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RESEARCH LETTER

Cardiac Troponin I Is an Independent Predictor for Mortality in Hospitalized Patients With COVID-19

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Since December 2019, coronavirus disease 2019 (COVID-19) has caused a global pandemic with thousands of pneumonia-related deaths.[1] Recently, Wang et al[2] reported the existence of myocardial injury in 7.2% of all patients with COVID-19 and in 22.2% of patients admitted to the intensive care unit versus only 2.0% patients not treated in the intensive care unit. Thus, we hypothesized that cardiac troponin I (cTNI), an established biomarker of cardiac injury, may be a clinical predictor of outcomes for patients with COVID-19.

Patients with laboratory-confirmed COVID-19 admitted to Union Hospital (West Campus), Huazhong University of Science and Technology from January 12 to March 12, 2020, were enrolled, and the final date of follow-up was March 20, 2020. This study was approved by the ethics committee of Union Hospital, Huazhong University of Science and Technology ([2020]0087) and conducted in accordance with the guidelines of the Declaration of Helsinki. Written informed consent was waived by the ethics commission based on the retrospective nature of the study and the emerging worldwide crisis caused by this infectious disease.

A total of 311 laboratory-confirmed COVID-19 cases were included on the basis of available cTNI concentrations measured during hospitalization. The data of laboratory and imaging tests performed for the first time after admission were used for analysis. The ARCHITECTSTAT high-sensitivity troponin I assay (Abbott Laboratories) was used to measure cTnI concentrations.[3] Cardiac injury was diagnosed if the level of serum cTNI with at least 1 value was above the 99th percentile upper reference limit during hospitalization. We defined the severity of COVID-19 on admission by using the Chinese management guideline for COVID-19 (version 6.0).[4] The primary composite end point was all-cause death. The included patients were assigned to 1 of 2 groups according to clinical outcomes: the discharged group and the nonsurvivor group. To explore the risk factors associated with mortality, univariable and then multivariable logistic regression models (backward elimination) were applied. We chose age, sex, comorbidity, body temperature, blood oxygen saturation, disease severity, lymphocyte count, D-dimer, C-reactive protein, and cTNI as the 10 variables for our multivariable logistic regression model on the basis of our univariable analysis results and previous findings.[4] With the exception of age and blood oxygen saturation, the continuous variables of laboratory and imaging indicators were included with log2 transformation and report odds ratio (OR) per doubling of concentration (Table). A 2-tailed $P<0.05$ was considered to be statistically significant. All analyses were performed with SPSS version 13.0 (SPSS).

For 311 included patients, the median age was 63 years (interquartile range [IQR], 54–70 years), and 190 (61.1%) patients were male. Overall, 62.7% of patients had at least 1 comorbidity, including hypertension, cardiovascular disease (coronary heart disease/arrhythmia/heart failure), cerebrovascular disease, chronic obstructive pulmonary disease, diabetes mellitus, malignancy, chronic kidney disease, and

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Key Words: biomarkers ■ COVID-19 ■ heart injuries ■ hospital mortality ■ patient outcome assessment ■ troponin I

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Table. Risk Factors for Mortality in Patients With COVID-19 by Univariable and Multivariable Analysis

Risk Factors	Univariable Analysis		Multivariable Analysis	
	Wald	Unadjusted OR (95% CI)	Wald	Adjusted OR (95% CI)
Sex				
Female		1 (ref)		1 (ref)
Male	16.74	2.96 (1.76–4.97)	0	1.01 (0.33–3.10)
Age, y*	39.71	1.08 (1.06–1.11)	0.05	1.00 (0.96–1.03)
Current smoking				
No		1 (ref)		
Yes	7.15	3.66 (1.41–9.46)		
Comorbidity				
No		1 (ref)		1 (ref)
Yes	27.57	4.56 (2.59–8.04)	11.38	9.07 (2.52–32.66)
Hypertension				
No		1 (ref)		
Yes	27.65	3.80 (2.31–6.25)		
Coronary heart disease				
No		1 (ref)		
Yes	0.38	1.26 (0.60–2.67)		
Arrhythmia				
No		1 (ref)		
Yes	3.32	4.67 (0.89–24.47)		
Heart failure				
No		1 (ref)		
Yes	0.04	1.21 (0.20–7.32)		
Cerebrovascular disease				
No		1 (ref)		
Yes	3.75	2.85 (0.99–8.24)		
Diabetes mellitus				
No		1 (ref)		
Yes	5.79	2.13 (1.15–3.95)		
Body temperature, °C				
≤37.3		1 (ref)		1 (ref)
>37.3	12.62	2.65 (1.55–4.52)	0.25	1.31 (0.45–3.81)
Blood oxygen saturation, %*	57.83	0.76 (0.71–0.82)	10.67	0.85 (0.77–0.94)
Disease severity				
Moderate		1 (ref)		1 (ref)
Severe /critical	37.68	11.19 (5.18–24.20)	0.43	1.55 (0.42–5.70)
White blood cell count, $\times 10^9$/L	33.55	3.24 (2.18–4.82)		
Neutrophil count, $\times 10^9$/L	51.33	3.69 (2.58–5.28)		
Lymphocyte count, $\times 10^9$/L	67.50	0.21 (0.15–0.31)	4.55	0.52 (0.29–0.95)
Platelet count, $\times 10^9$/L	29.87	0.34 (0.23–0.50)		
D-Dimer, μg/mL	74.44	2.25 (1.87–2.70)	7.23	1.55 (1.13–2.13)
Prothrombin time, s	24.61	40.52 (9.39–174.92)		
Fibrinogen, g/L	5.17	0.67 (0.48–0.95)		
Total bilirubin, μmol/L	20.78	2.13 (1.54–2.96)		
Alanine aminotransferase, U/L	17.20	1.70 (1.32–2.18)		
Aspartate aminotransferase, U/L	24.95	2.29 (1.65–3.17)		
Albumin, g/L	42.86	0.03 (0.01–0.08)		
Creatinine, μmol/L	14.18	2.16 (1.44–3.22)		
C-reactive protein, mg/L	56.82	2.49 (1.97–3.16)	11.90	1.98 (1.34–2.92)
Cardiac troponin I, ng/L	69.80	2.50 (2.02–3.10)	17.66	1.92 (1.41–2.59)
Creatine kinase-MB, ng/mL	45.15	4.02 (2.68–6.03)		
Creatine kinase, U/L	27.63	1.64 (1.36–1.96)		
Lactate dehydrogenase, U/L	82.74	19.24 (10.18–36.39)		
Numbers of pulmonary lobes involved	6.95	1.90 (1.18–3.07)		

COVID-19 indicates coronavirus disease 2019; OR, odds ratio; and Ref, reference.
*Per 1 U increase.

thyroid disease. The most common symptoms on admission were fever (77.5%), cough (32.5%), and dyspnea (24.4%). With regard to disease severity on admission, there were 101 patients (32.5%) with moderate-type, 180 (57.9%) with severe-type, and 30 (9.6%) with critical-type COVID-19. One hundred eleven patients died during hospitalization and 200 were discharged. The median time from illness onset to death was 23 days (IQR, 15–32 days). In laboratory findings, the lymphocyte count (0.5×10^9/L [IQR, $0.4–0.8\times10^9$/L] versus 1.2×10^9/L [IQR, $0.9–1.7\times10^9$/L]) was lower in the nonsurvivor group than in the discharged group. The concentrations of D-dimer (4.0 μg/mL [IQR, 1.2–8.0 μg/mL] versus 0.5 μg/mL [IQR, 0.2–1.5μg/mL]), C-reactive protein (80.2 mg/L [IQR, 48.4–121.8 mg/L] versus 8.1 mg/L [IQR, 2.4–43.6 mg/L]), and cTNI (32.5 ng/L [IQR, 11.4–304.4 ng/L] versus 2.8 ng/L [IQR, 1.5–5.8 ng/L]) in the nonsurvivor group were elevated in comparison with those in the discharged group. There were 103 patients (33.1%) with cardiac injury, including 12 patients in the discharged group and 91 patients in the nonsurvivor group. Multivariable logistic regression analysis identified cTNI concentration (OR, 1.92 [95% CI, 1.41–2.59]), lymphocyte count (OR, 0.52

[95% CI, 0.29–0.95]), C-reactive protein concentration (OR, 1.98 [95% CI, 1.34–2.92]), D-dimer concentration (OR, 1.55 [95% CI, 1.13–2.13]), comorbidity (OR, 9.07 [95% CI, 2.52–32.66]), and blood oxygen saturation (OR, 0.85 [95% CI, 0.77–0.94]) as independent risk factors for death in patients with COVID-19 (Table).

Although respiratory symptoms are the primary clinical manifestations of COVID-19, a portion of patients will experience severe cardiovascular injury.[2,5] cTnI is the most important biomarker of cardiac injury. Our results indicate that the serum cTnI concentration was significantly higher in nonsurviving patients with severe acute respiratory syndrome coronavirus 2 infection than in discharged patients, and the further multivariable logistic regression identified increased cTnI concentration as an independent predictor of mortality in patients with COVID-19.

This study is limited by selection bias based on cTnI measurement. The determination of whether cTnI would be measured in each case was an individual decision by the clinician. The results do not totally represent the epidemiological data of COVID-19.

ARTICLE INFORMATION

The data that support the findings of this study are available from the corresponding author upon reasonable request by email.

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Disclosures

None.

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