 to 10 days.[12] Combining the length of stay and sample size factors, the diagnostic criteria for SCM used in this study were: occurrence of LVEF < 50% within 72h of admission.[13]

Plasma PTX3 Concentration Measurement

Venous blood samples were collected from all participants at three time points, admission, day 3, and day 7 using EDTA anticoagulant tubes. Plasma was separated by centrifugation and stored at −80 °C until analysis. PTX3 concentrations were measured using a double-sandwich enzyme-linked immunosorbent assay, ELISA. The experimental procedure was strictly followed according to the instructions provided by the reagent kit, Shijiazhuang Huiyou Biotechnology Co., Ltd. A standard curve was generated, and PTX3 concentrations were determined by correlating the absorbance, A values of the samples with the curve.

Other Laboratory Indicators

Laboratory parameters collected at admission included cardiac troponin I, cTnI, CK-MB, MYO, N-terminal brain natriuretic peptide, white blood cell count, procalcitonin, PCT, C-reactive protein, CRP, and lactic acid, Lac. Additionally, the levels of cardiac troponin I, CK-MB, and MYO were measured on the second day of the study.

Statistical Methods

Statistical analyses were performed using SPSS 24.0. Quantitative data were assessed for normality prior to analysis. Normally distributed data were expressed as mean ± standard deviation, x ± s and were compared between groups using independent samples *t*-tests. Non-normally distributed data were expressed as median and interquartile range [M, Q1, Q3] and were compared using the Mann–Whitney *U*-test. Unordered categorical variables were presented as percentages, % and were analyzed using chi-square tests. Correlation analyses were conducted using Pearson's or Spearman's rank correlation coefficients, depending on the data distribution. Multivariate logistic regression analysis was employed to identify factors associated with the development of SCM. The receiver operating characteristic, ROC curve was utilized to evaluate the predictive ability of PTX3 for SCM, with the relative risk expressed as odds ratio, OR and 95% confidence interval, CI. The DeLong test was used for AUC comparisons. A non-parametric test, Kruskal–Wallis H-test was applied to analyse the differences between the three groups, and further two-by-two comparisons were made using the Dunn-Bonferroni method. A two-tailed p-value <0.05 defined statistical significance. Given the exploratory aim to screen potential biomarkers, multiple testing correction was not performed, and all results should be interpreted as hypothesis-generating.

Results

Comparison of General Data and Clinical Indicators between Groups

Among the 122 patients with septic shock included in the study, 30 developed SCM, resulting in an incidence rate of 24.6%. Compared to patients in the non-SCM group, those in the SCM group exhibited lower levels of CRP, 88.90, 37.74,149.00 mg/L vs 129.30, 57.70,215.87 mg/L, $p = 0.001$ and higher levels of PCT at admission, 21.91, 4.36,61.45

ng/mL vs 4.89, 1.19,29.57 ng/mL, $p = 0.021$, CK-MB, 2.45, 1.05,6.10 ng/mL vs 1.25, 0.70,3.58 ng/mL, $p = 0.023$, and MYO both at admission and on day 2, 318.55, 120.95,1107.25 ng/mL vs 139.10, 71.70,354.98 ng/mL, $p = 0.016$; 367.40, 126.58,686.05 ng/mL vs 138.60, 72.45,402.83 ng/mL, $p = 0.004$. Additionally, the SCM group demonstrated higher SOFA scores, 11, 8,12 vs 8, 7,10, $p < 0.001$ and APACHE II scores, 23, 18,29 vs 18, 14,23, $p = 0.001$. The length of stay in the intensive care unit, ICU was also significantly longer in the SCM group, 13, 7,19 d vs 7, 4,13 d, $p = 0.007$.

No statistically significant differences were observed between the groups in terms of gender, age, history of coronary heart disease, diabetes, MAP, or other laboratory indicators, $p > 0.05$, Table 1.

Comparison of Plasma PTX3 Concentrations between Groups

Plasma PTX3 concentrations differed significantly between the SCM and non-SCM groups. The plasma PTX3 concentration in the SCM group was significantly higher compared to the non-SCM group, 37.11, 20.40,53.58 ng/mL vs 14.28, 6.50,23.72 ng/mL, $p < 0.001$, Table 1.

Correlation between Plasma PTX3 Concentrations and Clinical Indicators

At admission, plasma PTX3 concentrations in both groups were significantly correlated with PCT, Lac, MYO, elevated levels of cTnI levels on day 2 compared to admission, SOFA score, APACHE II score, and ICU length of stay, $p < 0.05$, Table 2.

Table 1 Comparison of General Data, Clinical Indicators, and Plasma PTX3 Concentrations Between Non-SCM and SCM Groups

Indicator	Non-SCM Group, n = 92	SCM Group, n = 30	χ^2/Z/t value	*P* value
Male, n, %	55, 59.8	17, 56.7	0.091	0.763
Age, years	70, 61,76	72, 61,79	−0.686	0.493
Coronary artery disease, n, %	14, 15.22	6, 20.00	0.378	0.539
Diabetes, n, %	26, 28.3	7, 23.3	0.278	0.598
MAP, mmHg	90.52±19.48	92.93±21.80	−0.571	0.569
PTX3, ng/mL	14.28, 6.50,23.72	37.11, 20.40,53.58	−4.661	<0.001
Lac, mmol/L	2.00, 1.30,3.40	2.60, 1.58,5.63	−1.779	0.075
WBC, $\times 10^9$ /L^{-1}	12.72, 6.45,19.49	10.94, 6.90,15.19	−1.085	0.278
PCT, ng/mL	4.89, 1.19,29.57	21.91, 4.36,61.45	−2.301	0.021
CRP at enrolment, mg/L	129.30, 57.70,215.87	88.90, 37.74,149.00	−2.09	0.037
CK-MB at enrolment, ng/mL	1.25, 0.70,3.58	2.45, 1.05,6.10	−2.279	0.023
MYO, ng/mL	139.10, 71.70,354.98	318.55, 120.95,1107.25	−2.417	0.016
cTnI at enrolment, ng/mL	0.04, 0.01,0.19	0.07, 0.02,0.17	−0.886	0.376
NT-proBNP, pg/mL	2660.00, 759.50,8745.00	3230.00, 596.50,12,175.00	−0.687	0.492
AST, U/L	40.00, 25.25,71.50	42.50, 23.75,241.75	−1.058	0.290
ALT, U/L	21.00, 15.00,45.25	30.00, 16.00,141.25	−1.404	0.160
SCr at day 2, μmol/L	82.00, 58.25,139.50	107.50, 56.25,188.00	−1.189	0.234
CK-MB at day 2*, ng/mL	1.40, 0.60,4.25	2.25, 0.88,5.15	−1.734	0.083
MYO at day 2*, ng/mL	138.60, 72.45,402.83	367.40, 126.58,686.05	−2.896	0.004
cTnI*, ng/mL	0.05, 0.01,0.45	0.12, 0.06,0.77	−1.911	0.056
Positive blood culture	23, 25.00	10, 33.33	0.796	0.372
ICU length of stay, days	7, 4,13	13, 7,19	−2.677	0.007
SOFA, score	8, 7,10	11, 8,12	−3.761	<0.001
APACHEII, score	18, 14,23	23, 18,29	−3.224	0.001

Note: * denotes indicators measured on day 2 post-admission.

Abbreviations: MAP, mean arterial pressure; PTX3, Pentraxin 3; Lac, lactic acid; WBC, white blood cell; PCT, procalcitonin; CRP, C-reactive protein; CK-MB, Creatine Kinase-Myocardial Band; MYO, myoglobin; cTnI, cardiac troponin I; NT-proBN, precursor of N-terminal B-type natriuretic peptide; AST, aspartate aminotransferase; ALT, alanine aminotransferase; SCr, serum creatinine; SOFA, sequential organ failure score; APACHEII, Acute Physiology and Chronic Health Status Score II.

Table 2 Correlation Between Plasma PTX3 Concentration and Clinical Indicators

Indicator	PTX3		Indicator	PTX3	
	r value	*P* value		r value	*P* value
WBC	−0.179	0.055	NT-proBNP	0.065	0.491
PCT	0.235	0.011	cTnI	0.156	0.095
CRP	−0.036	0.704	Elevated cTnI value	0.217	0.019
Lac	0.285	0.002	SOFA score	0.271	0.003
CK-MB	0.153	0.102	APACHEII score	0.197	0.034
MYO	0.289	0.002	ICU length of stay, days	0.306	0.001

Note: The difference in cTnI refers to the increase in concentration on day 2 compared to admission.

Logistic Regression Analysis of Factors Influencing the Onset of SCM

A multivariate logistic regression analysis was conducted, using the occurrence of SCM as the dependent variable. A multivariate model was constructed using backward stepwise regression: ① a priori inclusion of age, sex, previous coronary heart disease, and diabetes mellitus; ② screening for variables with P<0.05 in univariate analysis, CRP, PCT, CK-MB, MYO, PTX3, SOFA, and the APACHE II score; ③ stepwise elimination of non-significant variables based on AIC minimisation criterion until the model parsimony was optimal. Model assumptions were validated: the Hosmer-Lemeshow test showed a good model fit, χ^2=9.19, p=0.327. The final results showed that after correcting for confounders, PTX3 concentration at admission and SOFA score emerged as independent predictors of SCM. The odds ratio, OR for PTX3 was 1.054, 95% CI: 1.024–1.084, $p < 0.001$, while the OR for the SOFA score was 1.369, 95% CI: 1.095–1.711, $p = 0.006$. For every 20 ng/mL increase in PTX3, the OR for developing SCM was 2.86, calculated using the formula: [OR' = Exp, 20B], Table 3.

Predictive Value of PTX3, SOFA, and Their Combination for SCM

Using the presence of SCM as the outcome variable, plasma PTX3, SOFA score, and a combined variable model incorporating both were evaluated as predictive indicators through the generation of ROC curves, Figure 1. The area under the curve, AUC of PTX3 was greater than that of the other indices, PCT, CKMB, myoglobin, SOFA, APACHEII. DeLong's test showed that the difference in AUC between PTX3 and PCT and myoglobin was statistically significant, $p < 0.05$, Table 4. AUC values, along with their 95% CI, were 0.784, 95% CI: 0.688–0.880 for PTX3, 0.727, 95% CI: 0.618–0.836 for SOFA, and 0.834, 95% CI: 0.749–0.918 for the combined model. The combined model demonstrated the highest AUC, indicating superior predictive performance. Using the threshold corresponding to the maximum Youden's index, the optimal cutoff value for PTX3 in predicting the occurrence of SCM was identified as 20.82 ng/mL, with a sensitivity of 76.7% and a specificity of 70.7%, Table 5.

Dynamic Changes in Plasma PTX3 Concentrations

Plasma PTX3 concentrations exhibited a downward trend in both groups as the disease progressed. Due to differences in ICU stay durations, the number of participants at each time point varied slightly. In the non-SCM group, 92 patients were evaluated

Table 3 Multivariate Logistic Regression Analysis of Factors Associated With SCM Occurrence, n = 122

Variable	B	SE	Wald	Exp, B	95% CI	*P* value
PTX3	0.052	0.015	12.967	1.054	1.024~1.084	<0.001
SOFA	0.314	0.114	7.601	1.369	1.095~1.711	0.006
APACHEII	0.069	0.037	3.450	1.072	0.996~1.153	0.063
Constant	−6.143	1.409	19.016	0.002		<0.001

https://doi.org/10.2147/JIR.S517566

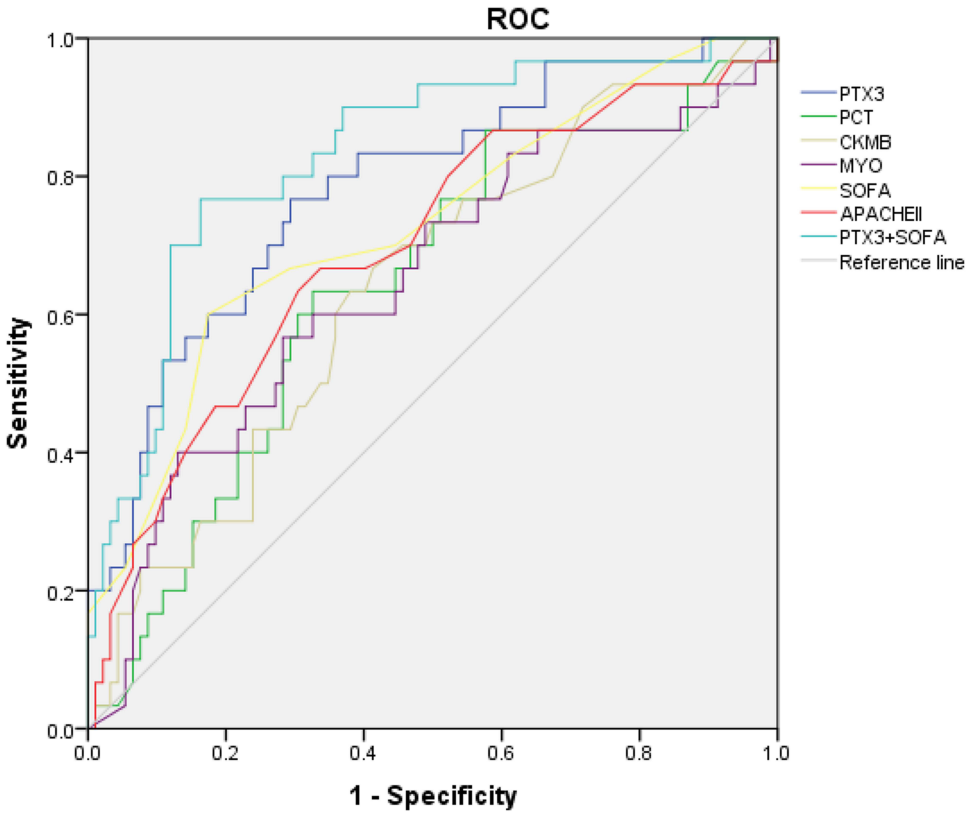

Figure 1 ROC curves for predicting SCM using PTX3, SOFA score, and various biomarkers at admission.

at admission, 87 on day 3, and 51 on day 7, whereas in the SCM group, 30 patients were evaluated at admission, 29 on day 3, and 23 on day 7. Kruskal–Wallis H-test showed that in the SCM group, there was a significant difference in PTX3 concentrations measured at three different time points, H=36.065, p<0.001, Dunn-Bonferroni post-hoc test showed that PTX3 concentrations on day 7, 8.20 [5.16,10.21] ng/mL were significantly lower than those at the time of admission, 37.11 [20.40,53.58] ng/mL and on the low 3 days, 23.26 [23.26,53.58] ng/mL., 37.11 [20.40,53.58] ng/mL at admission, corrected p<0.001 and 3 days lower, 23.26 [18.71,34.12] ng/mL, corrected p<0.001; there was no significant difference in PTX3 concentration between admission and day 3, corrected p=0.054. In the non-SCM group, there was a significant difference

Table 4 DeLong Test

Test Results	AUC Difference	z	*p*
PTX3 - PCT	0.144	2.601	0.009
PTX3 - CKMB	0.145	1.949	0.051
PTX3 - myoglobin	0.137	2.065	0.039
PTX3 - SOFA	0.057	0.789	0.43
PTX3 - APACHEII	0.088	1.262	0.207

Table 5 Predictive Utility of PTX3, SOFA, and Their Combination in SCM

Variable	AUC	95% CI	Optimal Cutoff Value	Youden's Index	Sensitivity	Specificity	*P* value
PTX3	0.784	0.688~0.880	20.82	0.474	0.767	0.707	<0.001
SOFA	0.727	0.618~0.836	10.5	0.426	0.600	0.826	<0.001
Combined variable	0.834	0.749~0.918	0.297	0.604	0.767	0.837	<0.001

Table 6 Comparison of Plasma PTX3 Concentrations Between Groups at Different Time Points

PTX3, ng/mL	SCM Group	Non-SCM Group	Z value	*P* value
At admission	37.11, 20.40,53.58	14.28, 6.50,23.72	4.661	<0.01
Day 3	23.26, 18.71,34.12	9.17, 5.26,13.46	5.518	<0.01
Day 7	8.20, 5.16,10.21	7.15, 4.30,9.16	1.524	0.127

between the PTX3 concentrations measured at the three different time points, H=34.833, p<0.001, Dunn-Bonferroni post hoc test showed that the PTX3 concentration on day 7, 7.15 [4.30,9.16] ng/mL was significantly lower than that at the time of admission, 14.28, 6.50,23.72 ng/ mL, corrected p<0.001 and day 3, 9.17[5.26,13.46]ng/mL, corrected p=0.019 and significantly lower on day 3 than on admission, corrected p=0.001.

On admission and day 3, plasma PTX3 concentrations were significantly higher in the SCM group compared to the non-SCM group, $p < 0.01$. By day 7, no statistically significant differences in PTX3 concentrations were observed between the two groups, $p > 0.05$, as shown in Table 6 and Figure 2.

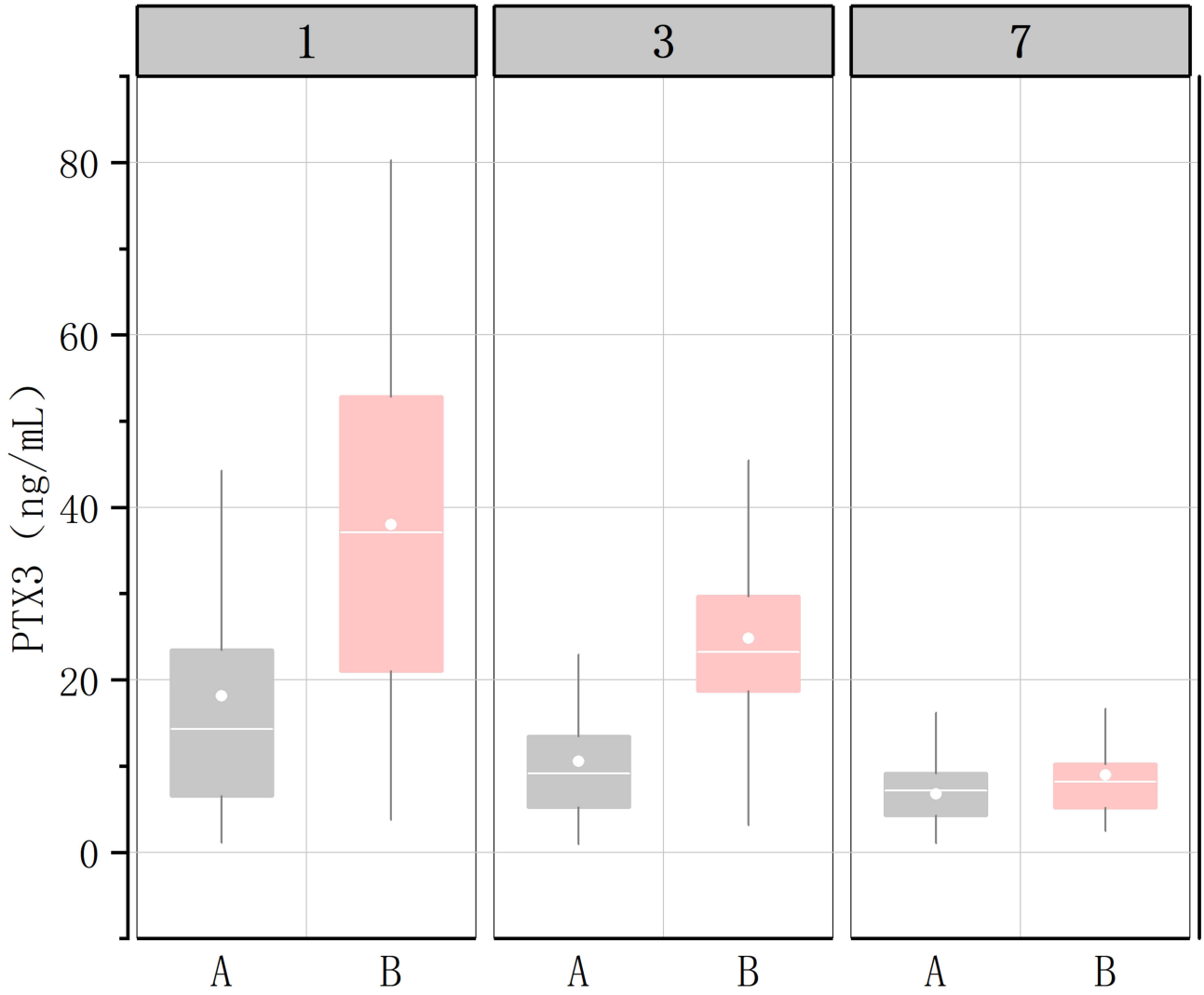

Figure 2 Dynamic changes in plasma PTX3 concentrations between the two groups of patients.
Note: The time points 1, 3, and 7 represent admission, day 3, and day 7 post-admission, respectively. Group A represents the non-SCM group, while Group B represents the SCM group.

https://doi.org/10.2147/JIR.S517566

Discussion

Sepsis is characterized by life-threatening organ dysfunction resulting from a dysregulated immune response to infection. SCM refers to myocardial suppression caused by sepsis and is associated with increased mortality among individuals with sepsis.[14] When SCM progresses to cardiogenic shock, the acute-phase mortality risk for patients may reach 70% to 80%. However, cardiac function in affected individuals often normalizes within 7 to 10 days if the critical phase is overcome. In this study, the incidence of SCM was 24.6%, consistent with the incidence rates reported both domestically and internationally.[4]

Cardiac dysfunction induced by sepsis frequently leads to circulatory failure, causing reduced blood flow, mitochondrial dysfunction, tissue hypoxia, metabolic disorders, and ultimately end-stage immune suppression. These pathophysiological processes may further aggravate cardiovascular failure, culminating in mortality among individuals with sepsis.[15] The intricate interactions between the immune system and invading pathogens often lead to severe complications.

Given these challenges, early detection, prompt recognition, and timely treatment of SCM, along with targeted interventions, are crucial for improving clinical outcomes. Despite these considerations, specific biomarkers capable of reliably predicting the onset of SCM remain lacking, underscoring the need for continued research to identify robust diagnostic indicators.

PTX3 is a recently identified inflammatory mediator belonging to the same superfamily as the short pentraxin CRP. Despite their shared classification, PTX3 and CRP differ significantly in gene structure, ligand recognition, induction signals, distribution, and sources, which confer distinct biological properties. Evidence suggests that PTX3 functions as an early inflammatory marker that correlates with disease severity and prognosis in individuals with sepsis.[9,10]

Elevated plasma PTX3 concentrations have been shown to assess the severity of infection and the critical condition of patients. Additionally, PTX3 levels are useful in evaluating therapeutic efficacy and predicting hospitalization duration.[16] Unlike CRP, PTX3 is produced and released by various cell types and tissues, mainly damaged myocardial cells, activated endothelial cells, and neutrophils.[17] In healthy individuals, peripheral blood PTX3 concentrations remain below 2 ng/mL. Following infection, inflammatory cells and local resident cells rapidly produce and release PTX3, causing a rapid increase in its concentrations within peripheral blood or tissues.

This process occurs significantly earlier than the release of CRP and serum amyloid protein from the liver. PTX3 concentrations peak 6 to 8 hours after tissue injury and exhibit a strong correlation with disease severity, whereas CRP levels in peripheral circulation rise 24–30 hours after injury and peak at approximately 48 hours.[18,19] Consequently, PTX3 serves as a superior acute-phase reactant biomarker compared to CRP, offering a more precise reflection of local tissue inflammation.

In cardiovascular disease research, PTX3 has been found to be synthesized locally in higher amounts in individuals with chronic heart failure. It is subsequently released into the circulation, serving as an inflammatory marker reflecting local cardiovascular inflammation and damage.[20] PTX3 shows potential as a biomarker for the early diagnosis of coronary artery disease, CAD, especially in patients in whom traditional screening methods, eg, lipid testing do not allow early detection of the disease, PTX3 provides additional diagnostic information.[21] PTX3 is strongly associated with prognosis in patients with CAD, and high circulating PTX3 concentrations are associated with an increased risk of adverse outcomes and a significantly higher risk of death.[22] PTX3 concentrations are significantly higher in patients with high Gensini scores, reflecting the severity of coronary artery disease, suggesting a strong correlation between PTX3 and the severity of coronary stenosis. In patients with acute ST-segment elevation myocardial infarction, STEMI, PTX3 levels were significantly elevated and strongly correlated with the severity of the disease and poor prognosis, especially when combined with other indices, such as NT-proBNP, which significantly improves the accuracy of prediction.[23] In patients with heart failure, HF, PTX3 showed high sensitivity and specificity, and was able to effectively predict the prognosis of patients. It has been shown that PTX3 can be used as a complementary indicator for risk stratification of HF patients, and when used in conjunction with existing scoring systems, eg, HFSS, MAGGIC, and SHFM, patient prognosis can be better assessed.[23] These findings highlight the potential value of PTX3 as a biomarker of inflammation and damage to the cardiovascular system.

The present study observed that patients with SCM had significantly higher plasma PTX3 concentrations upon admission to the ICU and experienced prolonged ICU stays compared to individuals without SCM. These findings align with the research conducted by Ma et al, which identified PTX3 as a key gene in the progression of SCM, primarily exhibiting anti-inflammatory effects.[11] Neutrophils and M2 macrophages were identified as the primary immune cells infiltrating myocardial tissue in SCM,

suggesting their potential as prognostic and therapeutic targets in the clinical management of SCM. Excessive anti-inflammatory activity and neutrophil infiltration may be the main causes of SCM development.

The dynamic assessment of PTX3 levels revealed a decline in plasma concentrations from admission to day 7 in both groups, consistent with findings by Vassalli et al.[24] Notably, on day 3 after admission, plasma PTX3 concentrations in the SCM group remained significantly higher than those in the non-SCM group. However, by day 7, no statistically significant differences were observed between the groups, possibly reflecting the reversible recovery of myocardial function and the overall improvement in the clinical condition of patients with SCM.

Further analysis demonstrated a strong association between PTX3 levels and disease severity. PTX3 concentrations were positively correlated with PCT, Lac, MYO, cTnI, and its dynamic elevation on day 2 relative to admission, as well as disease severity scores and ICU length of stay. These observations are consistent with the findings of Pietro et al, which indicate that higher plasma PTX3 concentrations may predict the occurrence of organ dysfunction.[25]

The binary logistic regression analysis conducted in this study identified PTX3 concentrations and SOFA scores as independent risk factors for the occurrence of SCM. This indicates that the occurrence of SCM is more closely associated with indicators of sepsis severity rather than conventional cardiac risk factors, such as myocardial biomarkers. These results corroborate the findings of Hanumanthu et al, who reported that increased myocardial biomarker levels do not reliably predict SCM occurrence.[14] In terms of diagnostic utility, PTX3 demonstrated superior AUC values compared to PCT, CK-MB, MYO, and APACHE II scores, indicating greater diagnostic accuracy for SCM. Additionally, the combined application of PTX3 and SOFA scores enhanced diagnostic performance, facilitating early detection of sepsis-related trends. This approach enables timely intervention and treatment, thereby improving the prognosis of patients with SCM.

Limitations

This study has several limitations that should be cautiously interpreted. First, the exploratory design allowed screening of potential biomarkers without strict multiplicity correction, which may increase the risk of type I errors. All reported associations should be regarded as hypothesis-generating findings and require validation in independent cohorts with pre-specified hypotheses and rigorous false discovery rate, FDR adjustments. Second, the relatively small sample size, constrained by data collection challenges, limits the generalizability of conclusions and underscores the necessity for replication in larger, multi-center cohorts, >500 patients with standardized sepsis subtyping. Third, although we focused on the relationship between PTX3 and septic cardiomyopathy, other inflammatory markers such as C-reactive protein, CRP and procalcitoninogen, PCT also play an important role in the development of sepsis and may have complex interrelationships with PTX3, making them potential confounders. Although we adjusted for some of the common inflammatory markers in our multivariate analyses, the interactions between these markers and their effects on the relationship between PTX3 and sepsis cardiomyopathy may not have been fully elucidated. Future studies need to explore the complex network of relationships between these inflammatory markers in more depth to further clarify the independent role of PTX3 in septic cardiomyopathy. Fourth, the impact of infection sites on the incidence of SCM was not statistically analyzed, and patient prognoses were not tracked. These aspects require further investigation and more comprehensive data collection.

Conclusion

PTX3 is a reliable biomarker for predicting the occurrence of SCM and serves as an independent risk factor for its development. Additionally, PTX3 levels correlate with the extent of organ dysfunction in individuals with septic shock. Clinically, PTX3 demonstrates potential for early detection of SCM, facilitating timely interventions and contributing to improved patient outcomes.

Abbreviations

PTX3, pentraxins 3; SCM, septic cardiomyopathy; SOFA, sequential organ failure assessment; APACHE II, acute physiology and chronic health evaluation II; ICU, Intensive Care Unit; ELISA, enzyme-linked immunosorbent assay; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end diastolic volume; cTnI, cardiac troponin I; CK-MB, creatine kinase MB; MYO, myoglobin; NT-proBNP, N-terminal brain natriuretic peptide; WBC, white blood cell count; PCT, procalcitonin; CRP, C-reactive protein; Lac, lactic acid; MAP, mean arterial pressure; OR, odds ratio; AUC, area under the curve; YI, Youden index.

https://doi.org/10.2147/JIR.S517566

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of Affiliated Hospital of Hebei University, Approval number is HDFYLL-KY-2023-167. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Acknowledgments

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

Funding

Hebei University Affiliated Hospital Young Scientific Research Fund Project, 2023QA05; Government-funded Training Programme for Excellence in Clinical Medicine, ZF2025261.

Disclosure

The authors declare that they have no competing interests.

References

1. Yin J, Chen Y, Huang JL, et al. Prognosis-related classification and dynamic monitoring of immune status in patients with sepsis: a prospective observational study. *World J Emerg Med*. 2021;12, 3:185–191. PMID: 34141032; PMCID: PMC8188286. doi:10.5847/wjem.j.1920-8642.2021.03.004
2. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock, sepsis-3. *JAMA*. 2016;315, 8:801–810. PMID: 26903338; PMCID: PMC4968574. doi:10.1001/jama.2016.0287
3. Liu YC, Yao Y, Yu MM, et al. Frequency and mortality of sepsis and septic shock in China: a systematic review and meta-analysis. *BMC Infect Dis*. 2022;22, 1:564. PMID: 35729526; PMCID: PMC9210671. doi:10.1186/s12879-022-07543-8
4. Sato R, Nasu M. A review of sepsis-induced cardiomyopathy. *J Intensive Care*. 2015;3:48. PMID: 26566443; PMCID: PMC4642671. doi:10.1186/s40560-015-0112-5
5. Sanfilippo F, Corredor C, Fletcher N, et al. Left ventricular systolic function evaluated by strain echocardiography and relationship with mortality in patients with severe sepsis or septic shock: a systematic review and meta-analysis. *Crit Care*. 2018;22, 1:183. PMID: 30075792; PMCID: PMC6091069. doi:10.1186/s13054-018-2113-y
6. Zhen J, Li L, Yan J. Advances in biomarkers of myocardial injury in sepsis. *Chin Crit Care Med*. 2018;30, 07:699–702. doi:10.3760/cma.j.issn.2095-4352.2018.07.017
7. Lu N, Yu J, Shao J, et al. Study on the relationship between ventricular function parameters obtained by echocardiography and prognosis of patients with sepsis. *Chin Crit Care Med*. 2022;34, 07:740–745. doi:10.3760/cma.j.cn121430-20210826-01281
8. Hamed S, Behnes M, Pauly D, et al. Diagnostic value of pentraxin-3 in patients with sepsis and septic shock in accordance with latest sepsis-3 definitions. *BMC Infect Dis*. 2017;17, 1:554. PMID: 28793880; PMCID: PMC5550951. doi:10.1186/s12879-017-2606-3
9. Wang G, Jiang C, Fang J, Li Z, Cai H. Pentraxin-3 as a predictive marker of mortality in sepsis: an updated systematic review and meta-analysis. *Crit Care*. 2022;26, 1:167. PMID: 35676730; PMCID: PMC9175505. doi:10.1186/s13054-022-04032-x
10. Milas GP, Issaris V, Niotis G. Pentraxin-3 and neonatal sepsis: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med*. 2023;36, 1:2205986. PMID: 37127619.. doi:10.1080/14767058.2023.2205986
11. Ma D, Qin X, Zhong ZA, Liao H, Chen P, Zhang B. Systematic analysis of myocardial immune progression in septic cardiomyopathy: immune-related mechanisms in septic cardiomyopathy. *Front Cardiovasc Med*. 2023;9:1036928. PMID: 36911241; PMCID: PMC10002421. doi:10.3389/fcvm.2022.1036928
12. L'Heureux M, Sternberg M, Brath L, Turlington J, Kashiouris MG. Sepsis-induced cardiomyopathy: a comprehensive review. *Curr Cardiol Rep*. 2020;22, 5:35. PMID: 32377972; PMCID: PMC7222131. doi:10.1007/s11886-020-01277-2
13. Hasegawa D, Ishisaka Y, Maeda T, et al. Prevalence and prognosis of sepsis-induced cardiomyopathy: a systematic review and meta-analysis. *J Intensive Care Med*. 2023;38, 9:797–808. PMID: 37272081. doi:10.1177/08850666231180526
14. Hanumanthu BKJ, Nair AS, Katamreddy A, et al. Sepsis-induced cardiomyopathy is associated with higher mortality rates in patients with sepsis. *Acute Crit Care*. 2021;36, 3:215–222. PMID: 34311515; PMCID: PMC8435447. doi:10.4266/acc.2021.00234
15. Carbone F, Liberale L, Preda A, Schindler TH, Montecucco F. Septic cardiomyopathy: from pathophysiology to the clinical setting. *Cells*. 2022;11, 18:2833. PMID: 36139408; PMCID: PMC9496713. doi:10.3390/cells11182833
16. Song J, Moon S, Park DW, et al. Biomarker combination and SOFA score for the prediction of mortality in sepsis and septic shock. *Medicine*. 2020;99:e20495. doi:10.1097/MD.0000000000020495
17. Gustin C, Delaive E, Dieu M, Calay D, Raes M. Upregulation of pentraxin-3 in human endothelial cells after lysophosphatidic acid exposure. *Arterioscler Thromb Vasc Biol*. 2008;28, 3:491–497. PMID: 18162608. doi:10.1161/ATVBAHA.107.158642

18. Davoudian S, Piovani D, Desai A, et al. A cytokine/PTX3 prognostic index as a predictor of mortality in sepsis. *Front Immunol*. 2022;13:979232. PMID: 36189302; PMCID: PMC9521428. doi:10.3389/fimmu.2022.979232
19. Porte R, Davoudian S, Asgari F, et al. The long pentraxin PTX3 as a humoral innate immunity functional player and biomarker of infections and sepsis. *Front Immunol*. 2019;10:794. PMID: 31031772; PMCID: PMC6473065. doi:10.3389/fimmu.2019.00794
20. Huang X, Lu J, Lin Y, Liu L, Shi Y. Advances on novel biological markers of heart failure]. *Shandong Med J*. 2019;59, 04:102–105.
21. Azami P, Mohammadzadeh S, Seirafi S, Razeghian-Jahromi I. A review of cutting-edge biomarkers for diagnosing coronary artery disease. *Medicine*. 2025;104, 4:e41377. PMID: 39854741; PMCID: PMC11771658. doi:10.1097/MD.0000000000041377
22. Kamarullah W, Nurcahyani, Multazam RB, Josephine CM. Pentraxin 3 concentration is associated with poor outcomes in patients with coronary artery disease: a systematic review and dose-response meta-analysis. *Acta Cardiol*. 2022;77, 5:385–394. PMID: 34281479. doi:10.1080/00015385.2021.1948715
23. Ye X, Wang Z, Lei W, et al. Pentraxin 3: a promising therapeutic target for cardiovascular diseases. *Ageing Res Rev*. 2024;93:102163. PMID: 38092307. doi:10.1016/j.arr.2023.102163
24. Vassalli F, Masson S, Meessen J, et al. Troponin T, N-terminal Pro-B-type natriuretic peptide in septic patients. *Shock*. 2020;54, 5:675–680. PMID: 32941388. doi:10.1097/SHK.0000000000001543
25. Caironi P, Masson S, Mauri T, et al.; ALBIOS Biomarkers Study Investigators. Pentraxin 3 in patients with severe sepsis or shock: the ALBIOS trial. *Eur J Clin Invest*. 2017;47, 1:73–83. PMCID: PMC5414835. doi:10.1111/eci.12704