The prognostic value of myocardial injury in COVID-19 patients and associated characteristics

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Abstract

Background: Since December 2019, coronavirus disease 2019 (COVID-19) has emerged as an international pandemic. COVID-19 patients with myocardial injury might need special attention. However, an understanding on this aspect remains unclear. This study aimed to illustrate clinical characteristics and the prognostic value of myocardial injury to COVID-19 patients.

Methods: This retrospective, single-center study finally included 304 hospitalized COVID-19 cases confirmed by real-time reverse-transcriptase polymerase chain reaction from January 11 to March 25, 2020. Myocardial injury was determined by serum high-sensitivity troponin I (Hs-TnI). The primary endpoint was COVID-19-associated mortality.

Results: Of 304 COVID-19 patients (median age, 65 years; 52.6% males), 88 patients (27.3%) died (61 patients with myocardial injury, 27 patients without myocardial injury on admission). COVID-19 patients with myocardial injury had more comorbidities (hypertension, chronic obstructive pulmonary disease, cardiovascular disease, and cerebrovascular disease); lower lymphocyte counts, higher C-reactive protein (CRP; median, 84.9 vs. 28.5 mg/L; \( p < .001 \)), procalcitonin levels (median, 0.29 vs. 0.06 ng/ml; \( p < .001 \)), inflammatory and immune response markers; more frequent need for non-invasive ventilation, invasive mechanical ventilation; and was associated with higher mortality incidence (hazard ratio [HR] = 7.02; 95% confidence interval [CI], 4.45–11.08; \( p < .001 \)) than those without myocardial injury. Myocardial injury (HR = 4.55; 95% CI, 2.49–8.31; \( p < .001 \)), senior age, CRP levels, and novel coronavirus pneumonia types on admission were independent predictors to mortality in COVID-19 patients.

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**Conclusions:** COVID-19 patients with myocardial injury on admission is associated with more severe clinical presentation and biomarkers. Myocardial injury and higher Hs-TnI are both strongest independent predictors to COVID-19-related mortality after adjusting confounding factors.

**KEYWORDS**
clinical characteristics, coronavirus disease 2019, myocardial injury, prognosis

**1 | BACKGROUND**

Coronavirus disease 2019 (COVID-19) is a newly recognized infection which was first reported in Wuhan, China. Since the beginning of the outbreak, COVID-19 has emerged as a pandemic globally, and the number of cases is rising at an exponential rate. As of June 18, 2021, there have been a total of more than 176,693,988 laboratory-confirmed cases of COVID-19 globally, and it poses a great threat to public health in the world as evidenced by 3,830,304 deaths. COVID-19 is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The clinical spectrum appears to be very wide, including asymptomatic infection, mild upper respiratory disease, and severe viral pneumonia with respiratory failure, and even death. The condition of some patients with COVID-19 may deteriorate rapidly, particularly in older patients with underlying comorbidities including cardiovascular disease. Furthermore, SARS-CoV-2 can affect the cardiovascular system in multiple ways, increasing morbidity in patients with potential cardiovascular disease and causing myocardial injury and dysfunction. High-sensitivity troponin I (Hs-TnI) provides the potential to earlier identify myocardial injury and assists treatment. Some studies provide insights into the incidence of cardiac complications associated with SARS-CoV-2, while imaging manifestations, cytokine levels, and the prognostic value of cardiovascular risk factors in COVID-19 patients are poorly understood. We aimed to comprehensively define clinical characteristics, laboratory results, outcomes, and management strategies of COVID-19 patients, then to find whether there is an association of myocardial injury and other biomarkers with mortality. This study may also provide clues to potential mechanisms associated with myocardial injury.

**2 | METHODS**

**2.1 | Study design and patients**

In this study, we retrospectively enrolled 320 COVID-19 patients admitted to the Renmin Hospital of Wuhan University from January 11, 2020 to March 25, 2020 with approval from the Research Ethics Committee of the Renmin Hospital of Wuhan University, Wuhan, China (approval number: WDRY2020-K038). Sixteen cases without significant biomarkers, including Hs-TnI and creatinine kinase–myocardial band (CK-MB) levels, were excluded. Thus, a total of 304 patients were finally included in the study. The confirmed diagnosis of COVID-19 was defined as a positive result by using real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) detection for routine
Research Article

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Title: Cardiac biomarkers and myocardial injury in COVID-19 patients: A single-center cohort study

Abstract

Background: The COVID-19 pandemic has posed a global threat. Cardiac biomarkers are often elevated in patients with COVID-19; however, the clinical significance of these elevations remains unclear.

Methods: We consecutively enrolled COVID-19 patients with laboratory-confirmed COVID-19 diagnosed in our hospital from January 1, 2020 to March 31, 2020. Patients were divided into two groups based on the presence or absence of myocardial injury. The clinical characteristics, laboratory data, and outcomes were compared between the two groups.

Results: Of the 304 COVID-19 patients, 198 patients (65.1%) had myocardial injury. Patients with myocardial injury were older, more males, and more likely to have pre-existing comorbidities and were associated with more severe presentation. Cardiac biomarkers were significantly elevated in patients with myocardial injury compared to those without myocardial injury.

Conclusions: Myocardial injury is common in COVID-19 patients and is associated with a more severe presentation and worse outcomes. Cardiac biomarkers may be useful in predicting myocardial injury and guiding clinical management.

Keywords: COVID-19, myocardial injury, cardiac biomarkers, clinical presentation.
D-dimer levels (all \( p < .001 \)) compared with patients without myocardial injury. Figure 2 shows the dynamic change of NT-proBNP of COVID-19 patients from admission to hospitalization.

The imaging manifestations of the 304 patients with COVID-19 were listed in Table S1. One hundred and thirty-five patients (44.4%) underwent examination of electrocardiogram (ECG) after admission, and 83 of 135 ECGs (61.5%) indicated cardiac abnormalities, including T-wave depression and inversion, ST-segment depression, and atrioventricular block. Thirty-four patients (11.2%) underwent examination with echocardiography and 27 patients (79.4%) showed abnormalities, and the more common abnormalities are cardiac diastolic dysfunction, and other complex abnormalities (tricuspid regurgitation). All patients underwent CT or DR examinations and 221 (72.6%) patients presented with pulmonary abnormalities including ground-glass opacities or consolidation (Figure S1). There was no statistically significant difference in the other imaging findings between patients with or without myocardial injury, only the patients with complex echo abnormalities had significant difference.

Oxygen treatment was provided to 206/304 patients (67.8%). Sixty-two (20.4%) patients received noninvasive ventilation, and 10.2% of the patients (31 patients) were placed in mechanical ventilation. The proportion treated with antiviral therapy was the highest (304, 100%), followed by high-dose glucocorticoid therapy (142, 46.7%), intravenous immunoglobulin therapy (122, 40.1%), antibiotic therapy (118, 38.8%) and hemoperfusion (20, 6.6%). Only 8 patients (2.6%) among all participants were given plasmapheresis therapy. Overall, 100 patients (27.3%) had kidney injury during hospitalization, and 65 patients (21.4%) had hepatic injury.

Compared with those without myocardial injury, more COVID-19 patients with myocardial injury required oxygen inhalation, noninvasive ventilation, invasive mechanical ventilation, antibiotic treatment, and hemoperfusion therapy (all \( p < .001 \)) (Table 3). However,

| TABLE 1 | Clinical characteristics and complications of COVID-19 patients |
|----------|---------------------------------------------------------------|
| Characteristic | All patients (\( n = 304 \)) | Myocardial injury | p value |
| Male (%) | 160 (52.6) | 61 (63.5) | 99 (47.6) | .010 |
| Age, median (IQR) | 65.0 (54.0–74.0) | 70.5 (60.1–79.0) | 62.0 (52.0–69.0) | <.001 |
| NCP types (%) | | | | |
| Mild/common | 117 (38.5) | 22 (22.9) | 95 (45.7) | <.001 |
| Severe | 147 (48.4) | 49 (51.0) | 98 (47.1) | |
| Critically severe | 40 (13.2) | 25 (26.0) | 15 (7.2) | |
| Comorbidities (%) | 198 (65.1) | 76 (79.2) | 122 (58.7) | <.001 |
| Diabetes | 50 (16.4) | 17 (17.7) | 33 (15.9) | .687 |
| Hypertension | 130 (42.8) | 52 (54.2) | 78 (37.5) | .006 |
| COPD | 21 (6.9) | 12 (12.5) | 9 (4.3) | .009 |
| Cardiovascular disease | 49 (16.1) | 27 (28.1) | 22 (10.6) | <.001 |
| Coronary artery disease | 32 (10.5) | 18 (18.8) | 14 (6.7) | .002 |
| Cerebrovascular disease | 21 (6.9) | 13 (13.5) | 8 (3.8) | .002 |
| Kidney disease | 12 (3.9) | 4 (4.2) | 8 (3.8) | 1 |
| Hepatic disease | 8 (2.6) | 3 (3.1) | 5 (2.4) | .711 |
| Cancer, autoimmune disease | 32 (10.5) | 11 (11.5) | 21 (10.1) | .719 |

Note: \( p \) values are calculated by Student's \( t \) test, Mann–Whitney \( U \) test, or \( \chi^2 \) test as appropriate. \( p \) values less than .05 was statistical significant (Boldface).

Abbreviations: COPD, chronic obstructive pulmonary disease; IQR, interquartile range; NCP, novel coronary pneumonia.
| Characteristic | Normal range | All patients (n = 304) | Myocardial injury With (n = 96) | Without (n = 208) | p value |
|---------------|--------------|------------------------|-----------------------------|--------------------|---------|
| **Immunologic markers, median (IQR)** | | | | | |
| Leucocyte counts (10⁹/L) | 3.5–9.5 | 6.3 (4.3–8.1) | 7.1 (5.0–10.1) | 6.0 (4.4–7.8) | .058 |
| Neutrophil counts (10⁹/L) | 1.8–6.3 | 4.9 (3.0–7.4) | 6.7 (4.2–10.3) | 4.4 (2.8–6.4) | <.001 |
| Lymphocyte counts (10⁹/L) | 1.1–3.2 | 0.9 (0.6–1.3) | 0.6 (0.4–1.0) | 1.0 (0.7–1.3) | <.001 |
| Platelet counts (10⁹/L) | 130–175 | 200.0 (145.0–258.0) | 151.5 (105.0–237.2) | 210.0 (165.5–264.0) | <.001 |
| Hemoglobin (g/L) | 125–350 | 123.0 (111.3–136.0) | 122.0 (110.0–137.0) | 123.0 (113.0–135.2) | .872 |
| CD3 counts (per µl) | 723–2737 | 502.0 (275.8–765.0) | 317.5 (177.3–591.0) | 539.5 (324.0–862.5) | <.001 |
| CD4 counts (per µl) | 404–1612 | 287 (161.5–464.5) | 193.5 (98.8–322.8) | 340.5 (201.8–528.3) | <.001 |
| CD8 counts (per µl) | 220–1129 | 152.0 (73.0–278.0) | 77 (40.8–161.5) | 191.0 (106.0–304.0) | <.001 |
| CD4/CD8 ratio | 0.9–2.0 | 1.8 (1.3–1.7) | 2.0 (1.3–3.4) | 1.8 (1.3–2.7) | .127 |
| IgG (g/L) | 7.0–16.0 | 12.3 (10.2–15.4) | 13.7 (11.2–16.6) | 11.7 (9.6–14.6) | .003 |
| IgM (g/L) | 0.4–2.3 | 1.0 (0.7–1.3) | 1.0 (0.7–1.3) | 1.0 (0.7–1.2) | .143 |
| IgA (g/L) | 0.7–4.0 | 2.4 (1.8–3.3) | 2.8 (2.1–3.8) | 2.2 (1.7–3.0) | .002 |
| C3 (g/L) | 0.9–1.8 | 1.0 (0.9–1.1) | 1.0 (0.8–1.1) | 1.0 (0.9–1.2) | <.001 |
| CK-MB (ng/ml) | 0–5 | 1.2 (0.7–2.6) | 4.2 (1.9–8.3) | 0.9 (0.7–1.5) | <.001 |
| **Cardiac, hepatic, and kidney injury markers, median (IQR)** | | | | | |
| Myoglobin (µg/L) | 0–110 | 49.1 (27.4–130.9) | 177.4 (82.5–765.7) | 35.0 (25.0–59.7) | <.001 |
| Hs-Tnl (ng/ml) | 0–0.04 | <0.006 (<0.006–0.068) | 0.22 (0.09–1.83) | <0.006 (<0.006–0.011) | <.001 |
| NT-proBNP<sup>a</sup> (pg/ml) | 0–300 | 285.8 (86.7–835.8) | 799.7 (267.7–1719.0) | 220.1 (54.0–456.5) | <.001 |
| NT-proBNP<sup>b</sup> (pg/ml) | 0–300 | 647.8 (237.2–1996.3) | 2543.0 (953.0–9022.0) | 389.0 (141.0–1046.0) | <.001 |
| LDH (U/L) | 100–300 | 266 (202.8–413.3) | 433.5 (306.5–677.5) | 221.0 (188.0–284.0) | <.001 |
| ALT (U/L) | 9–50 | 24.0 (17.0–46.0) | 27.0 (18.0–48.0) | 24.0 (16.8–43.3) | .662 |
| AST (U/L) | 15–40 | 27.0 (19.0–43.5) | 42.0 (24.0–65.0) | 23.5 (17.3–32.0) | <.001 |
| ALP (U/L) | 90–130 | 71.0 (56.4–94.0) | 75.0 (58.8–105.0) | 69.0 (56.0–90.3) | .219 |
| ALB (g/L) | 40–55 | 37.0 (33.5–40.0) | 33.8 (30.1–37.1) | 38.7 (35.8–41.0) | <.001 |
| Urea (mmol/L) | 3.6–9.5 | 5.4 (3.8–9.0) | 9.5 (5.4–19.4) | 4.6 (3.5–6.5) | <.001 |
| Creatinine (mmol/L) | 57–111 | 58.0 (48.0–79.0) | 71.0 (53.0–126) | 56.0 (46.0–70.8) | <.001 |
| Potassium (mmol/L) | 3.5–5.5 | 4.2 (3.8–4.5) | 4.1 (3.6–4.6) | 4.3 (3.9–4.5) | .255 |
| Sodium (mmol/L) | 135–155 | 142.0 (139.0–146.0) | 141.0 (138.0–146.0) | 142.0 (139.0–146.0) | .542 |
| **Inflammation markers, median (IQR)** | | | | | |
| PCT (ng/ml) | <0.1 | 0.10 (0.05–0.32) | 0.29 (0.10–1.09) | 0.06 (0.04–0.14) | <.001 |
| C-reactive protein (mg/L) | 0–10 | 51.3 (10.9–104.0) | 84.9 (53.7–173.8) | 28.5 (5.7–82.2) | <.001 |
| IL-6 (pg/ml) | <10 | 10.5 (6.1–26.5) | 23.5 (10.7–98.1) | 9.0 (5.8–20.6) | <.001 |
| **Coagulation markers, median (IQR)** | | | | | |
| PT (s) | 9–13 | 12.4 (11.5–13.5) | 13.4 (12.2–14.4) | 12.1 (11.3–13.1) | <.001 |
| APTT (s) | 25–31.3 | 28.6 (26.2–31.5) | 29.2 (27.7–33.2) | 28.2 (25.9–31.0) | <.001 |
| D-dimer (mg/L) | 0–0.55 | 2.5 (0.7–13.8) | 7.0 (1.9–21.7) | 1.6 (0.6–8.2) | .001 |

Abbreviations: ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, active partial thromboplastin time; AST, aspartate aminotransferase; C3, complement 3; CD, cluster of differentiation; CK-MB, creatinine kinase-myocardial band; ECG, electrocardiogram; Hs-Tnl, high-sensitivity troponin I; Ig, immunoglobulin; IL-6, interleukin 6; IQR, interquartile range; LDH, lactate dehydrogenase; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PCT, procalcitonin; PT, prothrombin time.

Note: p values are calculated by Student’s t test, Mann–Whitney U test, or χ² test as appropriate. p values less than 0.05 was statistical significant (Boldface).

<sup>a</sup>NT-proBNP levels on admission.

<sup>b</sup>NT-proBNP levels during hospitalization.
intravenous immunoglobulin treatment (24.0% vs. 47.6%; p < .001) was lower in patients with myocardial injury. The comparison of typical managements, comorbidities, complications, and time duration from symptom onset to death were made in 20 random patients with myocardial injury or not (Figure 3), indicating that myocardial injury may be associated with more severe presentation.

During the median durations for about 45.4 days from onset of symptoms to follow-up (range: 3–84 days), a total of 88/304 patients (27.3%) died, among which 61 patients had myocardial injury, while 27 patients did not have myocardial injury (Table 3). In the univariable analysis, the mortality rate was significantly higher in patients with myocardial injury (63.5% vs. 13.0%; p < .001; Table 3). The Kaplan–Meier survival curves indicated significant survival differences between the patients with or without myocardial injury (p < .001; Figure 4). The multivariate Cox proportional hazard regression model showed significantly higher risk of death in patients with myocardial injury than in those without myocardial injury from symptom onset (hazard ratio [HR], 4.55; 95% confidence interval [CI], 2.49–8.31; p < .001) to primary endpoint, after adjusting for age, sex, pre-existing comorbidities, CRP levels, D-dimer levels, NCP types (Table 4). Under this Cox regression model with Hs-TnI as continuous variable showed that higher Hs-TnI was also associated with mortality (HR, 3.33; 95% CI, 1.96–5.66; p < .001) (Table S2).

4 | DISCUSSION

This study summarizes the clinical characteristics, laboratory, cardiac, and radiographic findings in a large cohort of 304 hospitalized COVID-19 patients, and provides novel information of the prognostic value of pre-existing comorbidities and myocardial injury. Myocardial injury, senior age, NCP types, and CRP levels were independently associated with higher risk of mortality during hospitalization. The myocardial injury was probably associated with inflammation response. The prognostic value of elevated Hs-TnI in patients with COVID-19 should be of great interest to a broad readership, as a simple blood biomarker test was such a strong predictor of mortality and that sophisticated, expensive, and time-consuming cardiac testing with CT and magnetic resonance imaging are not needed.

With the high infectivity, COVID-19 has managed to supersede severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) in 2012 in terms of death toll. The median age was 65 years in our study, greater than previous studies (55.6 and 49 years),

FIGURE 1 Associations between CD3, CD4, CD8, and lymphocytes biomarkers. Strong correlations were found between CD3, CD4, CD8, and lymphocytes biomarkers. CD, cluster of differentiation of T cells
be older. This is supported by the evidence that the median age of patients is higher in group with myocardial injury than those without (70.5 vs. 62.0 years). COVID-19 patients with myocardial injury were prone to develop severe NCP types (77.0%), and more likely to have pre-existing comorbidities (79.2% vs. 58.7%), like hypertension, cardiovascular disease and cerebrovascular disease, also confirmed by other studies.9,15 Li et al.16 analyzed six studies involving 1527 COVID-19 patients with previous cardiovascular metabolic diseases, and indicated that this patient group may face a greater risk of developing into the severe condition and that comorbidities can also greatly affect the prognosis of the COVID-19 patients.

In our study, COVID-19 patients with myocardial injury had obviously elevated myoglobin, and NT-proBNP levels, providing independent corroborating evidence of myocardial injury.17 In addition, the correlations between Hs-TnI levels and NT-proBNP levels with urea nitrogen levels indicated multiorgan injury along with myocardial injury and worth early monitoring. In prior studies, no significant deviations in coagulation function from the normal range were found but some patients still presented with coagulation dysfunction.18,19 Our study further validated this result, especially in patients with myocardial injury or in critically severe and severe type. Hence, we speculate that coagulation may be not a very important pathophysiological process in all patients with COVID-19. Only some critically ill patients demonstrated abnormal coagulation function and multiple organ dysfunction at the end stage. COVID-19 patients with myocardial injury need active treatments to delay or reverse the progression of disease, supported by the fact that the clinical

**FIGURE 2** Progression of NT-proBNP in COVID-19 patients on admission and during hospitalization, and correlation between serum high-sensitivity TnI and NT-proBNP, urea nitrogen. When Hs-TnI levels was <0.006 ng/ml, it was recorded as 0.006 ng/ml at convenience. Hs-TnI, high-sensitivity troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide.
presentation and the severity of COVID-19, as well as more comorbidities in patients with myocardial injury group. However, patients without myocardial injury received more intravenous immunoglobulin therapy than patients with myocardial injury, and this may be attributable to rapid progression of COVID-19 disease in the later cohort, which makes it too late to use intravenous immunoglobulin therapy.

Two prior studies indicated that there was a strong correlation between myocardial injury and prognosis of COVID-19 patients during hospitalization. Adding to previous reports, our study further confirmed that myocardial injury, senior age, CRP levels, and NCP types are all independent prognostic indicators of mortality in COVID-19 patient. Among these risk factors, myocardial injury, determined by serum Hs-TnI, was the strongest both as dichotomous and continuous variable. The Hs-TnI marker can be an ally for earlier identifying myocardial injury, rather than myocardial infarction, thus guiding timely intervention.7

To date, the exact mechanism of cardiac involvement in COVID-19 remains under investigation. Current studies suggested immune change in patients with MERS, SARS and influenza, especially changes in peripheral blood T cells, which may contribute to understanding the characteristics, diagnosis, monitoring, prevention, and treatment of the disease. Many investigations have already reported that the pathophysiology of myocardial injury in COVID-19 patients may be linked to dysregulation of immune response, presenting with lower lymphocyte counts, higher leukocytes counts, and significantly reduced CD4+ and CD8+ T lymphocytes levels. In our study, the CD3, CD4, CD8 counts correlated well with lymphocytes counts and CRP levels, and elevated inflammation reaction (CRP) and suppressive immune response (CD4+, CD8+) were observed in COVID-19 patients at admission. In addition, traditional cardiovascular risk factors such as diabetes and hyperlipidemia impact immune function, and conversely, dysregulated immunologic status corresponds with elevated risk of incident cardiovascular disease. Another possible mechanism is the direct invasion via angiotensin converting enzyme 2 (ACE2) receptors in cardiovascular system. In our study, we not only found that COVID-19 patients with comorbidities were associated with higher mortality, but also the CRP levels are significantly associated with mortality in multivariate Cox analysis, which indicated there would be inflammation response and this was associated with worse outcomes. In addition, IL-6 cytokines were elevated in COVID-19 patients with myocardial injury, justifying the emergence of severity of inflammation, also immune-related markers, like CD3, CD4, CD8 molecules counts and lymphocyte counts were all reduced, more significant in

### TABLE 3
Managements and clinical outcomes of COVID-19 patients

| Characteristic | All patients (n = 304) | Myocardial injury |
|---------------|-----------------------|-------------------|
|               | With (n = 96) | Without (n = 208) | p value |
| Managements, n (%) |
| Oxygen inhalation | 206 (67.8) | 85 (88.5) | 121 (58.2) | <.001 |
| Noninvasive ventilation | 62 (20.4) | 35 (36.5) | 27 (13.0) | <.001 |
| Invasive mechanical ventilation | 31 (10.2) | 20 (20.8) | 11 (5.3) | <.001 |
| Immunoglobulin | 122 (40.1) | 23 (24.0) | 99 (47.6) | <.001 |
| Antiviral | 304 (100) | 96 (100) | 208 (100) | - |
| Antibiotic | 118 (38.8) | 65 (67.7) | 53 (25.5) | <.001 |
| Glucocorticoids | 142 (46.7) | 44 (45.8) | 98 (47.1) | .835 |
| Hemoperfusion | 20 (6.6) | 12 (12.5) | 8 (3.8) | .005 |
| Plasmapheresis | 8 (2.6) | 5 (5.2) | 3 (1.4) | .114 |

Clinical outcomes, n (%)

|               | n (%) | n (%) | n (%) |
|---------------|-------|-------|-------|
| Death | 88 (27.3) | 61 (63.5) | 27 (13.0) |
| In hospital | 83 (28.9) | 11 (11.5) | 72 (34.6) |
| Discharge | 133 (43.8) | 24 (25.0) | 109 (52.4) |

Note: p values are calculated by Student’s t test, Mann–Whitney U test, or χ² test as appropriate. p values less than 0.05 was statistical significant (Boldface).
patients with myocardial injury. This was consistent with a previous study, which indicated that lymphopenia was an independent risk factor of myocardial injury in the setting of COVID-19. It was reasonable to presume that invasive coronavirus may dysregulate the immune system, and further lead to severe damage to myocardial tissues. The data from all these studies taken together, suggest that clinicians should consider myocardial injury on presentation, NCP types and inflammation and immune dysregulation when caring for COVID-19 patients.

**FIGURE 3** Days from symptom onset to death of COVID-19 patients with or without myocardial injury and their comorbidities, complications, managements. Comparison of days from symptom onset to death of typical 20 patients with COVID-19 with myocardial injury (10 patients) or without myocardial injury (10 patients) randomly selected from dead patients. Patients with myocardial injury were more likely to have comorbidities, severe presentation, and complications, shock and ICU managements. However, no significant difference was found for time duration from symptom onset to death in two groups. This figure tells us that myocardial injury may be associated with more severe presentation. ICU, intensive care unit; NCP, novel coronary pneumonia

**FIGURE 4** Mortality during hospitalization between patients with versus without myocardial injury. Kaplan–Meier survival curves for mortality from symptom onset to follow-up date.

| No. | Comorbidities | January, 2020 | February, 2020 | March, 2020 | Time duration | NCP types | Complications, managements |
|-----|---------------|---------------|----------------|-------------|---------------|------------|-----------------------------|
| 1   |               | 15            | 20             | 25          | 31            | 5          | 10                          |
| 2   |               | 11            | 4#             | 11          | 4*            | 11          | 4#                         |
| 3   |               | 24            | 4#             | 24          | 4# IC#        | 24          | 4#                         |
| 4   |               | 12            | 4#             | 12          | 4# IC#        | 12          | 4#                         |
| 5   |               | 15            | 3#             | 15          | 3#           | 15          | 3#                         |
| 6   |               | 21            | 2              | 21          | 2             | 21          | 2                          |
| 7   |               | 16            | 3#             | 16          | 3# IC#        | 16          | 3# IC#                     |
| 8   |               | 17            | 4#             | 17          | 4#           | 17          | 4#                         |
| 9   |               | 14            | 2              | 14          | 2             | 14          | 2                          |
| 10  |               | 15            | 3              | 15          | 3             | 15          | 3                          |
| 11  |               | 17            | 4              | 17          | 4             | 17          | 4                          |
| 12  |               | 18            | 4#             | 18          | 4#           | 18          | 4#                         |
| 13  |               | 21            | 3#             | 21          | 3# IC#        | 21          | 3# IC#                     |
| 14  |               | 23            | 4#             | 23          | 4# IC#        | 23          | 4# IC#                     |
| 15  |               | 15            | 4              | 15          | 4             | 15          | 4                          |
| 16  |               | 11            | 4              | 11          | 4             | 11          | 4                          |
| 17  |               | 24            | 3#             | 24          | 3#           | 24          | 3#                         |
| 18  |               | 18            | 2ICU           | 18          | 2ICU         | 18          | 2ICU                       |
| 19  |               | 37            | 3#             | 37          | 3# IC#        | 37          | 3# IC#                     |
| 20  |               | 8             | 3#             | 8           | 3#           | 8           | 3#                         |

**FIGURE 3** Days from symptom onset to death of COVID-19 patients with or without myocardial injury and their comorbidities, complications, managements. Comparison of days from symptom onset to death of typical 20 patients with COVID-19 with myocardial injury (10 patients) or without myocardial injury (10 patients) randomly selected from dead patients. Patients with myocardial injury were more likely to have comorbidities, severe presentation, and complications, shock and ICU managements. However, no significant difference was found for time duration from symptom onset to death in two groups. This figure tells us that myocardial injury may be associated with more severe presentation. ICU, intensive care unit; NCP, novel coronary pneumonia

**FIGURE 4** Mortality during hospitalization between patients with versus without myocardial injury. Kaplan–Meier survival curves for mortality from symptom onset to follow-up date.

| Without Myocardial injury | With Myocardial injury |
|---------------------------|------------------------|
| Number at risk            | 192 191 177 173 169    |
|                           | 112 98 70 50 47        |

| Survival probability (%) | Time (days) |
|--------------------------|-------------|
| Without Myocardial injury|             |
| With Myocardial injury   |             |
The exact mechanism of myocardial injury merits further investigation, but the findings presented here highlight the prognostic value in identifying myocardial injury with noninvasive biomarker testing on admission in COVID-19 patients and raise the possibility that providers should consider close management of immune response, inflammation, and comorbidities in COVID-19 hospitalized patients.

We acknowledge some limitations in our study. First, this was a retrospective, single-center study of patients admitted to hospital; multi-center investigations for a larger cohort would be better to assess the clinical characteristics and confirm the outcomes of myocardial injury after infection with COVID-19. Second, because of the logistical limitations at the onset of these emerging infections in Wuhan, some data, such as inflammation biomarker and imaging data were lacking on admission, which limits further confirmation of potential mechanisms of myocardial injury. Third, the data in this study permit a preliminary assessment of the clinical course and outcomes of patients with COVID-19. The causes of death may involve multiple organ dysfunction in most cases, and it is difficult to differentiate the myocardial injury as the main and direct cause in an individual case. Long-term observation and prospective study design on the effectiveness of treatments specific for the myocardial injury are needed.

## CONCLUSIONS

In conclusion, myocardial injury is common in patients hospitalized with COVID-19. Patients with myocardial injury had more severe presentation and complex comorbidities. Furthermore, myocardial injury is independently associated with increased in-hospital mortality in patients with COVID-19.

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ETHICS STATEMENT
This study obtained approval from the Research Ethics Committee of the Renmin Hospital of Wuhan University, Wuhan, China (approval number: WDRY2020-K038). Written consent was obtained from all participants.

AUTHOR CONTRIBUTIONS
Jian He, Bicheng Zhang, Quan Zhou, Wenjing Yang, Jing Xu, Tingting Liu, Haijun Zhang, Zhiyong Wu, Dong Li, Qing Zhou, Jie Yan, Cuizhen Zhang: Data curation; formal analysis. Bicheng Zhang, Quan Zhou, JZ: Data curation; resources; investigation; Jian He, Wenjing Yang, Jing Xu: Writing; methodology. Haiyan Qian, Minjie Lu, Xiaoyang Zhou: Methodology, project administration, conceptualization. Minjie Lu and Xiaoyang Zhou: Conceptualization; validation; supervision; funding acquisition. All authors have read and approved the manuscript.

DATA AVAILABILITY STATEMENT
The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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