Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Covid Rapid Reports

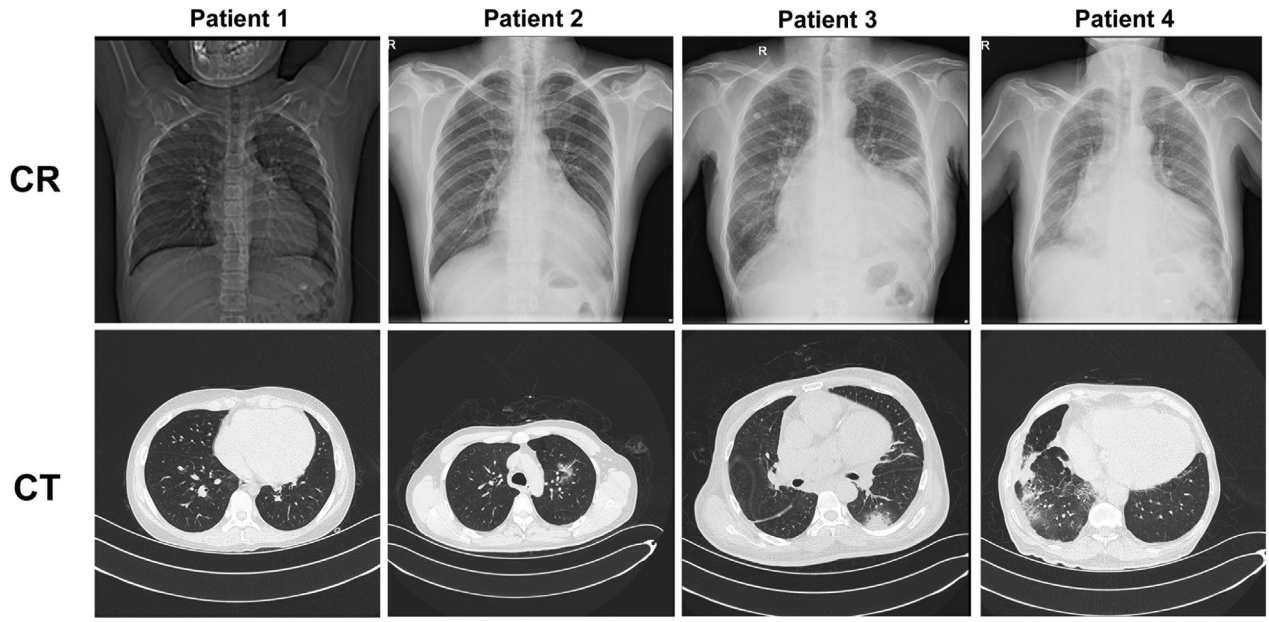
End-Stage Heart Failure With COVID-19

Strong Evidence of Myocardial Injury by 2019-nCoV

A novel coronavirus (2019-nCoV) was identified as the cause associated with emerging pneumonia (COVID-19) detected in Wuhan on January 7, 2020. Because the number of patients has risen rapidly worldwide, COVID-19 has become a thorny international public health event. As of Mar 24, 2020, China has cumulatively diagnosed 81,747 cases and 147 new cases, while the number of cases in other countries has grown rapidly to a total of 291,070 confirmed cases and 22,027 new cases identified every day, as of this writing. 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. This paper reports 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 the authors' department were screened for 2019-nCoV infection by nucleic acid test and chest computed tomography scans. Demographic information and clinical, biochemical, and radiological characteristics and treatment and outcome data were retrieved from electronic medical records. According to China Centers for Disease Control protocol, duplex reverse transcription-polymerase chain reaction or serum antibody test was performed to detect 2019-nCoV infection in throat swabs or blood samples. If respiratory samples tested positive by both open reading frame 1aboratory gene and nucleocapsid protein gene, the case was

FIGURE 1 Chest Radiography and Computed Tomography



Chest radiography and computed tomography of 4 end-stage heart failure patients with COVID-19.

TABLE 1 Characteristics of 4 Hospitalized End-Stage Heart Failure Patients Infected With COVID-19

	Patient #1	Patient #2	Patient #3	Patient #4
Demographics				
Age, yrs	11	38	57	67
Sex	Male	Male	Male	Male
DiagNosis	Myocarditis, 10 yrs after TOF operation	DCM, moderate MI	DCM, severe MI, severe AI	Severe AS and AI, severe MI
LVEDD (cm)	5.5	7.2	10.8	8.5
LVEF (%)	22	26	22	30
NYHA functional class	IV	IV	IV	IV
Heart failure course	1 month	2 yrs	5 yrs	6 yrs
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 appetite, fatigue	Cough	Chest tightness, cough	Cough, sputum
Laboratory findings				
White blood cell count (Normal range: 3.5-9.5 g/l)	8.48	5.56	5.40	12.18
Lymphocyte count (Normal range: 1.1-3.2 g/l)	2.63	1.40	0.67	0.52
Lymphocyte% (Normal range: 20%-50%)	31.0	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	2,085.7	82,22.1	4,450.0
Latest BNP (Normal range: 100 pg/ml)	109.8	603.0	20,700	>5,000
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	3,749.6	1,518.2
Plasma albumin (Normal range: 35-55 g/l)	38.0	41.9	33.7	26.5
D-dimers (Normal range: 0.5 mg/l FEU)	0.22	0.23	0.47	20.0
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 drugs				
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
Interfero-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
Mechanical ventilation	No	No	No	No
Outcome	Under therapy	Under therapy	Death	Death

ARDS = acute respiratory distress syndrome; BNP = brain natriuretic peptide; CRP = C-reactive protein; CT = computed tomography; FEU = fibrinogen equivalent units; IgM = immuNoglobulin M; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; TNI = troponin I.

considered laboratory-confirmed. Presumed hospital-related transmission was suspected if hospitalized patients in the same wards became infected in a certain time period.

Four hospitalized patients with severe heart failure were retrospectively included who had been infected with COVID-19 between January 7, 2020, and March 15, 2020, in the authors' department. All patients were

transferred to an isolation ward since the diagnosis was confirmed or highly suspected. Three patients were suspected of having received 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 were observed in 4 patients, and all had New York Heart Association functional class IV. Interestingly, Patient #1 was had negative results for 2 consecutive nucleic acid tests but positive result for serum antibodies (immunoglobulin M [IgM] 69.12 AU/ml). Only 2 patients had typical ground-glass imaging changes on lung computed tomography scans (**Figure 1**). With exacerbations, Patient #3 and #4 were transferred to intensive care units, and both died 10 days after the first positive nucleic acid test result. Three patients had elevated troponin I (TNI) in the later period, especially in Patients #3 and #4, TNI increased significantly a few days before death. Moreover, the levels of C-reactive protein (CRP) and brain natriuretic peptide in patients 3 and 4 were significantly higher than those in the remaining 2 patients. It is also worth mentioning that testing results for patient 2 turned positive again after 2 consecutive negative test results for nucleic acid. The detailed information and treatment of patients are shown in **Table 1**.

This study reported for the first time 4 end-stage heart failure patients who were infected with COVID-19, 2 with severe presentation and the others mild. These patients showed some similar characteristics as described in previous reports (3). For instance, all 4 patients were male, consistent with previous findings that higher percentages of infection were found in men than in women. In addition, critically ill COVID-19 patients with heart failure also had typical lymphopenia and significantly increased CRP levels.

Patients with end-stage heart failure seemed to have a high mortality rate after infection with pneumonia. Older age, more comorbidities, poor general condition, and severe myocardial injury may be risk factors. The most novel finding was that the TNI levels of the 2 critically ill patients were 20-fold increased, indicating myocardial injury. Although there have been previous reports of myocardial damage in COVID-19 patients (4,5), those reports chose mainly nonspecific indicators such as creatine kinase-MB (CK-MB) and lactate dehydrogenase (LDH), which could be confounded by many other factors in clinic. In addition, CK-MB and LDH were not, in fact, significantly increased in those reports. The present 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 present and previous 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 in a larger cohort of heart failure patients would help to understand the prognosis of the disease.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Heart Failure* author instructions page.

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