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The use of high-sensitivity cardiac troponin I in assessing cardiac involvement and Disease prognosis in idiopathic inflammatory myopathy

Hao Zhang[1†], Huihui Chi[1†], Liangzhe Xie[2†], Yue Sun[1], Honglei Liu[1], Xiaobing Cheng[1], Junna Ye[1], Hui Shi[1], Qiongyi Hu[1], Jianfen Meng[1], Zhuochao Zhou[1], Jialin Teng[1], Chengde Yang[1*] and Yutong Su[1*]

Abstract

Objectives Cardiac involvement is one of the most serious complications of idiopathic inflammatory myopathy (IIM) that indicates poor prognosis. However, there is a lack of effective biomarkers for the identification of cardiac involvement and the prediction of prognosis in IIM. Here, we aimed to explore the value of different cardiac biomarkers in IIM patients.

Methods A total of 142 IIM patients in the Department of Rheumatology and Immunology, Ruijin Hospital from July 2019 to October 2022 were included in this study. The clinical characteristics, laboratory tests, treatments and prognosis were recorded. The disease activity was assessed according to the core set measures. The correlations of the serum cardiac biomarkers levels with disease activity were analyzed by the Spearman correlation test. Risk factors for cardiac involvement were evaluated by multivariate logistic regression analysis.

Results Higher high-sensitivity cardiac troponin I (hs-cTnI) levels were associated with cardiac involvement (n = 41) in IIM patients [adjusted OR 7.810 (95% CI: 1.962–31.097); $p = 0.004$], independent of other serum cardiac biomarkers. The abnormal hs-cTnI had the highest AUC for distinguishing of cardiac involvement in IIM patients (AUC = 0.848, 95% CI: 0.772,0.924; $p < 0.001$). Besides, we found that high serum levels of hs-cTnI were significantly correlated with disease activity. Moreover, patients with higher serum levels of hs-cTnI tended to suffer from poor prognosis.

Conclusions Serum hs-cTnI testing may play a role in screening for cardiac involvement in IIM patients. Abnormal levels of serum hs-cTnI were associated with increased disease activity and poor prognosis.

†Hao Zhang, Huihui Chi and Liangzhe Xie contributed equally to this work.

*Correspondence:
Chengde Yang
yangchengde@sina.com
Yutong Su
suyt2015@163.com

Full list of author information is available at the end of the article

Key Points

1.Among all the cardiac biomarkers, the serum levels of hs-cTnI were independently associated with cardiac involvement in IIM patients.

2.The serum levels of hs-cTnI were significantly correlated with disease activity in IIM patients.

3.The abnormal hs-cTnI levels were correlated with poor prognosis in IIM patients.

Keywords Idiopathic inflammatory myopathy, Cardiac involvement, High-sensitivity cardiac troponin I, Biomarker, Disease activity, Prognosis

Introduction

Idiopathic inflammatory myopathy (IIM) is a group of autoimmune diseases characterized with skeletal muscle injury and multisystem involvement [1]. In adults, IIM contains dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy (IMNM), antisynthetase syndrome (ASS) and inclusion body myositis (IBM) [2]. Cardiac involvement is one of the leading causes of poor prognosis, which occurs in 9–72% of the IIM patients [3–5]. Because of the atypical early clinical symptoms, the incidence of cardiac involvement in IIM patients might be underestimated. Early detection and intervention are important to improve the prognosis of cardiac involvement in IIM patients. Endomyocardial biopsy contributes to the diagnosis of myocarditis, myocardial ischemia and fibrosis, but it is not routinely performed in clinical practice. Electrocardiography (ECG), echocardiogram, and cardiac magnetic resonance (MR) help to demonstrate heterogeneous severe cardiac involvement in IIM patients. However, asymptomatic patients with subclinical cardiac involvement might be unrecognized through these diagnostic techniques.

Serum cardiac biomarkers are more convenient and could be dynamically monitored, which include creatine kinase (CK), creatine kinase MB (CK-MB), high-sensitivity cardiac troponin I (hs-cTnI), myoglobin (Mb) and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Cohort studies based on general population have found that those cardiac biomarkers had promising predictive value for cardiac injury. Previous studies have demonstrated that cardiac troponin was associated with inflammatory cardiovascular involvement in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) [6, 7]. Those data highlight the value of these biomarkers in autoimmune disease. However, it is known that some of these indicators, such as cardiac troponin T (cTnT) or CK, can also increase when skeletal muscle is damaged, as a result, they lack specificity for the myocardium. Therefore, further studies are needed for assessing the application of these biomarkers in IIM patients. Nowadays, it is reported that serum troponins have utility in screening for cardiac involvement and disease activity in IIM patients [8]. However, more data are needed to evaluate the value of the cardiac biomarkers in IIM patients. The relationship between the serum cardiac biomarkers and the prognosis in IIM patients is still unknown. Therefore, in this study, we aimed to evaluate the potential of serum cardiac biomarkers in assessing cardiac involvement and prognosis in IIM.

Methods

Patients

A total of 142 IIM patients admitted to the Department of Rheumatology and Immunology, Ruijin Hospital from July 2019 to October 2022 were consecutively enrolled and followed up. All patients fulfilled the Bohan and Peter IIM criteria or 2004 European Neuromuscular Centre (ENMC) criteria or the 2017 EULAR/ACR criteria [9–11]. The diagnosis was performed independently by at least two well-trained rheumatologists. Patients with a history of ischemic heart disease or heart failure, evidence of severe lung infection or malignancy were excluded. Informed consent was obtained from all patients, and the clinical records were anonymized before analysis. This survey was approved by the Institutional Research Ethics Committee of Ruijin Hospital (ID: 2016–62) and was conducted following the Principles of the Declaration of Helsinki. Patients received regular outpatient or telephone follow-up after discharge.

Assessments

Clinical data including demographic characteristics, clinical manifestations, laboratory tests, and treatment strategies were recorded. Serological markers were measured at admission, every 3–5 days during hospitalization and at monthly outpatient follow-up after discharge. Cardiac involvement was defined as the occurrence of rhythm disturbances, conduction defects, myocarditis, pericarditis and heart failure due to the IIM disease process, and assessment was conducted by at least two clinicians. The ECG changes were new-onset and could not be explained by other causes. In our study, all patients performed echocardiogram and some patients performed cardiac magnetic resonance during hospitalization. The clinician that evaluated the criteria for cardiac involvement was blinded to patients' lab results.

The disease activity of each patient was assessed according to the core set measures (CSMs) from International Myositis Assessment and Clinical Studies Group

(IMACS). The assessment included physician global activity (PhGA), patient global activity (PGA), manual muscle testing-8 (MMT-8), health assessment questionnaire (HAQ), muscle enzyme activities and extramuscular disease activity based on the myositis disease activity assessment tool (MDAAT). The remission phase was defined as the period during which the glucocorticoid dose could be reduced for more than 3 months without a relapse [12]. All assessments of the enrolled patients were performed by a well-trained clinician. In this study, patients were all screened for myositis-specific antibodies (MSAs) and myositis-associated antibodies (MAAs) using a commercial immunoblot assay with sixteen autoantigens.

Statistics

Continuous data were expressed as the mean with standard deviation (SD) or median with interquartile range (IQR) and were evaluated by using Student's t-test or the Mann-Whitney U-test, respectively. Categorical data were presented as frequency counts (percentages) and were compared by $\chi 2$ test or Fisher's exact test, as appropriate. We used the Spearman correlation test to analyze the correlation between serum cardiac biomarkers with different aspects of disease activity. The receiver operating characteristic (ROC) curve was used to determine the related cut-off values and the maximum Youden index. Univariate and multivariate logistic regression analyses were used to evaluate different factors that could predict cardiac involvement in IIM. Variables that were significant in the univariate analysis were included in the multivariate analysis. The Kaplan-Meier survival curve and the log-rank test were used to compare survival rates. A two-tailed p-value <0.05 was considered statistically significant. All statistical analysis was performed using the IBM SPSS statistics 26.0. Figures were presented using the GraphPad Prism version 9.0.

Results

Clinical characteristics of IIM patients

A total of 142 patients with IIM were recruited. In our study, 98 patients were new-onset and 44 patients were relapsed. They were hospitalized with clinical symptoms due to the activity or recurrence of the disease. The clinical characteristics and laboratory parameters of the patients were shown in Table 1. Of all the cases, 81 had DM, 14 had PM, 33 had ASS and 14 had IMNM. The age of the patients ranged from 19 to 82 years, with a median age of 55 years. The majority of patients were women (71.8%) and the median disease course was 5 months. We identified that 41 (28.9%) IIM patients had cardiac involvement. The types of cardiac involvement were detailed in supplementary Table 1. The distribution of antibody in patients with cardiac involvement was presented in Supplementary Fig. 1. We observed that patients with positive anti-signal recognition particle (SRP) autoantibody had the highest rate (50%) of cardiac involvement, followed by anti-glycyl (EJ) autoantibody (40%) and anti-histidyl (Jo-1) autoantibody (33.3%). We found that patients with cardiac involvement were older (61 years vs. 52 years, $p<0.001$) and had higher levels of white blood cell (WBC) (10.6 *10^9/L vs. 8.1 *10^9/L, $p=0.014$), C-reactive protein (CRP) (5 mg/L vs. 3 mg/L, $p=0.047$), erythrocyte sedimentation rate (ESR) (12 mm/h vs. 7 mm/h, $p=0.044$). As for cardiac biomarkers, CK-MB (5.4 ng/mL vs. 1.4 ng/mL, $p<0.001$), hs-cTnI (37.6 pg/mL vs. 4.8 pg/mL, $p<0.001$), Mb (73.6 ng/mL vs. 22.6 ng/mL, $p=0.001$), NT-proBNP (419.7 pg/mL vs. 84.2 pg/mL, $p<0.001$), lactate dehydrogenase (LDH) (334 IU/L vs. 240IU/L, $p=0.001$) and aspartate aminotransferase (AST) (42 IU/L vs. 27 IU/L, $p=0.022$) were significantly higher in patients with cardiac involvement than those without cardiac involvement. Furthermore, higher indicators of disease activity were observed in patients with cardiac involvement, including PhGA (4 vs. 3.2, $p=0.013$), HAQ (0.5 vs. 0.3, $p=0.040$), and MDAAT (3 vs. 2, $p<0.001$).

The correlations between serum cardiac biomarkers and Disease activity in IIM patients

To further explore the relationship between serum cardiac biomarkers and disease activity, we performed the Spearman correlation test between the levels of CK, CK-MB, hs-cTnI, Mb, NT-proBNP and disease activity score (Table 2). All these biomarkers showed significant correlations with the disease activity. The hs-cTnI had significant correlations with PhGA ($r=0.403$, $p<0.001$), PGA ($r=0.296$, $p<0.001$), HAQ ($r=0.254$, $p<0.001$), MMT-8 (r = -0.187, $p=0.026$) and MDAAT ($r=0.342$, $p<0.001$). The CK-MB showed significant correlations with PhGA ($r=0.431$, $p<0.001$), PGA ($r=0.299$, $p<0.001$), HAQ ($r=0.283$, $p=0.001$) and MMT-8 (r = -0.351, $p<0.001$). The Mb was highly correlated with PhGA ($r=0.466$, $p<0.001$), PGA ($r=0.252$, p=0.002), HAQ ($r=0.270$, $p=0.001$) and MMT-8 (r = -0.303, $p<0.001$). The serum CK levels was also correlated with PhGA ($r=0.311$, $p<0.001$), PGA ($r=0.203$, p=0.015), HAQ ($r=0.227$, $p=0.007$) and MMT-8 (r = -0.279, $p=0.001$). The NT-proBNP showed significant correlations with PhGA ($r=0.307$, $p<0.001$), PGA ($r=0.227$, $p=0.007$) and MDAAT ($r=0.305$, $p<0.001$). In addition, we evaluated the serum cardiac biomarkers before and after treatment in Supplementary Fig. 2. We found that all these indicators significantly decreased after remission.

Table 1 Demographic and clinical features in IIM patients

	Total (*n* = 142)	**With cardiac involvement (*n* = 41)**	**Without cardiac involvement (*n* = 101)**	***p* -values**
Classification of the disease				
Dermatomyositis, *n* (%)	81 (57.0)	21 (51.2)	60 (59.4)	0.273
Polymyositis, *n* (%)	14 (9.9)	5 (12.2)	9 (8.9)	
Anti-synthetase syndrome, *n* (%)	33 (23.2)	13 (31.7)	20 (19.8)	
Immune-mediated necrotizing myopathy, *n* (%)	14 (9.9)	2 (4.9)	12 (11.9)	
Demographics				
Age, median (IQR), years	55.0 (45.8–64.0)	61.0 (52.0–69.5)	52.0 (43.0–61.0)	**< 0.001**
Female gender, *n* (%)	102 (71.8)	29 (70.7)	73 (72.3)	0.853
Disease course, median (IQR), months	5.0 (2.8–12.0)	7 (2.5–24.0)	5.0 (2.5–12.0)	0.170
BMI, mean ± SD	23.7 ± 3.9	22.8 ± 4.0	24.0 ± 3.8	0.090
Clinical features				
Fever, *n* (%)	38 (26.8)	13 (31.7)	25 (24.8)	0.396
muscle weakness, *n* (%)	52 (36.6)	17 (41.5)	35 (34.7)	0.445
Arthralgia, *n* (%)	45 (31.7)	10 (24.4)	35 (34.7)	0.234
Dysphagia, *n* (%)	8 (5.6)	2 (4.9)	6 (5.9)	0.803
Skin involvement, *n* (%)	85 (59.9)	26 (63.4)	59 (58.4)	0.582
Interstitial lung diseases, *n* (%)	83 (58.5)	29 (70.7)	54 (53.5)	0.058
Cardiovascular risk factors				
Hypertension, *n* (%)	24 (16.9)	9 (22)	15 (14.9)	0.306
Diabetes mellitus, *n* (%)	10 (7.0)	2 (4.9)	8 (7.9)	0.521
Hyperlipemia, *n* (%)	18 (12.7)	5 (12.2)	13 (12.9)	0.913
smoke current, *n* (%)	16 (24.5)	3 (7.3)	13 (12.9)	0.343
Laboratory tests				
WBC, median (IQR), *10^9/L	8.6 (6.1–11.5)	10.6 (6.5–12.8)	8.1 (6.0–11.0)	**0.014**
CRP, median (IQR), mg/L	3.0 (1.0–10.6)	5.0 (1.0–32.0)	3.0 (1.0–7.0)	**0.047**
ESR, median (IQR), mm/h	9.0 (5.8–24.0)	12.0 (6.0–28.5)	7.0 (5.0–19.0)	**0.044**
CK, median (IQR), IU/L	79.5 (50.0–175.3)	108.0 (62.0–453.5)	73.0 (48.0–160.5)	0.058
CK-MB, median (IQR), ng/mL	2.1 (0.8–9.1)	5.4 (2.3–36.4)	1.4 (0.7–6.0)	**< 0.001**
hs-cTnI, median (IQR), pg/mL	6.5 (2.6–32.0)	37.6 (17.0–109.1)	4.8 (2.3–10.0)	**< 0.001**
Mb, median (IQR), ng/mL	25.0 (14.3–90.2)	73.6(19.8–315.4)	22.6 (12.8–48.5)	**0.001**
NT-proBNP, median (IQR), pg/mL	129.1 (49.5–372.8)	419.7 (176.9–1609.5)	84.2 (41.5–183.0)	**< 0.001**
LDH, median (IQR), IU/L	254.0 (207.8–382.8)	334.0 (234.5–552.0)	240.0 (196.5–332.5)	**0.001**
AST, median (IQR), IU/L	30.0 (19.0–53.3)	42.0 (25.0–70.0)	27.0 (18.5–43.5)	**0.022**
ALT, median (IQR), IU/L	25.0 (14.0–59.3)	21.0 (14.0–57.0)	26.0 (14.0–59.5)	0.855
eGFR, mean ± SD, mL/min/1.73m2	99.4 ± 19.3	94.2 ± 20.9	101.5 ± 18.3	0.055
Disease activity measures				
PhGA, median (IQR)	3.5 (2.8–4.5)	4.0 (3.0–5.2)	3.2 (2.4–4.0)	**0.013**
PGA, median (IQR)	4.5 (3.0–6.0)	4.5 (3.0–6.3)	4.5 (3.0–6.0)	0.483
HAQ, median (IQR)	0.4 (0–0.8)	0.5 (0.2–1.0)	0.3 (0–0.6)	**0.04**
MMT-8, median (IQR)	76.0 (70.8–78.0)	74.0 (70.0–80.0)	76.0 (72.0–78.0)	0.784
MDAAT, median (IQR)	2.0 (2.0–3.0)	3.0 (2.5–4.0)	2.0 (1.0–3.0)	**< 0.001**

Values are presented as mean with standard deviation or median with interquartile range for continuous variables, and as numbers with percentage for categorical variables. $P < 0.05$ is shown in bold type. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; CK: creatine kinase; CK-MB: creatine kinase MB; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; ESR: erythrocyte sedimentation rate; HAQ: health assessment questionnaire; hs-cTnI: high-sensitivity cardiac troponin I; IQR: interquartile range; LDH: lactate dehydrogenase; Mb: myoglobin; MDAAT: myositis disease activity assessment tool; MMT-8: manual muscle testing-8; NT-proBNP: N-terminal pro-B-type natriuretic peptide; PGA: patient global activity; PhGA: physician global activity; SD: standard deviation; WBC: white blood cell

The value of serum cardiac biomarkers in identifying cardiac involvement

To evaluate the ability of different serum biomarkers in distinguishing cardiac involvement, we performed the ROC analysis. We found that the hs-cTnI in the active period had the best predictive value (AUC = 0.848, 95%CI: 0.772,0.924; $p < 0.001$) (Fig. 1). The cut-off value at 13.8 pg/ml had a sensitivity of 80.5% and a specificity of 79.2%. Similarly, we calculated the AUC for the other four indicators including NT-proBNP (AUC = 0.835,

Table 2 Correlation of serum cardiac biomarkers levels with disease activity in IIM patients

	CK		CK-MB		hs-cTnI		Mb		NT-proBNP	
	r	*p*-values	*r*	*p*-values	*r*	*p*-values	*r*	*p*-values	*r*	*p*-values
PhGA	0.311	**< 0.001**	0.431	**< 0.001**	0.403	**< 0.001**	0.466	**< 0.001**	0.307	**< 0.001**
PGA	0.203	**0.015**	0.299	**< 0.001**	0.296	**< 0.001**	0.252	**0.002**	0.227	**0.007**
HAQ	0.227	**0.007**	0.283	**0.001**	0.254	**< 0.001**	0.270	**0.001**	0.148	0.079
MMT-8	-0.279	**0.001**	-0.351	**< 0.001**	-0.187	**0.026**	-0.303	**< 0.001**	-0.058	0.497
MDAAT	0.018	0.830	0.154	0.068	0.342	**< 0.001**	0.137	0.104	0.305	**< 0.001**

r: Spearman's rank correlation coefficient. CK: creatine kinase; CK-MB: creatine kinase MB; HAQ: health assessment questionnaire; hs-cTnI: high-sensitivity cardiac troponin I; Mb: myoglobin; MDAAT: myositis disease activity assessment tool; MMT-8: manual muscle testing-8; NT-proBNP: N-terminal pro-B-type natriuretic peptide; PGA: patient global activity; PhGA: physician global activity

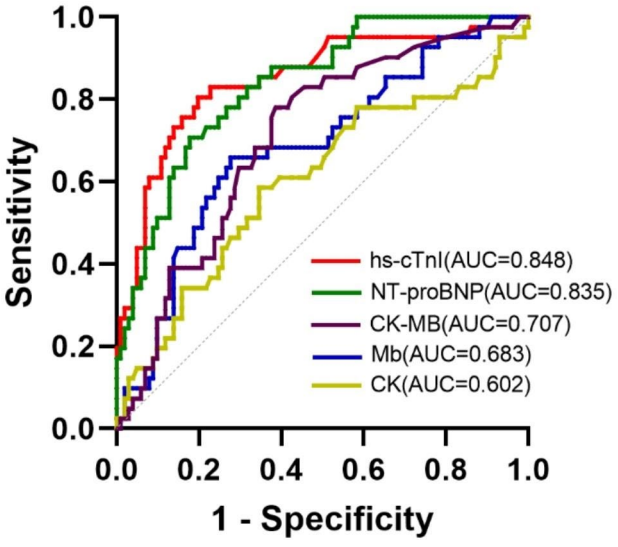

Fig. 1 Receiver operating characteristic (ROC) curves of the predictive capacity of the serum cardiac biomarkers to distinguish cardiac involvement in IIM patients. The area under the curve (AUC) was 0.848 (95%CI: 0.772,0.924; p < 0.001) for hs-cTnI, 0.835 (95%CI: 0.767,0.904; p < 0.001) for NT-proBNP, 0.707 (95%CI: 0.616,0.797; p < 0.001) for CK-MB, 0.683 (95%CI: 0.586,0.781; p = 0.001) for Mb and 0.602 (95%CI: 0.493,0.710; p = 0.058) for CK. CK: creatine kinase; CK-MB: creatine kinase MB; hs-cTnI: high-sensitivity cardiac troponin I; Mb: myoglobin; NT-proBNP: N-terminal pro-B-type natriuretic peptide

95%CI: 0.767,0.904; $p<0.001$), CK-MB (AUC=0.707, 95%CI: 0.616,0.797; $p<0.001$), Mb (AUC=0.683, 95%CI: 0.586,0.781; $p=0.001$) and CK (AUC=0.602, 95%CI: 0.493,0.710; $p=0.058$). Although the markers were similarly useful in identifying cardiac involvement, they were still less efficient than hs-cTnI. Furthermore, we performed the logistic regression analysis to evaluate the potential risk factors of cardiac involvement in IIM patients (Table 3). Univariate logistic regression analysis showed that the age (>49.5 years), the initial levels of WBC (>11.4*10^9/L), CRP (>11.5 mg/L), ESR (>9.5 mm/h), CK-MB (>2.1 ng/mL), hs-cTnI (>13.8 pg/ml), Mb (>38.3 ng/mL), NT-proBNP (>247 pg/ml), LDH (>405 IU/L) and AST (>49.5 IU/L) were highly associated with cardiac involvement. Multivariate logistic regression analysis demonstrated that age (>49.5 years) and the serum hs-cTnI (>13.8 pg/ml) were independent risk factors of cardiac involvement with an odds ratio (OR) of 5.560 (95% CI: 1.264, 24.468; $p=0.023$) and 7.810 (95% CI: 1.962, 31.097; $p=0.004$), respectively.

The value of hs-cTnI in predicting the treatment and prognosis in IIM patients

To evaluate the effect of hs-cTnI on the treatment and prognosis, we divided the patients into two groups

Table 3 Logistic regression of risk factors for cardiac involvement in IIM patients

	univariate analysis			multivariate analysis		
	OR	95%CI	*p*-values	OR	95%CI	*p*-values
Age > 49.5 years	9.017	2.609–31.166	**0.001**	5.560	1.264–24.468	**0.023**
WBC > 11.4*10^9/L	3.982	1.793–8.843	**0.001**	2.247	0.747–6.755	0.149
CRP > 11.5 mg/L	3.763	1.658–8.538	**0.002**	1.307	0.332–5.155	0.702
ESR > 9.5 mm/h	2.756	1.300-5.841	**0.008**	1.680	0.492–5.741	0.408
CK-MB > 2.1 ng/mL	5.652	2.438–13.107	**< 0.001**	1.461	0.336–6.351	0.613
hs-cTnI > 13.8 pg/mL	16.706	6.695–41.686	**< 0.001**	7.810	1.962–31.097	**0.004**
Mb > 38.3 ng/mL	5.028	2.308–10.955	**< 0.001**	1.176	0.277–4.987	0.826
NT-proBNP > 247 pg/mL	11.144	4.792–25.915	**< 0.001**	2.858	0.889–9.188	0.078
LDH > 405 IU/L	3.867	1.724–8.671	**0.001**	0.245	0.049–1.211	0.084
AST > 49.5 IU/L	3.498	1.595–7.669	**0.002**	2.647	0.577–12.151	0.211

ROC analyses were used to determine values at the maximum Youden index as cut-off points for continuous variables. Variables identified in the univariate logistic regression analysis ($p<0.05$) were entered into a conditional forward multivariable logistic regression model to predict risk factors for cardiac involvement. $P<0.05$ is shown in bold type. AST: aspartate aminotransferase; CI: confidence interval; CK-MB: creatine kinase MB; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; hs-cTnI: high-sensitivity cardiac troponin I; LDH: lactate dehydrogenase; Mb: myoglobin; NT-proBNP: N-terminal pro-B-type natriuretic peptide; OR: odds ratio; WBC: white blood cell

according to the levels of hs-cTnI (Table 4). Our results showed that patients with abnormal levels of hs-cTnI (>30 pg/mL) were prescribed higher doses of glucocorticoids ($p=0.001$). Besides, the beta blocker, angiotensin converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB) ($p=0.002$) and antiplatelet/anticoagulant treatment ($p<0.001$) were more frequently used in patients with elevated hs-cTnI (>30 pg/mL). During a median follow-up of 15 months, the overall survival tended to be lower in patients with elevated hs-cTnI (>30 pg/mL) ($p=0.004$) (Fig. 2A). Three deaths were recorded, and the causes of death were heart failure ($n=2$) and respiratory failure ($n=1$). In addition, an increased risk of cardiac involvement during follow-up was observed in the group with initial elevated levels of hs-cTnI (>30 pg/mL) ($p<0.001$) (Fig. 2B).

Discussion

Cardiac troponins have irreplaceable value in assessing myocardial injury in the general population. Recent studies have found that cardiac biomarkers were closely related to the myocardial events in several kinds of autoimmune and autoinflammatory diseases, such as SLE, RA, and psoriasis [6, 7, 13, 14]. However, there has been limited research on the serum cardiac biomarkers in IIM so far. In this study, we investigated the serum cardiac biomarkers in IIM patients, and we found that the elevated levels of hs-cTnI in active IIM patients were independently associated with cardiac involvement. We also demonstrated that higher levels of hs-cTnI were significantly correlated with disease activity. Furthermore, we firstly explored the relationship between serum hs-cTnI levels and prognosis in IIM patients.

IIM is a heterogeneous group of autoimmune diseases that is usually associated with skeletal muscle inflammation. Cardiac involvement is a serious organ involvement linked to high mortality in IIM patients. According to different literature, the presence of cardiac involvement varies from 9 to 72% in IIM patients [15]. James B Lilleker et al. observed a 9% rate of cardiac involvement in 1715 IIM patients [16]. Charles E. Denbow et al. investigated 20 autopsied IIM patients. They found that 72% of patients had abnormal electrocardiograms, and 45% of patients had congestive heart failure [4]. In our study, we identified that 28.9% of IIM patients had cardiac involvement. The relatively higher incidence in our cohort may be related to the enrolment of only hospitalized patients in a tertiary hospital. It is reported that the occurrence of cardiac involvement in IIM was associated with significantly increased morbidity and mortality [17]. However, due to the lack of awareness, the true incidence of cardiac involvement in IIM patients might be underestimated. A majority of cardiac involvement in IIM patients is subclinical and usually lacks specificity, so early detection

Table 4 The treatments and outcomes of IIM patients according to the levels of hs-cTnI.

	Total ($n=142$)	**hs-cTnI < 30pg/mL ($n=105$)**	**hs-cTnI > 30pg/mL ($n=37$)**	***p*-values**
Treatments				
Highest methyprednisolone dose (mg/day), median (IQR)	50.0 (40.0–80.0)	40.0 (20.0–80.0)	80.0 (80.0–80.0)	**<0.001**
Application of MTX, *n* (%)	7 (4.9)	6 (5.7)	1 (2.7)	0.467
Application of CTX, *n* (%)	10 (7.0)	7 (6.7)	3 (8.1)	0.768
Application of IVIG, *n* (%)	23 (16.2)	14 (13.3)	9 (24.3)	0.119
Application of biologic agents, *n* (%)	6 (4.2)	1 (2.7)	5 (4.8)	0.592
Application of PE, *n* (%)	5 (3.5)	3 (2.9)	2 (5.4)	0.470
Application of beta blocker and ACE inhibitor/ARB, *n* (%)	18 (12.7)	8 (7.6)	10 (27.0)	**0.002**
Application of statin, *n* (%)	3 (2.1)	2 (1.9)	1 (2.7)	0.772
Application of antiplatelet/anticoagulant treatment, *n* (%)	14 (9.9)	4 (3.8)	10 (27.0)	**<0.001**
Outcomes				
Death, *n* (%)	3 (2.1)	0 (0.0)	3 (8.1)	**0.004**

Values are presented as median with interquartile range for continuous variables, and as numbers with percentage for categorical variables. $P<0.05$ is shown in bold type. ACE: angiotensin converting enzyme; ARB: angiotonin receptor blocker; CTX: Cyclophosphamide; IVIG, intravenous immunoglobulin; MTX, methotrexate; PE: plasma exchange

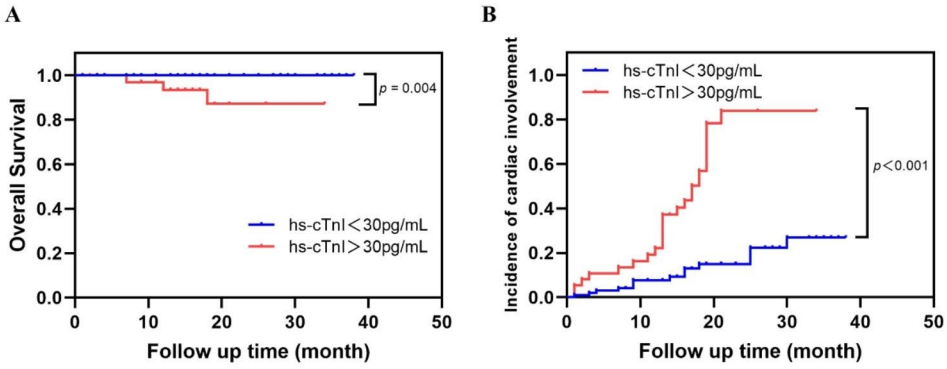

Fig. 2 The survival curve in different groups of patients according to the levels of hs-cTnI. The overall survival (A) and the incidence of cardiac involvement (B). hs-cTnI: high-sensitivity cardiac troponin I

methods are necessary to improve the prognosis of cardiac involvement in IIM patients [15].

The serum cardiac biomarkers, which could suggest myocardial damage, are a convenient way to assess heart function. It is initially released in a free state when cardiomyocytes undergo necrosis due to ischemia or hypoxia. With the progression of injury, it could be continuously released from the bound state as a result of cellular destruction. In addition, the use of high-sensitivity assays was more sensitivity, which allowed the measurement of biomarker concentrations below conventional levels of detection [18]. According to a recent report, abnormally elevated serum cardiac biomarkers could be observed in IIM patients. It was reported that the elevation of cTnT was more common, and the increased levels of cTnT were associated with weakness, lower MMT-8 scores and reduced daily living function, but not associated with cardiac involvement [8, 19]. The lack of association between cTnT and cardiac involvement might result from its re-expression in regenerating skeletal muscle fibers [20]. Similarly, the detection of traditional CK or CK-MB could not distinguish their origin from regenerated skeletal muscles or cardiac injury in IIM. According to the literature, approximately 51% of IIM patients without clinical evidence of cardiac involvement had elevated CK-MB levels and 41% of those patients also had elevated cTnT levels in clinical practice [21]. Therefore, it is necessary to find indicators with better sensitivity and specificity.

CTnI was a biomarker which was more specific for cardiac involvement in IIM patients. Previous study reported that both cTnT and cTnI were associated with increased risk of cardiac involvement in IIM patients, but only cTnI was independently associated with cardiac involvement after adjustment of overall disease activity [8]. High sensitivity (97%) and specificity (84%) of cTnI for myocarditis in IIM patients were also reported in another research [22]. Moreover, the levels of troponin were also reported significantly elevated in inflammatory myositis with cardiac involvement secondary to infectious diseases, such as COVID-19, which suggested the use of the troponin as a diagnostic tool [23]. As cTnI is unlikely to be found in non-cardiac muscle, any elevation of this myocardial-specific cTnI isoform is more likely to indicate myocardial damage. These results were similar to our observations that the levels of hs-cTnI were significantly higher in IIM patients with cardiac involvement. Moreover, our results suggested that hs-cTnI had the best performance of distinguishing cardiac involvement among all the cardiac biomarkers. In addition, the serum levels of hs-cTnI were also independent risk factors for cardiac injury in IIM patients. However, a recent study reported that elevated cTnI with normal echocardiogram and cardiac MRI evaluation in a patient of polymyositis after mRNA COVID-19 vaccination, which suggested the presence of interfering antibodies as the most likely explanation. Whether the elevated troponin truly reflected myocardial damage or a laboratory phenomenon in the context of generally increased antibodies in IIMs required further investigation [24].

Besides, we examined the association of cardiac biomarkers with disease activity. We found that the serum levels of hs-cTnI, CK, CK-MB, Mb and NT-proBNP were positively correlated with disease activity. The levels of these biomarkers decreased along with the remission of the disease after treatment. As the patients with cardiac involvement had significantly worse overall disease activity, it was important to screen for cardiac involvement in those highly active patients. Cardiac biomarkers should be dynamically monitored. Further examination, consultation with a cardiologist and aggressive treatment should be considered if any abnormalities are identified.

So far, cardiac biomarkers were found to be associated with prognosis in several diseases. In light-chain amyloidosis, the combination of hs-cTnT and NT-proBNP could be the best prognostic markers [25]. Similarly, NT-proBNP has also been found to be relevant to higher all-cause mortality in patients with early inflammatory

arthritis and RA [26]. The results of our study showed the early elevation of hs-cTnI in the acute phase was associated with poor prognosis and a relatively lower survival rate in IIM patients. What's more, patients with abnormal levels of hs-cTnI tended to have a higher risk of cardiac involvement during follow-up. We also found that patients with abnormal levels of hs-cTnI had a higher probability of application with high dose of glucocorticoids, beta blocker, ACE inhibitor/ARB and antiplatelet/anticoagulant treatment. These patients might be more severe and have a higher risk of cardiac related discomfort.

There are still some limitations in this study. First of all, the patients enrolled in our research had a relatively small sample size with regards to cardiac involvement, which prevented in-depth analysis of different clinical subtypes of IIM. Therefore, it is necessary to obtain further confirmation through a larger sample size and a longer follow-up period for IIM patients in the future. Second, our study reported that elevated serum levels of hs-cTnI in active IIM patients could be a marker of cardiac involvement and prognosis, however, longitudinal studies are required to explore the role of troponin as a marker for early detection and its role in the ambulatory setting during patient's follow-up. Lastly, the lack of cardiac MR and biopsy prevented a more comprehensive assessment of cardiac involvement, which should be included in further study.

Conclusion

In conclusion, our study suggests that the elevated serum levels of hs-cTnI in active IIM patients were independently associated with cardiac involvement. Hs-cTnI could be an effective biomarker of cardiac involvement among all the serum cardiac biomarkers in IIM patients. Furthermore, the levels of hs-cTnI were significantly correlated with disease activity, and patients with higher serum levels of hs-cTnI tended to suffer from poorer prognosis. Further studies with larger cohorts are needed to confirm these results.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

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Authors' contribution
All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Su had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study conception and design: Yutong Su, Chengde Yang, Hao Zhang, Liangzhe Xie. Acquisition of data: Yutong Su, Chengde Yang, Hao Zhang, Liangzhe Xie, Huihui Chi, Yue Sun, Honglei Liu, Xiaobing Cheng, Junna Ye, Hui Shi, Qiongyi Hu, Jianfen Meng, Zhuochao Zhou, Jialin Teng. Drafting and revising the article: Yutong Su, Hao Zhang, Liangzhe Xie, Huihui Chi. Analysis and interpretation of data: Yutong Su, Hao Zhang, Liangzhe Xie.

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Avaliability of data and materials
All data and materials generated or analysed during this study are included in this published article (and its supplementary information files).

Declarations

Ethical approval and consent to participate
The study was performed in accordance with the Declaration of Helsinki and the Principles of Good Clinical Practice. Biological samples were obtained under a protocol approved by the Institutional Research Ethics Committee of Ruijin Hospital (ID: 2016-62), Shanghai, China. All subjects gave written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Rheumatology and Immunology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, No. 197 Ruijin Second Road, Shanghai 200025, China
[2]Department of Laboratory Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

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References

1. Lundberg IE, Fujimoto M, Vencovsky J, Aggarwal R, Holmqvist M, Christopher-Stine L, et al. Idiopathic inflammatory myopathies. Nat Rev Dis Primers. 2021;7(1):86.
2. Lundberg IE, de Visser M, Werth VP. Classification of myositis. Nat Rev Rheumatol. 2018;14(5):269–78.
3. Sultan SM, Ioannou Y, Moss K, Isenberg DA. Outcome in patients with idiopathic inflammatory myositis: morbidity and mortality. Rheumatology (Oxford). 2002;41(1):22–6.
4. Denbow CE, Lie JT, Tancredi RG, Bunch TW. Cardiac involvement in polymyositis: a clinicopathologic study of 20 autopsied patients. Arthritis Rheum. 1979;22(10):1088–92.
5. Dankó K, Ponyi A, Constantin T, Borgulya G, Szegedi G. Long-term survival of patients with idiopathic inflammatory myopathies according to clinical features: a longitudinal study of 162 cases. Med (Baltim). 2004;83(1):35–42.
6. Divard G, Abbas R, Chenevier-Gobeaux C, Chanson N, Escoubet B, Chauveheid MP, et al. High-sensitivity cardiac troponin T is a biomarker for Atherosclerosis in systemic lupus erythematous patients: a cross-sectional controlled study. Arthritis Res Ther. 2017;19(1):132.
7. Karpouzas GA, Estis J, Rezaeian P, Todd J, Budoff MJ. High-sensitivity cardiac troponin I is a biomarker for occult coronary plaque burden and

cardiovascular events in patients with rheumatoid arthritis. Rheumatology (Oxford). 2018;57(6):1080–8.
8. Lilleker JB, Diederichsen ACP, Jacobsen S, Guy M, Roberts ME, Sergeant JC, et al. Using serum troponins to screen for cardiac involvement and assess Disease activity in the idiopathic inflammatory myopathies. Rheumatology (Oxford). 2018;57(6):1041–6.
9. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975;292(7):344–7.
10. Hoogendijk JE, Amato AA, Lecky BR, Choy EH, Lundberg IE, Rose MR, et al. 119th ENMC international workshop: trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis, 10–12 October 2003, Naarden, the Netherlands. Neuromuscul Disord. 2004;14(5):337–45.
11. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, et al. 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory myopathies and their major subgroups. Arthritis Rheumatol. 2017;69(12):2271–82.
12. Matsuo T, Sasai T, Nakashima R, Kuwabara Y, Kato ET, Murakami I, et al. ECG changes through immunosuppressive therapy Indicate Cardiac Abnormality in Anti-MDA5 antibody-positive clinically amyopathic Dermatomyositis. Front Immunol. 2021;12:765140.
13. Chezel J, Costedoat-Chalumeau N, Laouénan C, Rouzaud D, Chenevier-Gobeaux C, Le Guern V, et al. Highly sensitive serum cardiac troponin T and cardiovascular events in patients with systemic Lupus Erythematosus (TROPOPLUS study). Rheumatology (Oxford). 2021;60(3):1210–5.
14. Colaco K, Lee KA, Akhtari S, Winer R, Welsh P, Sattar N, et al. Association of Cardiac biomarkers with Cardiovascular outcomes in patients with psoriatic arthritis and psoriasis: a longitudinal cohort study. Arthritis Rheumatol. 2022;74(7):1184–92.
15. Zhang L, Wang GC, Ma L, Zu N. Cardiac involvement in adult polymyositis or dermatomyositis: a systematic review. Clin Cardiol. 2012;35(11):686–91.
16. Lilleker JB, Vencovsky J, Wang G, Wedderburn LR, Diederichsen LP, Schmidt J, et al. The EuroMyositis registry: an international collaborative tool to facilitate myositis research. Ann Rheum Dis. 2018;77(1):30–9.
17. Limaye V, Hakendorf P, Woodman RJ, Blumbergs P, Roberts-Thomson P. Mortality and its predominant causes in a large cohort of patients with biopsy-determined inflammatory myositis. Intern Med J. 2012;42(2):191–8.
18. Westermann D, Neumann JT, Sörensen NA, Blankenberg S. High-sensitivity assays for troponin in patients with cardiac Disease. Nat Rev Cardiol. 2017;14(8):472–83.
19. Aggarwal R, Lebiedz-Odrobina D, Sinha A, Manadan A, Case JP. Serum cardiac troponin T, but not troponin I, is elevated in idiopathic inflammatory myopathies. J Rheumatol. 2009;36(12):2711–4.
20. Bodor GS, Survant L, Voss EM, Smith S, Porterfield D, Apple FS. Cardiac troponin T composition in normal and regenerating human skeletal muscle. Clin Chem. 1997;43(3):476–84.
21. Erlacher P, Lercher A, Falkensammer J, Nassonov EL, Samsonov MI, Shtutman VZ, et al. Cardiac troponin and beta-type myosin heavy chain concentrations in patients with polymyositis or dermatomyositis. Clin Chim Acta. 2001;306(1–2):27–33.
22. Liu Y, Fang L, Chen W, Zhu Y, Lin X, Wang Y, et al. Identification of characteristics of overt Myocarditis in adult patients with idiopathic inflammatory myopathies. Cardiovasc Diagn Ther. 2020;10(3):405–20.
23. Freund O, Eviatar T, Bornstein G. Concurrent myopathy and inflammatory cardiac Disease in COVID-19 patients: a case series and literature review. Rheumatol Int. 2022;42(5):905–12.
24. Ciofani JL, Ward L, Liulu X, Chan RCF, Sampedro S, Soh HC, et al. Polymyositis and raised troponin after mRNA COVID-19 vaccination. Intern Med J. 2022;52(10):1840–2.
25. Palladini G, Barassi A, Klersy C, Pacciolla R, Milani P, Sarais G, et al. The combination of high-sensitivity cardiac troponin T (hs-cTnT) at presentation and changes in N-terminal natriuretic peptide type B (NT-proBNP) after chemotherapy best predicts survival in AL amyloidosis. Blood. 2010;116(18):3426–30.
26. Provan S, Angel K, Semb AG, Atar D, Kvien TK. NT-proBNP predicts mortality in patients with rheumatoid arthritis: results from 10-year follow-up of the EURIDISS study. Ann Rheum Dis. 2010;69(11):1946–50.

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