Analysis of myocardial enzyme spectrum in 230 COVID-19 patients of Chongqing, China.

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Research

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Abstract

Background

A novel coronavirus disease COVID-19 outbreak caused pandemic in China and worldwide. In addition to pneumonia, Cardiac failure is also a clinical outcome of coronavirus (COVID-19) patients and one of the leading causes for the death of COVID-19 patients. This study focused on a spectrum of cardiac enzymes to provide biomarkers for the severity of cardiomyopathy, and provide guidance of clinical treatment.

Methods

230 coronavirus patients (182 mild and 48 severe cases) enrolled in Three Gorges Hospital of Chongqing University from January to March 2020 were analyzed for a spectrum of cardiac injury enzymes including α-hydroxybutyric dehydrogenase (αHBDH), lactic acid dehydrogenase (LDH), creatine kinase (CK), and creatine kinase isoenzyme (CK-MB).

Results

The severe cases had significantly higher myocardial enzyme levels than mild cases, regardless of male and females. Males appeared to be more susceptible than females to COVID-19 induced heart injury, having higher CK and CK-MB in mild cases, and higher αHBDH and LDH levels in severe cases. Age is also a susceptible factor to COVID-19, but affected males were younger than females.

Conclusions

This study reveals that the heart is also a major target of COVID-19 infection, and myocardial enzyme spectrum assays could help the diagnosis, prognosis and guide the treatments to prevent heart failure in COVID-19 patients.

Background

The novel coronavirus (COVID-19) pneumonia has caused a pandemic in China and even the world since its discovery in Wuhan in December 2019. It is a respiratory infectious disease caused by beta coronavirus subtypes. The pneumonia diagnosis and treatment plan (Trial Version 7)[1] explicitly proposes that based on autopsy and puncture tissue pathological observations, the virus may accumulate the heart and degenerate and necrotize myocardial cells. However, no changes in myocardial enzymes have been reported after the onset of the disease. There are currently over 2,200,000 infected patients worldwide, so the summary of myocardial enzymes in these patients is of significance for understanding the disease and for subsequent guidance of clinical treatment.

Study Subjects

The study subjects were patients with COVID-19 pneumonia clinically diagnosed from the Three Gorges Hospital of Chongqing University from January 2020 to March 2020. All cases met the clinical diagnostic criteria for new type of coronavirus pneumonia [1] promulgated by the National Health and Health Commission at different times; severe patients included severe and critically ill patients, based on the above diagnosis standard; mild patients include light and general patients with the above diagnostic criteria.

Table 1.Demographics of COVID-19 patients

Case	Gender	Number (age range)	Age (mean ± SD)
Mild	Male	n = 101 (9-71)	44.16 ±27.69
	Female	n = 81 (7-65)	42.16 ±13.77
Severe	Male	n = 26 (31-79)	57.35 ±14.22
	Female	n = 22 (25-87)	65.18 ±14.84

A total of 230 patients with COVID-19 pneumonia were included this time, of which 127 were male, 101 were mild, and 26 were severe; 103 were female, 81 were mild, and 22 were severe; the average age of the patients was (49.01 ± 15.41) years.

Methods

This retrospect analysis includes 230 COVID-19 patients in 943 assays (each patient was subjected to 3-5 assays). The myocardial enzyme spectrum assays include α-hydroxybutyrate dehydrogenase (α-HBDH), lactate dehydrogenase (LDH), creatine kinase (CK), and creatine kinase isoenzyme (CK-MB), routinely performed in the Three Gorges Hospital. The data analysis was designed by Cardiac Vascular Surgery Department and analyzed by Statistician.

Statistics

Data were expressed as Mean ± SD (standard deviation) and analyzed with SPSS 22.0 software. The data was subjected to ANOVA analysis, followed by Chi-Square tests and multivariable tests, and Student's *t* tests. The criteria of significance were set at $p < 0.05$.

Results

Myocardial enzyme spectrum in 230 COVID-19 patients

In 230 patients (182 of whom were mild), a two-sample independent t-test was performed on changes in myocardial enzymes in the mild and severe groups. The results are as follows: all indicators are statistically different, and each indicator of the severe patients is relatively high; and there was a statistical difference between the average age of the mild group and the severe group, and the age of the severe group was higher.

Table 2.Myocardial enzyme spectrum in mild and severe COVID-19 female patients

Assays	Normal range	Cases	N (assays)	Mean ± SD	T	P
α-HBDH	76-195 U/L	Mild	81(296)	149.9 ± 42.56	-12.27	0.000
		Severe	22 (127)	251.6 ± 88.84		
LDH	120-250 umol/L	Mild	81(296)	192.2 ± 58.94	-10.41	0.000
		Severe	22 (127)	328.4 ± 142.3		
CK	F: 40-200 U/L	Mild	81(296)	41.21 ± 23.93	-3.452	0.001
		Severe	22 (127)	100.7 ± 193.6		
CK-MB	0-25 U/L	Mild	81(296)	10.51 ± 4.476	-3.359	0.000
		Severe	22 (127)	15.83 ± 17.61		

In 103 female patients (81 of whom were mild), two independent sample t tests were performed on different myocardial enzymes according to the severity of the disease (mild and severe), and the results were as follows: the differences in the four detection indicators were statistically significant, and the various indicators of the severe patients were relatively high.

Table 3.Myocardial enzyme spectrum in mild and severe COVID-19 male patients

Assays	Normal range	Cases	N (assays)	Mean ± SD	T	P
α-HBDH	76-195 U/L	Mild	101(374)	152.3 ± 48.80	-12.98	0.000
		Severe	26 (145)	285.3 ± 119.6		
LDH	120-250 umol/L	Mild	101(374)	197.9 ± 64.96	-12.04	0.000
		Severe	26 (145)	380.2 ± 177.8		
CK	F: 50-310 U/L	Mild	101(374)	81.07 ± 125.2	-3.094	0.002
		Severe	26 (145)	119.2 ± 126.2		
CK-MB	0-25 U/L	Mild	101(374)	11.91 ± 5.487	-4.135	0.000
		Severe	26 (145)	15.24 ± 9.077		

In 127 male patients (101 of whom were mild), two independent sample t tests were performed on different myocardial enzymes according to the severity of the disease, and the results were as follows: the differences in the four detection indicators were statistically significant, and each indicator of the severe patient was relatively high.

Table 4.Sex-difference in enzyme spectrum in mild COVID-19 patients

Assays	Normal range	Cases	N (assays)	Mean ± SD	T	P
α-HBDH	76-195 U/L	Female	81 (296)	149.9± 42.53	-0.679	0.498
		Male	101 (374)	152.3± 48.80		
LDH	120-250 umol/L	Female	81 (296)	192.2± 58.94	-1.161	0.246
		Male	101 (374)	197.9± 64.96		
CK	F: 40-200 U/L	Female	81 (296)	42.21 ± 23.93	-6.017	0.000
	M: 90-310 U/L	Male	101 (374)	81.07 ± 125.3		
CK-MB	0-25 U/L	Female	81 (296)	10.51± 4.476	-3.541	0.000
		Male	101 (374)	11.91± 5.487		

182 mild patients (81 females) were tested by two independent samples for myocardial enzyme changes of different genders. The difference was statistically significant in CK (81.07 ± 125.28) U/L and CK-MB (11.91 ± 5.49) U/L.

Table 5.Sex-difference in myocardial enzyme spectrum in severe COVID-19 patients

Assays	Normal range	Cases	N (assays)	Mean ± SD	T	P
α-HBDH	76-195 U/L	Female	22 (127)	251.6± 88.84	-2.652	0.008
		Male	26 (145)	285.3± 119.6		
LDH	120-250 umol/L	Female	22 (127)	328.4± 142.3	-2.668	0.008
		Male	26 (145)	380.2± 177.8		
CK	F: 40-200 U/L	Female	22 (127)	100.7± 193.7	-0.942	0.347
	M: 90-310 U/L	Male	26 (145)	119.2± 126.1		
CK-MB	0-25 U/L	Female	22 (127)	15.83± 17.61	-0.356	0.722
		Male	26 (145)	15.24± 9.08		

Forty-eight patients with severe illness (including 22 females), two independent sample t tests were performed on changes in myocardial enzyme spectrum of different genders. The differences were statistically significant for α-HBDH, LDH, and age. Among them, male patients had higher detection values, respectively. α-HBDH (285.26 ± 119.57) U/L, LDH (380.24 ± 177.83) U/L.

Discussion

COVID-19 is a new deadly and highly contagious infectious disease. This new coronavirus resembles SARS coronavirus, and gets into cells via the ACE2 receptor, which is highly expressed in the lung and heart, and lung is the major target of the COVID-19, causing COVID-19 pneumonia leading to death[2]. Heart is also a major target of this new coronavirus, and clinical observation revealed cardiomyocytes injury[3, 4], however, the focus is on the Tropin (cTNI/cTNT), B-type natriuretic peptide (BNP) and N-termina pro-brain natriuretic peptide (NT-proBNP) [4, 5]

α-HBDB, LDH, CK, and CK-MB are routine clinically examined myocardial enzymes[6].They exist in normal cardiomyocytes, and under the normal conditions, serum levels these enzymes are low. If the corona blood flow is suddenly reduced, the permeability of cardiomyocytes increased, and these enzymes could then be released into blood, and their serum levels are regarded as acute cardiomyocytes injury and useful biomarkers to evaluate the severity of heart injury[7]. It is reported that the enzymes α-HBDH and CK are quickly increased 3–8 h during cardiac infarction, 10–36 h reached the peak, and therefore as a sensitive biomarkers of acute heart injury. In 12–36 h, CK-MB reached the peak; the more sever the heart injury the higher the enzymes. The myocardial enzyme spectrum is wildly used as the diagnosis and prognosis index. In addition, LDH increase also seen in liver injury and pulmonary embolism, and increases in CK-MB are also seen in angina pectoris, pericarditis, and other kinds of myocardial injury[8].

In this study, we examined myocardial enzyme spectrum in 230 COVID-19 patients with 943 repeated measures. Severe cases showed significantly higher myocardial enzymes than mild cases, and males were more susceptible to COVID-19 induced myocardial injury, and had higher enzyme activities than females, and in severe cases, the age in males is younger than females, suggesting that males is more vulnerable to heart injury than females, and young males are also vulnerable to the disease.

This gender difference in COVID-19 induced heart injury is probably due to X chromosomes and female sex hormones, which could render females more resistant to virus infection. In further analysis of mild vases and severe cases, the statistical significant changes are dramatic between mild and sever cases, and somewhat correlated with gender differences[9].

Compare with the light female patients, male light patients also had higher CK and CK-MB, suggesting that male patients could be more susceptible to heart infarction or viral myocarditis and prone to accompany liver and other major organ failures. This needs to be further investigated.

In regard to the severity of disease, severe patients had higher α-HBDH, LDH, CK and CK-MB than light patients, and the severe cases are older patients that mild cases. Thus, we conclude that severe patients

are more susceptible to coronavirus-induced heart injury, consistent with the observation of Li et al [10–12]. Thus, it is important to monitor these parameters in severe cases, the give early drug intervention to prevent heart failure. Whether the suddenly increased α-HBDH, LDH, CK, and K-MB could predict the prognosis needs further investigation to guide clinical treatment and management of severe COVID-19 patients.

Summary

This study clearly demonstrates that heart is a target of COVID-19 infection, and the mechanism needs to be further elucidated. For severe and critical patients, especially for elderly, in addition to lung injury, the cardiomyocytes injury should also be monitored with myocardial enzyme spectrum to guide drug interventions to prevent heart failure.

Abbreviations

αHBDH-α-hydroxybutyric dehydrogenase

LDH- lactic acid dehydrogenase

CK- creatine kinase

CK-MB- creatine kinase isoenzyme

BNP- B-type natriuretic peptide

cTNI/cTNT- Tropin

NT-proBNP- N-termina pro-brain natriuretic peptide

SARS-Severe acute respiratory syndrome coronavirus

COVID-19- novel coronavirus pneumonia

Declarations

Conflict of interest: The authors report no relationships that could be construed as a conflict of interest.

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Ethics approval and consent to participate

Ethics Committee of Three gorges Hospital of Chongqing University approved this study.

Consent for publication

Not applicable.

Availability of supporting data

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Cai-Ling Jiao and Wen-Fa Li designed the study and undertook most of the work, they should be regarded as co-first author. Ye-Hong Xie, Jia-Wei Miao□Yun-Fang Wu, Wan-Ning Tan participated in data collection and analysis. All authors have contributed to the last version of the manuscript. The authors read and approved the final manuscript.

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Figures

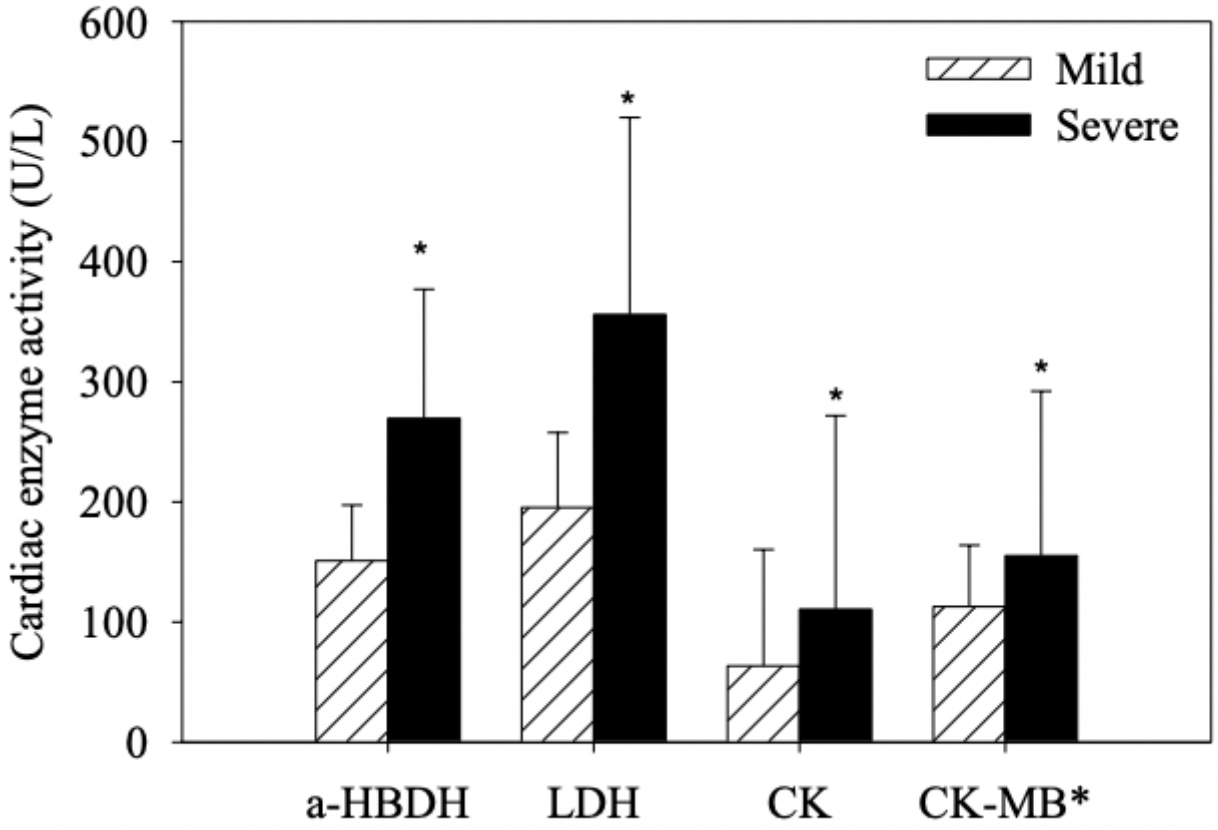

Figure 1

Myocardial enzyme spectrum in 230 COVID-19 patients. The myocardial enzyme spectrum assays including α-hydroxybutyrate dehydrogenase (α-HBDH), lactate dehydrogenase (LDH), creatine kinase (CK), and creatine kinase isoenzyme (CK-MB) in 230 COVID-19 patients were determined. Values for CK-MB* were multiplied 10-fold to allow the changes to be more visible. Data are mean ± SD. *Significantly different from Mild cases, $p < 0.05$.