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Troponin I, a risk factor indicating more severe pneumonia among patients with novel coronavirus infected pneumonia

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ABSTRACT

Background: In December 2019, a novel communicable disease, novel coronavirus infected pneumonia (NCIP) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) broke out. We aimed to analyze the characteristics and severity of patients with myocardial damage in NCIP.
Methods: We enrolled 215 adult patients with NCIP from January 2020 to February 2020. Outcomes were followed up until March 1st, 2020.
Results: 28.37% of the total patients showed increased level of TnI (>0.040 ng/ml). Patients were older and had more cardiovascular complications in increased TnI group. Higher CRP, NT-proBNP, lower immune CD3, CD4 and CD8 cell account and more involved lobes detected by CT scan in the lung were observed in increased TnI group. Patients with elevated TnI had higher CURB-65 scores and were more likely given glucocorticoid therapy and mechanical ventilation than patients in normal TnI group.
Conclusions: Markers of cardiomyocyte injury were elevated not least in elderly males with pre-existing cardiovascular disease. Patients with elevated TnI presented more severe situation, leading to multiple organ dysfunctions, which appeared as a pivotal feature of patients with NCIP that requires attention by clinicians in order to provide necessary treatment as soon as possible and improve patients' outcomes.
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Introduction

In December 2019, a novel coronavirus infected pneumonia (NCIP), originating from the Huanan Seafood Market in Wuhan broke out. Being highly transmissible through mainly air droplets and contact, this epidemic has spread throughout the globe and has caused a total of over 1,500,000 infections outside China as of April 10, 2020. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus responsible for this infection was soon isolated and sequenced by Chinese Center for Disease Control and Prevention [1]. SARS-CoV-2 within the subgenus *sarbecovirus*, *Orthocoronavirinae* subfamily, turns out to be another coronavirus that infect human currently.

In The Lancet, there are two research reported the clinical characteristics of patients with SARS-CoV-2 infection [2,3]. Symptoms, CT features, treatment, mortality, and comparison between ICU patients and non-ICU patients were reported [4].

Aside from pulmonary edema and hyaline membrane formation observed in lung, the biopsy samples taken from heart tissue from a severe case of NCIP showed a few interstitial mononuclear inflammatory infiltrates and indicated myocardial damage [5]. We also observed elevated myocardial enzymes in severe patients with NCIP. Therefore, we retrospectively analyzed the characteristics and severity of patients with myocardial damage in NCIP.

Methods

Study design and participants

From January 2020 to February 2020, patients with NCIP admitted to Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine in Shanghai and Tongji Hospital affiliated to Tongji Medical College of Hust, Tongji Medical College, Huazhong University of Science & Technology in Wuhan were enrolled in this study. The respiratory specimens including nasal and pharyngeal swabs, bronchoalveolar lavage fluid, sputum, or bronchial aspirates were collected and detected

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by real-time RT-PCR methods to confirm the presence of SARS-CoV-2. All participants underwent chest CT scans. The study was approved by Ruijin Hospital Ethics Committee and Tongji Hospital Ethics Committee, respectively. Written informed consent was waived for emerging infectious diseases.

Patients were divided into four types following the standards set up by the Chinese Diagnosis and Treatment of Pneumonia Caused by New Coronavirus Infection (Fifth Version) as follows

1. Mild type: patients with mild clinical symptoms and no radiological abnormality.
2. Common type: patients presented with fever, cough or other respiratory symptoms, positive radiological findings as pneumonia.
3. Severe type: if one of the following conditions was met:
   (1) Respiratory distress, RR ≥ 30 per min;
   (2) Finger oxygen saturation (SaO2) ≤ 93% in resting state;
   (3) Partial pressure of arterial oxygen (PaO2)/concentration of oxygen inhaled (FiO2) ≤ 300 mmHg.
4. Critical type: if one of the following conditions was met:
   (1) Respiratory failure occurs and mechanical ventilation is needed;
   (2) Shock occurs;
   (3) Patients with other organ dysfunction need intensive care unit (ICU) monitoring treatment.

Patients with incomplete data were excluded from this study.

Data collection

We collected demographic data, symptoms, laboratory, radiological characteristics, severity, and treatment from patients' electronic medical records. Two physicians reviewed the date collected to double check.

Outcomes

In this study, patients (n = 215) involved were divided into two groups: normal TnI group (n = 154) and increased TnI group (n = 61) according to their level of troponin I (TnI) at admission. The above collected characteristics were compared between the two groups.

Statistical analysis

Continuous measurements were presented as mean (SD) and independent T test or Oneway ANOVA were used if they are normally distributed. Otherwise median (IQR) and Mann–Whitney *U* test were adopted to express and compare the variable if its distribution is non-normal. χ^2 test or Fisher's exact test were used to compare categorical variables. The analysis of covariance (ANCOVA) was also used to adjust age and sex. All tests were two-sided and a $p < 0.05$ denoted statistical significance. P value and the one adjusted by age and sex were listed in Tables. All analyses were done by SPSS (version 26.0).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Patient and public involvement

This was a retrospective case series study and no patients were involved in the study design, setting the research questions, or the outcome measures directly. No patients were asked to advise on interpretation or writing up of results.

Results

Patient characteristics

Totally, there are 222 patients admitted in the hospital. Seven patients lack the measurement of TnI. Therefore these 7 patients were excluded from this study. The participation rate is 96.85%. The patients were divided into two groups as normal TnI group (0 ~ 0.040 ng/ml, n = 154) and increased TnI group (>0.040 ng/ml, n = 61) according to their TnI level on admission. The majority patients were men (53%). Patients in normal TnI group were about 13 years younger than those in increased TnI group ($p = 0.001$) (Table 1). 80% or so of study population alleged exposure history (Table 1). More patients had the complications of hypertension and coronary heart disease in increased TnI group than in normal TnI group (16.2% *vs*. 41.0% respectively; $p < 0.001$; 7.1% *vs*. 16.4%; $p = 0.039$) (Table 1).

Cases in increased TnI group had higher score of CURB-65 at admission than patients in normal TnI group ($p < 0.001$). Most patients had fever or cough (80.5% and 48.8%). The distribution of symptoms was similar between these two groups (Table 1).

Laboratory and radiologic findings

On admission, level of CRP, direct bilirubin, creatinine, myoglobin, NT-proBNP, procalcitonin and fibrinogen were higher in increased TnI group than those in normal TnI group (Table 2). Compared with normal TnI group, the patients with lymphocyte count less than $1*10^9$/L and D-

Table 1
Clinical features of patients with NCIP on admission and comparison between normal TnI group and increased TnI group.

	Total population (n = 215)	Normal TnI group (n = 154)	Increased TnI group (n = 61)	*P*-value	Adjusted *P*-value
Baseline characteristics					
Male sex	114 (53.0%)	74 (48.1%)	40 (65.6%)	0.023	
Age (median, IQR)	54 (37–65)	49.5 (35–63)	63 (41–68)	0.001	
Epidemiological history	171 (79.5%)	121 (78.6%)	50 (82.0%)	NS	
Hypertension	50 (23.3%)	25 (16.2%)	25 (41.0%)	<0.001	0.026
Diabetes	24 (11.2%)	14 (9.1%)	10 (16.4%)	NS	
Chronic obstructive pulmonary disease	5 (2.3%)	2 (1.3%)	3 (4.9%)	NS	
Coronary heart disease	21 (9.8%)	11 (7.1%)	10 (16.4%)	0.039	0.048
Cerebrovascular disease	2 (0.9%)	0 (0%)	2 (3.3%)	NS	
Cancer	2 (0.9%)	0 (0%)	2 (3.3%)	NS	
Other diseases[a]	36 (16.7%)	20 (13.0%)	16 (26.2%)	0.019	0.089
CURB-65 on admission					
0	151 (70.2%)	118 (76.6%)	33 (54.1%)	0.001	0.033
1	53 (24.7%)	33 (21.4%)	20 (32.8%)		
2	9 (4.2%)	3 (1.0%)	6 (9.8%)		
3	2 (0.9%)	0 (0.0%)	2 (3.3%)		
Symptoms					
Fever	173 (80.5%)	127 (82.5%)	46 (75.4%)	NS	
Chill	4 (1.8%)	3 (1.9%)	1 (1.6%)	NS	
Cough	105 (48.8%)	73 (47.4%)	32 (52.5%)	NS	
Sputum production	56 (26.0%)	35 (22.7%)	21 (34.4%)	NS	
Sore throat	18 (8.4%)	16 (10.4%)	2 (3.3%)	NS	
Chest pain	5 (2.3%)	3 (1.9%)	2 (3.3%)	NS	
Shortness of breath	17 (7.9%)	10 (6.5%)	7 (11.5%)	NS	
Myalgia	25 (11.6%)	19 (12.3%)	6 (9.8%)	NS	
Nausea	10 (4.7%)	10 (6.5%)	0 (0.0%)	NS	
Vomit	0 (0.0%)	0 (0.0%)	0 (0.0%)	NS	
Diarrhea	12 (5.6%)	8 (5.2%)	4 (6.6%)	NS	
Headache	14 (6.5%)	11 (7.1%)	3 (4.9%)	NS	
Dizziness	7 (3.3%)	7 (4.5%)	0 (0.0%)	NS	

TnI, troponin I; IQR, Inter Quartile Range; CURB-65, (C: disturbance of consciousness, U: urea nitrogen, R: respiratory rate, B: blood pressure, 65: age).
Data were shown as number (percentage) or median (IQR). P-values between two groups were calculated by Fisher's exact test, Chi-square test, or Mann–Whitney *U* test. Adjusted P-values were calculated by covariance analysis after adjusting age, sex.
[a] Other diseases referred to other organ diseases except for the above diseases.

Table 2
Laboratory findings of patients with NCIP on admission and comparison between normal TnI group and increased TnI group.

	Total population (n = 215)	Normal TnI group (n = 154)	Increased TnI group (n = 61)	*P*-value	Adjusted *P*-value
Blood routine examination					
White blood cell count (10^9/L)	4.85 (4.09–6.11)	4.89 (4.09–6.11)	4.64 (4.00–6.46)	NS	
<4	47 (21.9%)	32 (20.8%)	15 (24.6%)		
>10	8 (3.7%)	5 (3.2%)	3 (4.9%)		
Neutrophil count (10^9/L)	3.14 (2.48–4.06)	3.22 (2.45–4.03)	3.02 (2.57–4.45)	NS	
Lymphocyte count (10^9/L)	1.12 (0.77–1.49)	1.14 (0.87–1.55)	0.91 (0.64–1.31)	NS	
<1.0	90 (41.9)	57 (37.0%)	33 (54.1%)	**0.022**	0.026
CRP (mg/L)	11.8(0.6–37.2)	10.7 (0–22.8)	19.5 (3.9–81.9)	<**0.001**	**0.016**
Hemoglobin (g/L)	135 (124–148)	134 (124–148)	136 (121–150)	NS	
Platelet count (10^9/L)	179 (143–220)	178 (142–220)	177 (144–213)	NS	
<100	7 (3.3%)	4 (2.6%)	3 (4.9%)		
Blood biochemistry examination					
ALT (U/L)	22 (15–32)	21 (15–32)	23 (15–21)	NS	
AST (U/L)	24 (19–33)	24 (19–32)	26 (21–33)	NS	
Total bilirubin (μmol/L)	8.2 (6.3–10.4)	8.0 (6.4–9.7)	9.1 (6.3–13.2)	NS	
Direct bilirubin (μmol/L)	3.9 (2.9–5.0)	3.7 (2.9–4.7)	4.5 (3.3–6.7)	**0.001**	**0.005**
>8.6	8 (3.7%)	3 (1.9%)	5 (8.2%)	**0.043**	0.087
Albumin (g/L)	41 (38–44)	41 (38–43)	39 (26–43)	NS	
Urea nitrogen (mmol/L)	4.56 (3.67–5.51)	4.39 (3.54–5.42)	4.94 (4.07–5.95)	NS	
Creatinine (μmol/L)	64 (52–77)	63 (51–75)	70 (55–87)	**0.001**	0.012
>111	12 (5.6%)	3 (1.9%)	9 (14.8%)	<**0.001**	**0.006**
Sodium (mmol/L)	139 (137–141)	139 (137–141)	139 (137–141)	NS	
Potassium (mmol/L)	3.8 (3.5–4.1)	3.8 (3.5–4.0)	3.9 (3.6–4.1)	NS	
Other					
LDH (U/L)	232 (192–299)	220 (189–276)	269 (209–339)	NS	
>245	50 (23.3%)	12 (7.8%)	38 (62.3%)	<**0.001**	0.081
Creatine kinase (U/L)	80 (56–125)	76 (52–113)	93 (64–170)	NS	
CK-MB (U/L)	12 (10–15)	12 (9–14)	13 (11–16)	NS	
Myoglobin (μg/L)	7.6 (3.2–17.4)	5.4 (3.0–12.7)	11.6 (5.1–37.0)	**0.001**	0.016
>48.8	22 (10.2%)	9 (5.8%)	13 (21.3%)	**0.002**	0.024
Procalcitonin (μg/L)	0.03 (0.02–0.07) (n = 174)	0.03 (0.02–0.06) (n = 125)	0.04 (0.02–0.08) (n = 49)	**0.032**	**0.048**
≤0.1	124 (71.2%)	114 (91.2%)	39 (79.6%)	NS	
0.1–0.25	14 (0.8%)	7 (5.6%)	7 (14.3%)		
0.25–0.5	2 (1.1%)	2 (1.6%)	0 (0%)		
≥0.5	5 (2.9%)	2 (1.6%)	3 (6.1%)		
ESR (mm/h)	72 (35–94)	70 (32–91)	76 (38–101)	NS	
NT-proBNP (pg/ml)	40.1 (25.1–91.1) (n = 153)	33.2 (21.2–66.3) (n = 114)	79.4 (34.8–350.2) (n = 39)	<**0.001**	**0.001**
>250	18 (11.8%)	7 (6.1%)	11 (28.2%)	**0.004**	**0.019**
Lactate (mmol/L)	2.28 ± 0.71 (n = 160)	2.21 ± 0.68 (n = 120)	2.48 ± 0.75 (n = 40)	**0.039**	0.047
Fibrinogen (g/L)	4.34 (3.72–5.41)	4.21 (3.62–5.10)	4.97 (4.09–5.80)	**0.001**	0.052
D-dimer (μg/L)	0.43 (0.31–0.80)	0.41 (0.30–0.80)	0.50 (0.34–0.83)	NS	
≥0.5	79 (36.7%)	48 (31.2%)	31 (50.8%)	**0.007**	0.009
Arterial blood gas analysis					
PH	7.40 (7.37–7.43)	7.40 (7.38–7.43)	7.39 (7.37–7.42)	NS	
PaO2 (kPa)	12.3 (10.1–14.8)	12.6 (10.4–15.4)	11.8 (9.8–14.2)	NS	
≤7.98	7 (3.3%)	5 (3.2%)	2 (3.2%)		
PaCO2 (kPa)	5.24 (4.80–5.64)	5.25 (4.85–5.64)	5.21 (4.73–5.66)	NS	
≥6.65	4 (1.9%)	4 (2.6%)	0 (0%)		
Oxygen saturation (%)	97.6 (96.1–98.7)	97.6 (96.2–98.8)	97.4 (95.7–98.5)	NS	
≤90	6 (2.8%)	5 (3.2%)	1 (1.6%)		
Standard bicarbonate (mmol/L)	23.8 (22.7–25.1)	24.0 (22.8–25.1)	23.5 (22.5–24.7)	NS	
Base excess	−0.9 (−2.4–0.8)	−0.6 (−2.3–0.8)	−1.4 (−2.8–0.3)	NS	
Lactate (mmol/L)	1.4 (1.0–2.1)	1.4 (0.9–2.03)	1.30 (1.05–2.15)	NS	
Immune status					
CD3 count	721 (491–1041)	779 (505–1085)	629 (328–913)	**0.006**	0.008
<700	85 (39.5%)	50 (32.5%)	35 (57.4%)	<**0.001**	<**0.001**
CD4 count	425 (297–650)	450 (307–680)	395 (173–607)	**0.017**	0.019
<400	74 (34.4%)	42 (27.3%)	32 (52.5%)	<**0.001**	**0.015**
CD8 count	246 (154–389)	270 (161–409)	215 (133–321)	**0.031**	0.046
IgG	11.7 (10.1–13.6)	11.7 (9.9–13.4)	11.8 (10.6–13.8)	NS	
IgA	2.28 (1.76–3.05)	2.26 (1.71–2.97)	2.36 (1.90–3.27)	NS	
IgM	0.94 (0.70–1.22) (n = 203)	0.95 (0.70–1.21) (n = 143)	0.86 (0.69–1.28) (n = 60)	NS	

TnI, troponin I; CRP, C reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; CK-MB, creatine kinase MB; ESR, erythrocyte sedimentation rate; NT-proBNP, N-terminal - pro hormone BNP.
Data were shown as number (percentage) or median (IQR). P-values between two groups were calculated by Fisher's exact test, Chi-square test, or Mann–Whitney *U* test. Adjusted P-values were calculated by covariance analysis after adjusting age, sex. These numbers in bold indicate they are less than 0.05.

dimer more than 0.5 μg/L was more in increased TnI group (37.0% *vs.* 54.1%, 31.2% *vs.* 50.8% in normal TnI group and increased TnI group respectively; p = 0.022, p = 0.007) (Table 2). Arterial blood gas between the two groups showed no significant differences. Compared with cases in increased TnI group, patients in normal TnI group presented higher level in CD3 count, CD4 count and CD8 count than those in increased TnI group, while their level of antibodies (IgG, IgA, IgM) were similar (Table 2).

In the terms of CT examination, ground-glass opacities (94.9%) and pleural thickening (59.1%) were the most common manifestations (Table 3). Images suggested more patients with 4–5 lobes involved in increased TnI group (52.00% *vs.* 75.4% in normal TnI group and increased TnI group respectively; p = 0.006) (Table 3).

Severity and treatment

The proportion of severe and critical illness in increased TnI group was significantly higher than those in normal TnI group (11.9% *vs.* 14.8%, 2.8% *vs.* 11.5% in normal TnI group and increased TnI group respectively; p = 0.021) (Table 4). Regarding therapy situation, subjects in increased TnI group were more likely given glucocorticoid therapy and mechanical ventilation than patients in normal TnI group (Table 4).

Discussion

Coronavirus could result in severe respiratory syndrome [6]. However, myocardial lesions and the elevation of myocardial enzymes in coronavirus infections are limited. Our study found that SARS-CoV-2 induced elevated myocardial enzymes and myocardial injury. From the present study, 28.37% of the total patients showed increased level of TnI. Elevated TnI usually indicates myocardial damage. Previous study reported increased serum troponin concentration might be a biomarker to stratify risk in subjects with pneumonia [7]. Troponin elevation in sufferers with COVID-19 is likely to be due to multifactorial non-ischemic causes, and less likely to be on account of atherothrombotic coronary occlusion [8]. Biopsy heart specimens of a patient with SARS-CoV-2 showed a few interstitial mononuclear inflammatory infiltrates [5]. SARS-CoV-2 was reported to use the same cell entry receptor as SARS-CoV (human angiotensin-converting enzyme 2 [hACE2]) [9]. As a homolog of the key enzyme of renin-angiotensin system, ACE2 is highly expressed in arterial and venous endothelial cells and arterial smooth muscle cells aside from lungs, which account for myocardium's susceptibility of SARS-CoV-2 [10–12]. Previous study suggested SARS-CoV mediated myocardial inflammation and damage through down-regulating myocardial ACE2 system, which might serve as the mechanism of SARS-CoV-2 impairing heart as well [13].

On the one hand novel coronavirus directly invades the myocardium and results in myocardial damage. On the other hand, previous cardiovascular complications aggravate this process. Pneumonia and cardiac disease frequently coexist in the same patients [14]. New-onset or worsening cardiac complications, not least atrial fibrillation are well-characterized complications of acute pneumonia [15]. Researchers have showed during the course of community-acquired pneumonia, a high incidence of cardiac complications, was independently associated with increased short-term mortality [7]. Consistent with previous study [2,16], the comparison of baseline characteristics indicated elderly male with comorbidities including hypertension and coronary heart disease were more likely to present a high level of TnI. A prospective study of elderly persons reported pre-existing heart failure figures as a risk factor for the development of pneumonia and as well increased the risk of pneumonia-related death [17]. This phenomenon suggests that patients with underlying cardiovascular disease have less robust cardiac reserve function, therefore their cardiac systolic and diastolic dysfunction are more vulnerable when virus attacks the myocardium. Hypoxia caused by pneumonia leads to an increase in heart rate, which induces the shortening diastolic time and insufficient coronary perfusion, thereby aggravating myocardial ischemia and hypoxia, ultimately causing instability and even collapse of the circulatory system. In our research, that patients with elevated myocardial enzymes had higher CURB-65 scores and higher NT-proBNP- a biomarker of cardiac function confirm the above theory from another aspect.

With regard to laboratory tests and CT scan results, higher CRP, lower immune CD3, CD4 and CD8 cell account and more involved lobes in the lung were observed in increased TnI group indicating higher virus load and more severe inflammatory response, also known as cytokine storm, a phenomenon associated with a wide variety of infectious and noninfectious diseases [18]. The storm of inflammatory factors can further cause disorders in multiple organs and systems as patients in increased TnI group showed elevating bilirubin, creatinine and D-dimer. Creatinine is the product of muscle metabolism in the human body and is mainly excreted by the glomerular filtration. Increased creatinine concentration indicates kidney damage. As a specific degradation product of fibrin, D-dimer increase when hypercoagulability and secondary fibrinolysis take place in the body. Figuring as a biomarker of liver function, bilirubin elevates if liver damage happens. Aforementioned multiple organ disorders along with myocardial damage exacerbated patients' condition.

Table 3
CT manifestations of patients with COCID-19 and comparison between normal TnI group and increased TnI group.

	Total population (n = 215)	Normal TnI group (n = 154)	Increased TnI group (n = 61)	*P*-value	Adjusted *P*-value
Abnormalities on chest CT					
Pleural effusion	15 (7.0%)	9 (5.8%)	6 (9.8%)	NS	
Pleural thickening	127 (59.1%)	90 (58.4%)	37 (60.7%)	NS	
Ground-glass opacity	204 (94.9%)	145 (94.2%)	59 (96.7%)	NS	
Fibrous stripes	42 (19.5%)	33 (21.4%)	9 (14.8%)	NS	
Consolidation	62 (28.8%)	50 (32.5%)	12 (19.7%)	NS	
Numbers of involved lung lobes					
0–1	30 (14.0%)	26 (16.9%)	4 (6.6%)	**0.006**	**0.014**
2–3	59 (27.4%)	48 (31.1%)	11 (18%)		
4–5	126 (58.6%)	80 (52.0%)	46 (75.4%)		

TnI, troponin I; CT, computed tomography.
Data were shown as number (percentage).
P-values between two groups were calculated by Fisher's exact test, or Chi-square test. Adjusted P-values were calculated by covariance analysis after adjusting age, sex. These numbers in bold indicate they are less than 0.05.

Table 4
Treatment and severity in hospital of patients with NCIP and comparison between normal TnI group and increased TnI group.

	Total population	Normal TnI group	Increased TnI group	*P*-value	Adjusted *P*-value
Treatment					
Antibiotics	101/200 (50.5%)	70/143 (49.0%)	31/57 (54.4%)	NS	
Glucocorticoids	41/215 (19.1%)	24/154 (15.6%)	17/61 (27.9%)	**0.039**	NS
Assisted ventilation	34/205 (16.6%)	18/154 (11.7%)	16/61 (26.2%)	**0.008**	0.047
Severity in hospital					
Mild + common	164/201 (81.6%)	122/143 (85.3%)	42/58 (68.9%)	**0.021**	0.036
Severe	26/201 (12.9%)	17/143 (11.9%)	9/58 (14.8%)		
Critically severe	11/201 (5.5%)	4/143 (2.8%)	7/58 (11.5%)		

TnI, troponin I.
Data were shown as number/total numbers (percentage).
P-values between two groups were calculated by Fisher's exact test, or Chi-square test. Adjusted P-values were calculated by covariance analysis after adjusting age, sex. These numbers in bold indicate they are less than 0.05.

Our study suffers from three limitations: 1. As a cross-sectional study, we have not included data of dynamic changes in myocardial enzymes, echocardiography and not evaluated diastolic function and ejection fraction of heart. The relationship between heart damage and NCIP pneumonia could be better assessed if aforementioned data could be included. 2. The data in this study was from 2 centers and incomplete data has been excluded, possibly resulting in a certain degree of selection bias. 3. For part of patients were still hospitalized as of press, we failed to know their eventual prognosis. Nevertheless, this retrospective study suggested myocardial damage is not ought to be ignored in the diagnosis and treatment of patients with NCIP.

Conclusion

Myocardial enzymes were elevated in a significant proportion of patients with NCIP, not least in elderly males with pre-existing cardiovascular disease. Patients with elevated myocardial enzymes presented a stronger immune and inflammatory response, leading to multiple organ dysfunctions including heart, liver and kidney which appeared as a pivotal feature of patients with NCIP that requires attention by clinicians in order to provide necessary treatment as soon as possible and improve patients' outcomes.

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Authors' contributions

W Chen is a member of the first batch of medical teams from Shanghai to support Hubei. Conception or design of the work: JMQ and DL. Data collection: WC, YF, YSX, HHL and JYY. Data analysis and interpretation: WPH, HC and DL. Draft of the article: DL, QYY. Critical revision of the article: JMQ and DL.

Declaration of competing interest

The authors declare that they have no conflict of interest.

References

1. Qun Li, Xuhua Guan, Wu Peng, Wang Xiaoye, Lei Zhou, Yeqing Tong, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med. 2020:1–9. https://doi.org/10.1056/nejmoa2001316.
2. Nanshan Chen, Min Zhou, Dong Xuan, Jieming Qu, Fengyun Gong, Yang Han, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;6736(20):1–7. https://doi.org/10.1016/S0140-6736(20)30211-7.
3. Chaolin Huang, Wang Yeming, Xingwang Li, Lili Ren, Jianping Zhao, Hu Yi, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;6736(20):1–10. https://doi.org/10.1016/s0140-6736(20)30183-5.
4. Wang Dawei, Hu Bo, Hu Chang, Zhu Fangfang, Xing Liu, Jing Zhang, et al. Clinical characteristics of 138 hospitalized patients with 2019 Novel coronavirus-infected pneumonia in Wuhan, China. Jama. 2020:1–9. https://doi.org/10.1001/jama.2020.1585.
5. Xu Zhe, Lei Shi, Wang Yijin, Jiyuan Zhang, Lei Huang, Chao Zhang, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir. 2020;2600(20):19–21. https://doi.org/10.1016/S2213-2600(20)30076-X.
6. Alimuddin Zumla, Hui David S. Perlman Stanley. Middle East respiratory syndrome. Lancet. 2015;386(9997):995–1007. https://doi.org/10.1016/S0140-6736(15)60454-8.
7. Corrales-Medina Vicente F, Musher Daniel M, Wells George A, Chirinos Julio A, Li Chen, Fine Michael J. Cardiac complications in patients with community-acquired pneumonia: incidence, timing, risk factors, and association with short-term mortality. Circulation. 2012;125(6):773–81. https://doi.org/10.1161/CIRCULATIONAHA.111.040766.
8. Chapman Andrew R, Anda Bularga, Mills Nicholas L. High-sensitivity cardiac troponin can be an ally in the fight against COVID-19. Circulation. 2020. https://doi.org/10.1161/CIRCULATIONAHA.120.047008.
9. Peng Zhou, Yang Xing-Lou, Wang Xian-Guang, Hu Ben, Lei Zhang, Wei Zhang, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020. https://doi.org/10.1038/s41586-020-2012-7 10.1038/s41586-020-2012–7.
10. Danilczyk U, Eriksson U, Oudit GY, Penninger JM. Physiological roles of angiotensin-converting enzyme 2. Cell Mol Life Sci. 2004;61(21):2714–9. https://doi.org/10.1007/s00018-004-4241-6.
11. Anguiano L, Riera M, Pascual J, Soler MJ. Circulating ACE2 in cardiovascular and kidney diseases. Curr Med Chem. 2017;24(30):3231–41. https://doi.org/10.2174/0929867324666170414162841.
12. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203(2):631–7. https://doi.org/10.1002/path.1570.
13. Oudit GY, Kassiri Z, Jiang C, Liu PP, Poutanen SM, Penninger JM, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest. 2009;39(7):618–25. https://doi.org/10.1111/j.1365-2362.2009.02153.x.
14. Fry Alicia M, Shay David K, Holman Robert C, Curns Aaron T, Anderson Larry J. Trends in hospitalizations for pneumonia among persons aged 65 years or older in the United States, 1988-2002. JAMA. 2005;294(21):2712–9. https://doi.org/10.1001/jama.294.21.2712.
15. Corrales-Medina Vicente F, Suh Kathryn N, Gregory Rose, Chirinos Julio A, Steve Doucette, William Cameron D, et al. Cardiac complications in patients with community-acquired pneumonia: a systematic review and meta-analysis of observational studies. PLoS Med. 2011;8(6):e1001048. https://doi.org/10.1371/journal.pmed.1001048.
16. Shaobo Shi, Qin Mu, Shen Bo, Yuli Cai, Tao Liu, Yang Fan, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol. 2020:1–8. https://doi.org/10.1001/jamacardio.2020.0950.
17. Koivula I, Sten M, Mäkelä PH. Risk factors for pneumonia in the elderly. Am J Med. 1994;96(4):313–20. https://doi.org/10.1016/0002-9343(94)90060-4.
18. Tisoncik Jennifer R, Korth Marcus J, Simmons Cameron P, Jeremy Farrar, Martin Thomas R, Katze Michael G. Into the eye of the cytokine storm. Microbiol Mol Biol Rev. 2012;76(1):16–32. https://doi.org/10.1128/MMBR.05015-11.