# End-stage Heart Failure with COVID-19: Strong Evidence of Myocardial Injury by 2019-nCoV

Nianguo Dong, Jie Cai, Ying Zhou, Junwei Liu, Fei Li

PII: S2213-1779(20)30200-6

DOI: https://doi.org/10.1016/j.jchf.2020.04.001

Reference: JCHF 1250

To appear in: *JACC: Heart Failure*

Received Date: 31 March 2020

Accepted Date: 1 April 2020

Please cite this article as: Dong N, Cai J, Zhou Y, Liu J, Li F, End-stage Heart Failure with COVID-19: Strong Evidence of Myocardial Injury by 2019-nCoV, *JACC: Heart Failure* (2020), doi: https://doi.org/10.1016/j.jchf.2020.04.001.

# End-stage Heart Failure with COVID-19: Strong Evidence of Myocardial Injury by 2019-nCoV

[#]Nianguo Dong, [#]Jie Cai, Ying Zhou, Junwei Liu, Fei Li

Department of Cardiovascular Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

[#]These authors contributed equally to this work.

**Conflicts of interest:** The authors declare no conflicts of interest.

**Funding:** None

**Correspondence to:** Fei Li, Department of cardiovascular surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, China, Email: lifei_union@sina.com;

A novel coronavirus (2019-nCoV) was identified as the cause associated with emerging pneumonia (COVID-19) detected in Wuhan on Jan 7th. Since the number of patients rising rapidly worldwide, COVID-19 has become a throny international public health event. As of Mar 24th, China has cumulatively diagnosed 81747 cases and 147 new cases, while the number of cases in other countries is growing rapidly with a total of 291070 cases confirmed and 22027 new cases identified that day. Emerging studies suggest that COVID-19 preferentially afflicts the elderly, particularly those with chronic comorbidities[1, 2]. However, the clinical profiles of COVID-19 in refractory heart failure patients is unknown. Herein, we reported the clinical features in a group of end-stage heart failure patients with COVID-19, providing strong evidence of cardiac injury by the virus.

This study was approved by the institutional review board of Union Hospital, Tongj Medical College. All hospitalized patients in our department were screened for 2019-nCoV infection by nucleic acid test and chest CT scan. Demographic information, clinical, biochemical, and radiological characteristics and treatment and outcomes data were retrieved from electronic medical records. According to China CDC protocol, duplex RT-PCR or serum antibody test was performed to detect 2019-nCoV infection in throat swabs or blood samples. If respiratory samples were successfully tested positive by both open reading frame 1ab gene and nucleocapsid protein gene, the case was considered to be laboratory-confirmed. Presumed hospital-related transmission was suspected if hospitalized patients in the same wards became infected in a certain time period.

We retrospectively included four hospitalized severe heart failure patients infected with COVID-19 between Jan 7th and Mar 15th in our department. All patients were transferred to isolation ward since confirmed diagnosis or highly suspected. Three patients were suspected as hospital-related transmission because they were once in the same ward. None of the patients had fever during the illness, and they had just mild cough or fatigue at the time of diagnosis. Significantly enlarged left ventricle (Figure 1) and reduced left ventricular ejection fraction was observed in four patients, and all of them had New York Heart Function grade IV. Interestingly, patient 1 was

negative for two consecutive nucleic acid tests but positive for serum antibodies (IgM 69.12 AU/ml). Only two patients had typical ground-glass imaging changes in lung CT (Figure 1). With exacerbations, patient 3 and 4 were transferred to ICU and both died on ten days after the first positive nucleic acid test. Three patients had elevated troponin I (TNI) in the later period, especially in patient 3 and 4, TNI increased significantly a few days before death. Moreover, the levels of C-reactive protein (CRP) and brain natriuretic peptide of patient 3 and 4 were significantly higher than the rest two patients. It is also worth mentioning that patient 2 turned positive again after two consecutive negative test for nucleic acid. The detailed information and treatment on patients were shown in Table 1.

In this study, we reported for the first time four end-stage heart failure patients who were infected with COVID-19, two severe presentation and others mild. These patients showed some similar characteristics as described in previous reports[3]. For instance, all four patients were male, consistent with previous findings that higher percentages of infection in men than women. In addition, critically ill COVID-19 patients with heart failure also had typical lymphopenia and significantly increased CRP level.

Patients with end-stage heart failure seemed to have a high mortality rate after infection with the pneumonia. Older age, more comorbidities, poor general condition and severe myocardial injury may be risk factors. The most novel finding was that the TNI level of the two critically ill patients increased significantly by more than 20 folds, indicating myocardial injury. Although there have been previous reports of myocardial damage in COVID-19 patients[4,5], they mostly chose non-specific indicators such as CK-MB and LDH which could be confounded by many other factors in clinic. In addition, CK-MB and LDH were not significantly increased in those reports in fact. Our findings provided definitely stronger evidence of myocardial injury by COVID-19.

The exact mechanism of myocardial injury caused by 2019-nCoV is not completely clear, but through previous and our findings, it is clear that 2019-nCoV infection can cause myocardial injury and is closely related to disease progression.

The study was limited by small sample size, longitudinal studies on a larger cohort of heart failure patients would help to understand the prognosis of the disease.

**References:**


1. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Feb 7.
2. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020 Feb 24.
3. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Feb 28.
4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020 Feb 15;395(10223):507-513.
5. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020 Mar 13.

**Table 1. Characteristics of four hospitalized end-stage heart failure patients infected with COVID-19**

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| **Demographics** | | | | |
| Age | 11 | 38 | 57 | 67 |
| Gender | male | male | male | male |
| Diagnosis | myocarditis, 10 years after TOF operation | DCM, moderate MI | DCM, severe MI, severe AI | sever AS and AI, severe MI |
| LVEDD (cm) | 5.5 | 7.2 | 10.8 | 8.5 |
| LVEF | 22% | 26% | 22% | 30% |
| NYHA | IV | IV | IV | IV |
| Heart failure course | 1 month | 2 years | 5 years | 6 years |
| Comorbidities | tachycardia | ventricular arrhythmia | diabetes, COPD | hypertension,diabetes,ventricular premature beat |
| **Confirmation of COVID-19** | 12-Mar | 19-Feb | 10-Feb | 14-Feb |
| **Symptoms at onset** | poor apetite, fatigue | cough | chest tightness, cough | cough, sputum |
| **Labotary findings** | | | | |
| white blood cell count (normal range: 3.5-9.5 G/L) | 8.48 | 5.56 | 5.4 | 12.18 |
| lymphocyte count (normal range: 1.1-3.2 G/L) | 2.63 | 1.4 | 0.67 | 0.52 |
| lymphocyte% (normal range: 20-50%) | 31 | 25.2 | 12.4 | 4.3 |
| CRP (normal range: <8.0 mg/L) | <3.14 | <3.14 | 143 | 103 |
| first BNP (normal range: <100 pg/ml) | 250.4 | 2085.7 | 8222.1 | 4450 |
| latest BNP (normal range: <100 pg/ml) | 109.8 | 603 | 20700 | >5000 |
| first TNI (normal range: <26.2 ng/L) | 48.6 | 9.5 | 143.5 | 71.2 |
| latest TNI (normal range: <26.2 ng/L) | 3.8 | 71.3 | 3749.6 | 1518.2 |
| plasma albumin (normal range: 35-55 g/L) | 38 | 41.9 | 33.7 | 26.5 |
| D-diners (normal range: <0.5 mg/L FEU) | 0.22 | 0.23 | 0.47 | >20 |
| **2019nCoV nucleic acid test (throat swabs)** | twice negative | twice positive | twice positive | twice positive |
| **2019nCoV antibody (< 10 AU/ml)** | IgM 69.12 | no | no | no |
| **CT findings** | no abnormalities | mild infectious lesions in bilateral lung | patchy dense shadow and ground-glass changes in the lower lobe of bilateral lung | multiple ground-glass changes in bilateral pulmonary zone |
| **Anti-heart failure therapy** | | | | |
| beta-blocker | yes | yes | yes | yes |
| diuretics | yes | yes | yes | yes |
| sacubitril valsartan sodium tablets | no | yes | yes | yes |
| recombinant Human BNP | no | no | yes | yes |
| intravenous inotropes | yes | no | yes | yes |
| **Anti-COVID-19 treatment** | | | | |
| ribavirin | no | no | yes | no |
| antibiotic | no | yes | yes | yes |
| abidol | no | no | yes | no |
| Interferon α | yes | yes | yes | yes |
| glucocorticoids | no | no | no | no |
| intravenous immune globin | no | yes | no | no |
| oxygen supply | yes | yes | yes | yes |
| **Clinical course** | | | | |
| Intensive unit care | no | no | yes | yes |
| ARDS | no | no | yes | yes |
| mechnical ventilation | no | no | no | no |
| outcome | under thearpy | under therapy | death | death |

Abbreviations: LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; CRP, c-reactive protein; BNP, brain natriuretic peptide; TNI, troponin I; ARDS, acute respiratory distress syndrome.

**Figure 1. Chest radiography (CR) and computed tomography (CT) of four end-stage heart failure patients with COVID-19.**