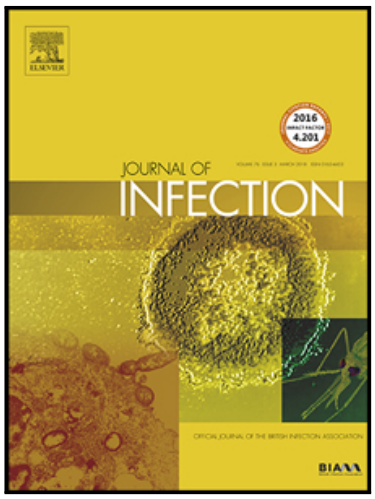

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The Clinical Characteristics of Myocardial injury [1] in Severe and Very Severe Patients with
2019 Novel Coronavirus Disease

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Dear Editor,

We read with interest the recent article published by Yang W et al.[1], which described the clinical characteristics and imaging manifestations of hospitalized patients with confirmed COVID-19 infection in Wenzhou, Zhejiang, China. The 2019 Novel coronavirus disease (COVID-19) has drawn global intensive attention[2-4]. Previous studies suggest that severe COVID-19 may present with acute cardiac injury[2-4]. However, few have investigated the cardiac lesion markers and their correlation to disease severity. In this letter, we explored the cardiac lesion biomarkers in patients with severe and very severe COVID-19.

We enrolled 34 COVID-19 patients admitted to the West District of Union Hospital of Tongji Medical College from February 5th to February 13rd, 2020. COVID-19 was diagnosed upon admission based on the New Coronavirus Pneumonia Prevention and Control Program (4th edition)[5]. Severe COVID-19 was defined as having either one of the flowing criteria: 1) Respiratory distress with respiratory rate more than 30 times/min; 2) Oxygen saturation ≤93%

in resting state; 3) PaO2/FiO2≤300mmHg (1mmHg=0.133kPa); and very severe either one of the flowing: 1) Respiratory failure in need of mechanical ventilation; 2) Shock; 3) Other organ dysfunction. Patients with medical history of cardiovascular disease were excluded. The study was approved by the ethics committee of the local hospital.

Demographic data and serum samples were collected upon admission. Laboratory confirmation of COVID-19 was done as recommended[5]. Laboratory test and cardiac lesion markers, including cardiac troponin I (cTnI), myoglobin (Myo), Creatine Kinase (CK), Creatine kinase–MB (CKMB), α-hydroxybutyrate dehydrogenase (HBDB), Lactate Dehydrogenase (LDH), and Aspartate Aminotransferase (AST), were tested by the laboratory department. Data were presented as percentages for categorical variables and median±IQR (Inter Quartile Range) for continuous variables. Simple t test and Mann-Whitney U test was used to compare continuous variables. Fisher's exact test was used to compare categorical variables.

We noted significantly increased cTnI, CK, HBDB and LDH levels in very severe group as compare to severe (Table 1). We then applied Fisher's exact test to determine the positive rate of cardiac lesion markers between severe and very severe patients. Increasingly, the percentage of very severe patients with elevated cTnI levels was markedly higher, with 8/8 patients exhibiting increased cTnI in very severe group, and only 1/26 patient in severe group (P value<0.001). In addition, the abnormal percentage of HBDB and LDH showed no significant difference between 2 groups (Table 2).

Recently, a number of studies have described the epidemiological and clinical characters of COVID-19[2-4]. A study of 41 patients with COVID-19 has suggested that 12% of the mild and

severe cases combined showed increased hyper sensitivity troponin I, suggesting acute myocardial injury[2]. It is also reported that severe acute respiratory syndrome coronavirus (SARS-CoV)[6] and Middle East respiratory syndrome coronavirus (MERS-CoV)[7] have caused critical cardiac lesions. In the present study, we have focused on cardiac lesion biomarkers in severe and very severe patients with COVID-19. We have proved elevation of cTnI, CK, HBDB, and LDH in critical cases. It is important to notify that, in very severe group, 8/8 patients exhibit cTnI above reference level; while 1/26 in severe group. This suggests that elevated cTnI could be a potential indicator for critically ill patients. It is worth notifying that among the 8 critically ill patients enrolled, the kidney and liver function markers are not as significantly disturbed as the cardiac lesion markers, suggesting that most patients enrolled have not been suffering from multiple organ dysfunction syndrome (MODS). Thus, the consistently high cTnI levels in very severe group point to the importance that the heart injury could be a distinct, or even lethal feature in very severe COVID-19. Protecting from myocardial injury could be of vital importance in clinical treatment for reducing the mortality rate. The study was limited by small sample size. And we haven't analyzed the echocardiography and MRI for the patients enrolled. Further analysis is needed to determine the etiology.

Author Contributions: BZ, XM and YW collected the clinical and laboratory data. JS processed statistical analysis. JS and BZ drafted the manuscript. XM and YW revised the final manuscript. XM and YW is responsible for all clinical and laboratory data.

Conflict of Interest Disclosures: We declare no competing interests.

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Table 1: Baseline Information and Cardiac Biomarkers in Severe and Very Severe Patients with COVID-19

	Median(IQR)		P Value	Reference
	Severe	Very Severe		
Number	26	8		
Sex(Male%)	46.15%	62.50%	ns	
age	63(58-69)	67(66-75)	ns	
CRE(μmol/L)	64.2(56.5-74.7)	82.6(69.6-98.6)	ns	57.0-111.0
AST(U/L)	32(25-45)	44(34-56)	ns	8-40
ALT（U/L）	34(27-67)	49(29-75)	ns	5-40
WBC count(*10^9/L)	5.93(4.77-7.45)	9.32(6.37-10.99)	ns	3.50-9.50

NEU%	78.20(71.10-84.70)	86.70(63.50-91.15)	ns	40.00-75.00
LYO%	14.30(11.90-18.90)	7.60(4.55-16.40)	ns	20.00-50.00
CRP(mg/L)	18.87(12.26-43.66)	73.00(36.57-116.95)	<0.05	0.00-8.00
Cardiac Biomarkers				
cTnI(ng/L)	4.8(2.5-8.4)	46.8(34.2-299.8)	<0.001	＜26.2
Myo(ng/mL)	62.8(33.0-87.7)	101.75(59.4-212.4)	ns	＜146.9
CK（U/L)	88(45-125)	199(77-285)	<0.05	24-194
CKMB(U/L)	10(17-13)	13(10-25)	ns	0-25
HBDB(U/L)	245(207-275)	453(347-547)	<0.01	72-182
AST(U/L)	32(25-45)	44(34-56)	ns	8-40
LDH(U/L)	287(246-331)	513(414-641)	<0.01	109-245

Abbreviations: IQR: inter quartile range; CRE: Creatine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; WBC: White blood count; NEU%: Neutrophil percentage; LYO%: Lymphocyte percentage; CRP: C reactive protein; cTnI: cardiac troponin I; Myo: myoglobin; CK: Creatine Kinase; CKMB: Creatine kinase–MB; HBDB: α-hydroxybutyrate dehydrogenase; AST: Aspartate aminotransferase; LDH: Lactate Dehydrogenase.

Table 2: Comparation of the severe and very severe patients with normal or elevated cardiac biomarkes

Group	**Number**	**cTnI(ng/L)**		**CK（U/L)**		**HBDB(U/L)**		**LDH(U/L)**	
		Normal	**Elevated**	**Normal**	**Elevated**	**Normal**	**Elevated**	**Normal**	**Elevated**
Severe	26	25	1	23	3	4	22	6	20
Very Severe	8	0	8	4	4	0	8	0	8
P value		＜0.001		<0.05		ns		ns	

Abbreviations: cTnI: cardiac troponin I; CK: Creatine Kinase; HBDB: α-hydroxybutyrate dehydrogenase; LDH: Lactate Dehydrogenase.