The absolute and relative change of high-sensitivity cardiac troponin I are associated with in-hospital outcome of patients with fulminant myocarditis

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Abstract

Background

we sought to describe the tendency and extent of high-sensitivity cardiac troponin I (hs-cTnI) changes in patients with fulminant myocarditis (FM) after admission, and to explore the relationship between in-hospital outcome of FM and the value of absolute and relative change of hs-cTnI within 24 h and 48 h after admission.

Methods

a total of 83 cases of FM patient admitted to our center from January 1, 2010 to December 31, 2019 were included, 69 patients survived and 14 patients died. The absolute and relative change of hs-cTnI within 24 h and 48 h were described as range distribution. Receiver operating characteristic (ROC) curves and Cox analysis were performed to determine the relationship between in-hospital outcome of FM and hs-cTnI change.

Results

In survive group, 78% patients experienced the decline of hs-cTnI within 24 h, while 36% of death group had the declined tendency of hs-cTnI ($P = 0.003$). Absolute and relative change of hs-cTnI within 24 h and 48 h were displayed as range distribution. Multivariate analysis revealed that the decline tendency of hs-cTnI change within 24 h, in addition with time from onset to hospital, intravenous immunoglobulin treatment and abnormal of creatinine, were associated with the outcome of FM (for the decline tendency of hs-cTnI within 24 h, OR = 0.10, 95% CI = 0.02−0.68, $P = 0.018$). ROC curve revealed optimized cutoff values of -0.618 ng/ml for absolute change within 24 h (AUC = 0.800, $P < 0.01$), -4.389 ng/ml for absolute change within 48 h (Area Under Curve = 0.711, $P < 0.01$), -28.46% for relative change within 24 h (AUC = 0.810, $P < 0.01$), -52.23% for relative change within 48 h (AUC = 0.795, $P < 0.01$). Absolute change and relative change of hs-cTnI within 24 h and 48 h were strong predictors of in-hospital mortality by COX regression analyzed, after the adjustment for gender, time from onset to admission, occurrence of ventricular tachycardia or ventricular fibrillation.

Conclusion

Most survive FM patients experienced the decline of hs-cTnI within 24 h. The absolute and relative change of hs-cTnI within 24 h and 48 h were strong predictors of in-hospital mortality.

1. Introduction

Myocarditis is an inflammatory disease of the myocardium which has a broad spectrum of clinical presentations, ranging from mild symptoms to life-threatening arrhythmias and/or severe heart failure (HF)[1]. Fulminant myocarditis (FM) is a rare but the most severe type of myocarditis and is characterized by sudden occurrence, rapid progress, and hemodynamic dysfunction[2]. Though endomyocardial biopsy (EMB) is the golden standard of myocarditis diagnosis, it is pragmatic to determine the treatment for the patients suspected of myocarditis by clinical diagnosis referred to clinical state as well as laboratory and imaging tests[2, 3]. To be exactly, FM can be clinically defined as patients presenting with a distinct onset of symptoms in the prior 2 weeks, severe symptoms of HF, and hypotension or overt cardiogenic shock needing inotropes, vasopressor, and/or mechanical circulation support[3]. As the technology advanced, gadolinium contrast-enhanced cardiac magnetic resonance (CMR) can afford tissue-level pathologies consistent with myocarditis, including myocardial edema and fibrosis (e.g., T2- and T1-weighted sequences and late gadolinium enhancement [LGE]) which has high diagnostic accuracy[4, 5].

Myocarditis is an inflammatory cardiac disorder induced predominantly by viruses[6]. The mechanisms of myocardial injury were recognized as the direct injury and the indirect immunogenic injury[7]. The former indicates the intracellular viral replication in the myocardium and other tissues, resulting in degeneration, necrosis, and dysfunction[8]. The latter is triggered by cytotoxic and antigen-antibody reaction which are caused by virus infection[9]. An elevated serum cardiac troponin (cTn) is almost always observed in patients with FM as myocardial injury, especially the assay of high-sensitivity troponin I (hs-cTnI) detection was more sensitive in reflecting the potential injury of myocardium. The same as hs-cTnI elevated, research in patients with myocardial infraction (MI) about the diagnostic and prognostic value of serial changes of hs-cTnI had been widely performed[10-15]. It is undetermined that the FM patients' hs-cTnI kinetic in the early phase after admission and the relationship between the serial change of hs-cTnI and patients' outcome.

Therefore, this retrospective research aimed to describe the serial changes of hs-cTnI, and to determine the prognostic value of the absolute (Δ) and relative(Δ%) changes in hs-cTnI within 24 h and 48 h after admission for FM patients' outcome in hospital.

2. Method

2.1 Study population and diagnosis of fulminant myocarditis

All patients were in-hospital patients in TongJi hospital, a tertiary teaching medical center in Wuhan, China. From January 1, 2010 to December 31, 2019. A total of 105 FM cases were retrospectively included in the study, of whom 22 cases were excluded (Fig. 1). The exclusive criteria include: 1) age less than 16 years old, 2) diagnosis of other severe disease, such as malignant tumor. 3) dead within 24 h after admission to hospital, 4) lack of serial hs-cTnI record within 48 h. At last, the final analysis consist of 83 FM patients.

FM is usually defined as myocardial inflammatory disease with a rapid outbreak complicated with severe hemodynamic dysfunction. FM is more likely to be a clinical diagnosis rather than a histological or pathological diagnosis. Therefore, FM was diagnosed in our center, predominantly as Chinese expert consensus statement recommended[2], by following signs: sudden attack, obvious premonitory symptoms of viral infection (especially severe fatigue and poor appetite), and rapid emerging severe hemodynamic dysfunction, serious myocardial injuries, and diffuse ventricular wall motion decrease. Since 2018, CMR was widely used in our center to ascertain the diagnosis of FM, 25 cases of 36 FM patients in that period performed CMR examination. EMB had been performed in 3 patients with unexplained heart failure as the guideline recommended[16]. Coronary angiography had been operated in 36 cases to distinguish from myocardial infraction for clinical signs as chest pain and elevated ST wave in electrocardiogram and elevated hs-cTnI[17]. All patients' ultimate diagnosis was ascertained by at least two cardiologists before admitted to the study.

2.2 Data collection and hs-cTnI detection

All patients at admission underwent clinical assessments including clinical history, physical examination, 12-lead electrocardiogram, echocardiography, and standard blood tests. Patients' outcome in hospital were recorded. All hs-cTnI value measured after admission within 7 days were recorded to describe the kinetic of hs-cTnI which was test by ARCHITECT i2000SR (Abbott Laboratories). The serial change of hs-cTnI was defined as follow: hs-cTnI baseline = $hs\text{-}cTnI_{0h}$, $hs\text{-}cTnI_{\Delta 24h}$ = $hs\text{-}cTnI_{24h}$ - $hs\text{-}cTnI_{0h}$, $hs\text{-}cTnI_{\Delta 48h}$ = $hs\text{-}cTnI_{48h}$ - $hs\text{-}cTnI_{0h}$, $hs\text{-}cTnI_{\Delta\%24h}$ = ($hs\text{-}cTnI_{24h}$ - $hs\text{-}cTnI_{0h}$)/$hs\text{-}cTnI_{0h}$, $hs\text{-}cTnI_{\Delta\%48h}$ = ($hs\text{-}cTnI_{48h}$ - $hs\text{-}cTnI_{0h}$)/$hs\text{-}cTnI_{0h}$.

2.3 Statistical analysis

The data are presented as proportions, mean ± SD, and median with interquartile range if variable was nonnormal distribution. Comparisons were made with the t test for normally distributed continuous variables, Mann-Whitney U test for nonnormally distributed continuous variables, χ^2 test for categorical variables. Receiver operating characteristic (ROC) curves were constructed to assess the relationship between in-hospital outcome of FM and the value of absolute (Δ) and relative (Δ%) changes of hs-cTnI within 24 hour and 48 hours after admission. Optimal cutoff values were derived from ROC curves as described by Youden, and sensitivity, specificity, were calculated. Cox regression analysis was performed to determine the prognostic value of optimal cutoff of absolute (Δ) and relative (Δ%) changes of hs-cTnI within 24 hour and 48 hours. All hypothesis testing was 2 tailed, and a P value of 0.05 was considered statistically significant. All statistical analyses were performed with SPSS 22.0 (SPSS Inc., Chicago, IL) for Windows (Microsoft Corp, Redmond, WA).

3. Result

3.1 characteristics of FM patients

The baseline characteristics of all 83 FM patients are shown in Table 1. The median age was 37 (Q1-Q3: 29–48) years old, 49.4% were women. Premonitory symptoms of viral infection, like fever, was observed in 75.9% of total population while the co-existing conditions including hypertension or diabetes mellitus were observed in less than 10% of patients. The median time from onset to admission was 3 days, which indicated that FM was an acute disease; while this period in survive group was significant shorter than in death group ($P = 0.028$). Chest distress (69.9%) was the most common symptoms of FM patients, and chest pain (22.9%), palpitation (22.9%), dizziness (25.3%), and disturbances of consciousness (21.7%) were also recorded. The incidence of severe arrhythmia, such as ventricular tachycardia or ventricular fibrillation, was significant higher in death group than in survive group (35.7% vs. 10.1%, $P = 0.026$). Higher level of creatinine rather than alanine transaminase was also observed at admission in death group than survive group ($P = 0.016$). 42% of survive group received CMR examination, all of the examination were performed in the recent two years, while no patients in death group received such examination as severe hemodynamic dysfunction. Coronary angiography was performed in 28.6% of death group and 46.4% of survive group. Patients in death group with so rapid illness progression as to all of them received vasoactive agent(100%), 50% of whom received intraaortic balloons pump(IABP) and mechanical ventilation therapy. The majority of patients (87%) in survive group were performed IABP to maintain hemodynamic stable. Vasoactive agent was used in 66.7% of survive patients and mechanical ventilation was used in 36.2% of survive patients. About 20% of patients in both group operated extracorporeal membrane oxygenation (ECMO).

Table 1
Baseline characteristics of FM

	total (n = 83)	death(n = 14)	survive(n = 69)	P
Female n;(%)	41(49.4)	6(42.9)	35(50.7)	0.591
age (year) Median[Q1-Q3]	37[29,48]	42.5[32.75,50.75]	37[27,47.5]	0.226
Premonitory symptoms of viral infection n; (%)	63(75.9)	10(71.4)	53(76.8)	0.735
Co-existing conditions n;(%)				
Hypertension	6(7.2)	1(7.1)	5(7.2)	1.000
Diabetes mellitus	4(4.8)	0	4(5.8)	1.000
Renal disease	1(1.2)	1(7.1)	0	0.169
Time from onset to admission (days) Median[Q1-Q3]	3[2, 5]	4.5[2.75,10.25]	3[1, 4.5]	0.028
Coronary angiography (n, %)	36(43.3)	4(28.6)	32(46.4)	0.220
CMR (n,%)	29(34.9)	0	29(42.0)	0.002
Clinical symptoms n ;(%)				
Chest pain	19(22.9)	2(14.3)	17(24.6)	0.506
Chest distress	58(69.9)	10(71.4)	48(69.6)	1.000
Palpitation	19(22.9)	3(21.4)	16(23.2)	1.000
Dizziness	21(25.3)	2(14.3)	19(27.5)	0.501
Disturbances of consciousness	18(21.7)	3(21.4)	15(21.7)	1.000
Ejection fraction at lowest %	33.7 ± 13.5	40.9 ± 15.3	32.5 ± 13.0	0.056
ECG n ;(%)				
ST-segment elevation	30(36.1)	4(28.6)	26(37.7)	0.518
Ventricular Tachycardia or Ventricular fibrillation	12(14.5)	5(35.7)	7(10.1)	0.026
Atrioventricular block	14(16.9)	2(14.3)	12(17.4)	1.000

CMR = cardiac magnetic resonance; ECG = electrocardiogram; ALT = Alanine aminotransferase; Crea = creatinine; IVIG = Intravenous immunoglobulin; IABP = Intraaortic balloons pump; ECMO = extracorporeal membrane oxygenation.

	total (n = 83)	death(n = 14)	survive(n = 69)	P
ALT(x ± s)	552 ± 1185	1133 ± 2156	434 ± 850	0.252
Crea(x ± s)	107 ± 110	205 ± 157	87 ± 86	0.016
Vasoactive agent n;(%)	60(72.3)	14(100)	46(66.7)	0.008
Anti-viral therapy n;(%)	81(97.6)	12(85.7)	69(100)	0.027
Glucocorticoid therapy n;(%)	83(100)	14(100)	69(100)	1.000
IVIG n;(%)	73(88.0)	8(57.1)	65(94.2)	0.001
Mechanical ventilation n;(%)	32(38.6)	7(50.0)	25(36.2)	0.335
IABP n;(%)	67(80.7)	7(50.0)	60(87.0)	0.004
ECMO n;(%)	19(22.9)	3(21.4)	16(23.2)	1.000
IABP + ECMO n;(%)	17(20.5)	3(21.4)	14(20.3)	1.000

CMR = cardiac magnetic resonance; ECG = electrocardiogram; ALT = Alanine aminotransferase; Crea = creatinine; IVIG = Intravenous immunoglobulin; IABP = Intraaortic balloons pump; ECMO = extracorporeal membrane oxygenation.

3.2 baseline and tendency of hs-cTnI

The baseline hs-cTnI was illustrated in Fig. 2A, which revealed no significant difference between the death and survive groups(value: survive patients 27.62 ± 2.4 ng/ml and death patients 31.05 ± 7.1 ng/ml, P = 0.81). hs-cTnI tested within 24 h lower than hs-cTnI baseline was defined as declined tendency, otherwise it was defined as not declined tendency. Figure 2B showed the significant difference of tendency of hs-cTnI change in death and survive FM patients within 24 h after admission, in survive group 78% patients experienced the declined hs-cTnI change, while 36% of death group had the declined tendency of hs-cTnI (P = 0.003).

3.3 absolute and relative hs-cTnI changes within 24 h and 48 h

As available hs-cTnI data was concentrate within 24 h and 48 h after admission, the absolute and relative changes of hs-cTnI in these periods were illustrated in Table 2 and Fig. 3. The absolute change of hs-cTnI in survival group within 24 h was mainly at the scale of -10 to 0 ng/ml, accounting for 39.68% of the patients, followed by the scale of -20 to -10 ng/ml which accounted for 19.05% of the patients. The relative change of hs-cTnI within 24 h was concentrated in -25% to -75%, accounting for 58.07% of patients. The absolute change of hs-cTnI within 48 h was concentrate in -10 to 0 ng/ml incorporating

32.3% patients and in -20 to -30 ng/ml, accounting for 22.03%. Survive patients with relative change of hs-cTnI within 48 h between − 50% to -100% account for 72.41%. In death group, the absolute change of hs-cTnI both within 24 h and 48 h were concentrated in 0 to 10 ng/ml, which account for 50% and 37.5% respectively. Main scale of relative change of hs-cTnI in death group changed from 0 to 25% within 24 h to -50% to -75% within 48 h, accounting for 46.67% and 25% of patients respectively. Main scale of hs-cTnI distribution in the survive group and death group within both 24 h and 48 h have significant statistic difference.

Table 2
Distribution of hs-cTnI change in survive group and death group within 24 h and 48 h

	Survive group proportion with 24 h	Death group proportion within 24 h	P	Survive group proportion within 48 h	Death group proportion within 48 h	P
	% (n = 63)	% (n = 14)		% (n = 58)	% (n = 8)	
Absolute change of hs-cTnI (ng/ml)						
[-50,-40)	1.59	0	1.000	5.08	0	1.000
[-40,-30)	4.76	0	1.000	10.17	12.50	1.000
[-30,-20)	14.29	0	0.198	22.03	0	0.338
[-20,-10)	19.05	14.29	1.000	18.64	12.50	1.000
[-10,0)	39.68	14.29	0.120	32.20	25.00	1.000
[0,10)	15.87	50.00	0.011*	5.08	37.50	0.019*
[10,20)	3.17	14.29	0.149	3.39	12.50	0.321
[20,30)	1.59	0	1.000	1.69	0	1.000
[30,40)	0	7.14	0.182	1.69	0	1.000
Relative change of hs-cTnI (*100%)						
[-1,-0.75)	11.29	0	0.334	31.03	0	0.095
[-0.75,-0.5)	30.65	6.67	0.098	41.38	25.00	0.464
[-0.5,-0.25)	27.42	6.67	0.170	10.34	12.50	1.000
[-0.25,0)	11.29	13.33	1.000	6.90	12.50	0.487
[0,0.25)	9.68	46.67	0.002*	1.72	25.00	0.037*
[0.25,0.5)	1.61	6.67	0.354	0	0	-
[0.5,0.75)	1.61	0	1.000	1.72	0	1.000
[0.75,1)	1.61	0	1.000	0	12.50	0.121
[1,2)	4.84	20.00	0.084	6.90	12.50	0.487

* means P value less than 0.05

3.4 Univariate analysis and multivariate analysis for outcome of FM

Univariate analysis was operated to select factors potentially associated with the outcome of FM, and the result was displayed in Table 3. There are 6 variables showing statistical significance, including the time from onset to hospital, occurrence of ventricular Tachycardia or ventricular fibrillation, abnormal of creatinine, the decline tendency of hs-cTnI change within 24 h, Intravenous immunoglobulin (IVIG) treatment and operation of IABP. Those variables were taken into multivariate analysis. The results showed that the decline tendency of hs-cTnI change within 24 h, in addition with the abnormal of creatinine, IVIG treatment and time from onset to hospital were associate with the outcome of FM (for time from onset to hospital, OR = 1.3, 95% CI = 1.02–1.75, P = 0.04; for abnormal of creatinine, OR = 7.85, 95% CI = 1.19–51.74, P = 0.032; for the decline tendency of hs-cTnI change within 24 h, OR = 0.10, 95% CI = 0.02–0.68, P = 0.018; for IVIG treatment, OR = 0.028, 95%CI = 0.003-0.3, P = 0.003).

Table 3
Univariate analysis and multivariate analysis for outcome of FM.

Factor	Univariate analysis		Multivariate analysis	
	OR(95%CI)	*P*	OR(95%CI)	*P*
Female	0.73(0.23−2.32)	0.592		
age (year)	1.02(0.98−1.07)	0.321		
Premonitory symptoms of viral infection	1.33(0.37−4.80)	0.668		
Time from onset to admission	1.22(1.03−1.45)	0.023	1.34(1.02−1.75)	0.038
Chest pain	1.96(0.40−9.66)	0.407		
Chest distress	0.91(0.26−3.25)	0.890		
Disturbances of consciousness	1.02(0.25−4.12)	0.979		
Ejection fraction at lowest %				
ST-segment elevation	0.66(0.19−2.33)	0.520		
Ventricular Tachycardia or Ventricular fibrillation	4.92(1.28−18.86)	0.020	6.68(0.87−51.04)	0.067
Atrioventricular block	0.79(0.16-4.00)	0.778		
ALT	1.33(0.38−4.70)	0.655		
Crea	9.82(2.68−36.02)	0.001	7.85(1.19−51.74)	0.032
IVIG	0.08(0.02−0.35)	0.001	0.03(0.003-0.3)	0.003
Mechanical ventilation	1.76(0.55−5.60)	0.338		
IABP	0.150(0.04−0.53)	0.003	-	-
ECMO	0.90(0.22−3.64)	0.886		
IABP + ECMO	1.07(0.26−4.37)	0.923		
Tendency of hs-cTnI within 24 h	0.09(0.02−0.32)	< 0.01	0.1(0.02−0.68)	0.018

ALT = Alanine aminotransferase; Crea = creatinine; IVIG = Intravenous immunoglobulin; IABP = Intraaortic balloons pump; ECMO = extracorporeal membrane oxygenation.

3.5 Value of absolute hs-cTnI change and relative hs-cTnI change in predicting hospital mortality

ROC curve was performed to calculate cutoff and to evaluate the value of absolute and relative hs-cTnI change in predicting in-hospital outcome of FM. Results including cutoff, area under curve(AUC),95% confidence interval were displayed as Fig. 4 and Table 4, showing that the predictable value of absolute hs-cTnI changes for hospital mortality of FM was high both within 24 h (cutoff=-0.618 ng/ml; AUC, 0.80; 95% confidence interval, 0.692 to 0.883) and within 48 h (cutoff=-4.389 ng/ml; AUC, 0.711; 95% confidence interval, 0.587 to 0.816). The accuracy of relative hs-cTnI change for predicting FM mortality in hospital also high both within 24 h (cutoff=-28.46%;AUC, 0.81; 95% confidence interval, 0.704 to 0.891) and within 48 h (cutoff=-52.23%;AUC, 0.795; 95% confidence interval, 0.678 to 0.885). There was no significant difference among the relative change and absolute change at both time points (P > 0.05 for comparison; Fig. 4 and Table 3). Cox regression analysis for mortality in FM patients grouped by cutoff of relative and absolute change of hs-cTnI within 24 h and 48 h were shown in Fig. 5 and Table 5. The factors that absolute change of hs-cTnI and relative change of hs-cTnI within both 24 h and 48 h in addition with elevated creatinine were strong predictors of in-hospital mortality, after adjustment for gender, time from onset to admission, occurrence of ventricular tachycardia and ventricular fibrillation ($hs\text{-}cTnI_{\Delta 24h}$ > -0.618 ng/ml: HR = 6.93 [1.88−25.64], P = 0.004; $hs\text{-}cTnI_{\Delta 48h}$ > -4.389 ng/ml: HR = 6.47 [1.29−32.42], P = 0.023; $hs\text{-}cTnI_{\Delta\%24h}$ > -28.46%: HR = 13.83 [1.76-108.95], P = 0.013; $hs\text{-}cTnI_{\Delta\%48h}$ > -52.23%: HR = 19.88 [2.40-164.79], P = 0.006).

Table 4
Diagnostic value of hs-cTnI Δ24h, hs-cTnI Δ48h, hs-cTnI Δ%24 h, hs-cTnI Δ%48 h for hospital mortality of patients with fulminant myocarditis.

	AUC	P	Cutoff	sensitivity	specificity
hs-cTnI $_{\Delta 24h}$	0.800	< 0.01	-0.618	78.57	79.03
hs-cTnI $_{\Delta 48h}$	0.711	< 0.01	-4.389	75.00	72.41
hs-cTnI $_{\Delta\%24h}$	0.810	< 0.01	-0.2846	92.86	67.74
hs-cTnI $_{\Delta\%48h}$	0.795	< 0.01	-0.5223	87.50	70.69

Table 5
Cox proportional hazards analysis for death in FM.

	HR	95%CI	P-Value
Model 1			
hs-cTnI$_{\Delta24h}$>-0.618 ng/ml	6.93	1.88−25.64	0.004
Elevated creatinine	4.63	1.41−15.19	0.011
Model 2			
hs-cTnI$_{\Delta48h}$>-4.389 ng/ml	6.47	1.29−32.42	0.023
Elevated creatinine	19.03	2.32-155.85	0.006
Model 3			
hs-cTnI$_{\Delta\%24h}$>-28.46%	13.83	1.76-108.95	0.013
Elevated creatinine	4.04	1.24−13.15	0.020
Model 4			
hs-cTnI$_{\Delta\%48h}$>-52.23%	19.88	2.40-164.79	0.006
Elevated creatinine	27.20	3.28−225.40	0.002
All models were adjusted for gender, time from onset to admission, occurrence of ventricular tachycardia or ventricular fibrillation.			

4. Discussion

The main findings of this study include three aspects: 1) we firstly described the tendency and extent of hs-cTnI change within 24 h and 48 h after admission in FM; 2) we determined the tendency of hs-cTnI change within 24 h was associated with in-hospital outcome of FM; 3) we further determined that the extent of hs-cTnI change as absolute change and relative change within 24 h and 48 h were significant factors to predict outcome of FM.

Detection of hs-cTnI at admission is recommended in guidelines regarding myocarditis[17, 18], for almost all patients showed elevated troponin. Enrico Ammirati reported a cohort study comprised 118 myocarditis patients with left ventricular ejection fraction (LVEF) less than 50% and 325 myocarditis patients with no such complications, above 99% of whom in both groups have increased troponin at admission[19]. Little research focused on the relationship between the serial change of cardiac troponin and the outcome of myocarditis, the majority of which explored hs-cTnI baseline prognostic value. There were studies demonstrated that the level of cardiac troponin was not associated with the outcome[20−22].

In contrary, other studies reported that elevated troponin in the early phase for myocarditis was associated with ECMO or worse prognosis[23, 24]. It is still debated that the prognostic value of cardiac troponin baseline in myocarditis.

Though the increased level of hs-cTnI in FM is well-recognized, it is unknown that the tendency and exact extent of hs-cTnI change in reality. This study described the situation of hs-cTnI change, revealing that it is regular for hs-cTnI change in FM. Most survive patients experienced decline of hs-cTnI change within 24 h while few patients in death group had decreased hs-cTnI, significantly differently compared to survive group. Within 24 h after admission, 40% of survive patients had absolute change of hs-cTnI dropped by 0–10 ng/ml and 58% of survive patients showed relative change of hs-cTnI dropped by 25%-75%. While patients in death group have absolute change of hs-cTnI increased by 0–10 ng/ml, accounting for 50%. The depiction of hs-cTnI change in FM is of importance for us to know more about fulminant myocarditis and give better treatment for patients.

Besides, the declined tendency of hs-cTnI change within 24 h was found to be associated with in-hospital outcome of FM, after the adjustment of the abnormal of creatinine, IVIG treatment and time from onset to hospital. The declined tendency may reveal that treatment for FM in our center was effective, including anti-viral therapy, immunomodulating therapy, circulation support, and respiratory support, resulting in the relief of inflammation reaction which caused myocardium injury and reduction of incidence of ventricular tachycardia or ventricular fibrillation. In contrary, the opposite tendency may inflected that inflammation reaction was still severe after treatment, with high incidence of arrhythmia.

Furthermore, the prognostic value of extent of hs-cTnI change, as absolute change and relative change, within 24 h and 48 h was explored. The results revealed that the concrete absolute and relative change within 24 h and 48 h were associated with in-hospital outcome of FM. Specifically, if FM patients have absolute change of hs-cTnI within 24 h dropped as to 0.618 ng/ml or relative change dropped as to 28.46%, it is more likely for them to survive, which can also be predicted by the absolute change of hs-cTnI within 48 h dropped as to 4.389 ng/ml or relative decline change dropped as to 52.23%. This result is beneficial for doctors to evaluate treatment regimen and patients' prognostication. If patients experience declined tendency within 24 h with the magnitude reached our proposed cutoff value, the outcome may be good. But the patient's hs-cTnI change within 24 h show increased tendency or the magnitude dropped not reach the cut-off value, it may remind doctor to reassess the treatment for better control of inflammation reaction.

There are still some limitations in the current study. The retrospective nature of this research may have introduced potential bias. Although we collect all FM patients in our singer center for 10 years, the cases are not enough for further subanalysis. The median time for patients from onset to hospital was three days, thus the peak time of hs-cTnI is undetermined for patients experienced declined tendency of hs-cTnI after admission. The prospective research with more regular and frequent detection of hs-cTnI need to be performed for better understanding of hs-cTnI change in FM.

5. Conclusion

Most survive FM patients have decline tendency of hs-cTnI change under treatment within the early phase. The absolute and relative changes of hs-cTnI within 24 h and 48 h have significant predictable value for the in-hospital outcome of FM.

Abbreviations

hs-cTnI: high-sensitivity troponin I; FM: fulminant myocarditis; ROC: Receiver operating characteristic; AUC: area under curve; HF: heart failure; EMB: endomyocardial biopsy; CMR: cardiac magnetic resonance; LGE: late gadolinium enhancement; cTn: cardiac troponin; MI: myocardial infraction; IABP: Intraaortic balloons pump; ECMO: extracorporeal membrane oxygenation; IVIG: Intravenous immunoglobulin; LVEF: left ventricular ejection fraction;

Declarations

Acknowledgements:

Not applicable.

Authors' contributions:

CL: data collection and manuscript writing. ZQW: manuscript writing and data analysis. KQC: data collection and management. GLC: data analysis. LYW: manuscript revision and data review. CC: manuscript revision. JGJ: research design and manuscript revision. All authors have read and approved the manuscript.

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Availability of data and materials

The information and data of the study population were acquired from Hospital Information System and were recorded manually in EXCEL to form the database. The datasets analyzed during the current study are not publicly available due to the protection of the individual privacy but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All methods were performed in accordance with the relevant guidelines and regulations. The study has been approved by the Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology Institutional Review Board (TJ-C20160202). Informed consent was obtained from all

participants. The database is not open to public, thus the individual privacy of the participants could be well protected.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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