

High-Sensitivity Troponin I is an Indicator of Poor Prognosis in Patients with Severe COVID-19 Related Pneumonia

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Objective: Critical covid-19 patients have complications with acute myocardial injury is still unclear. We observed a series of critically ill patients, paying particular attention to the impact of myocardial injury at admission on short-term outcome.

Methods: We prospectively collected and analyzed data from a series of severe covid-19 patients confirmed by real-time RT-PCR. Data were obtained from electronic medical records including clinical charts, nursing records, laboratory findings, and chest x-rays were from Feb 8, 2020, to April 7, 2020. The Acute Physiology and Chronic Health Evaluation (APACHE II) score, CURB-65 Pneumonia Severity Score, Sequential Organ Failure Assessment (SOFA) Score and pneumonia severity index (PSI) score were made within 24 hours of admission. Cardiac injury was diagnosed as hs-cTnI were above >28 pg/mL. The short-term outcome was defined as mortality in hospital.

Results: A total of 100 patients met the diagnostic criteria of severe patients with COVID-19 during 2020.02.08–2020.04.07. The CURB 65, APACH2, SOFA, and PSI score were significantly higher in Critical group than in Severe group. Univariate regression analysis showed that oxygen flow, PO₂/FiO₂, SOFA and hs-cTnI were closely related to short-term outcome. The corresponding ROC of hs-cTnI, oxygen flow and SOFA for patient death prediction were 0.949, 0.906 and 0.652. hs-cTnI at 47.8 ng/liter predicted death, sensitivity 92.8%, specificity 92.9%; Oxygen flow at 5.5 liter/minute predicted death sensitivity 100%, specificity 77.9%; SOFA score at 5 predicted death sensitivity 100%, specificity 73.8%.

Conclusion: Our cohort study demonstrated that inhaled oxygen flow, SOFA score, and myocardial injury at admission in critically ill COVID-19 patients were important indicators for predicting short-term death of patients, the hs-cTnI can be as a risk stratification, which may provide a simple method for the physicians to identify high-risk patients and give reasonable treatment in time.

Keywords: COVID-19, high-sensitivity cardiac troponin I, short-term outcome

Introduction

Coronavirus disease 2019 (Covid-19) is a global epidemic disease, most patients can be cured,^{1,2} but severe patients, especially elderly patients still have a higher mortality rate.^{1,3} Covid-19 is a systemic disease that damages various systems throughout the body. There are many basic diseases in elderly patients. After the merger of the new crown, the two superimposed the two, resulting in aggravation of the disease and increased mortality. Coronavirus 2 (SARS-CoV-2) infects host cells through ACE2 receptors, leading to coronavirus disease (COVID-19)-related pneumonia, while also causing acute myocardial injury and chronic damage to the cardiovascular system.⁴ Myocardial injury associated with the SARS-CoV-2 occurred in 5 of the first 41 patients diagnosed with COVID-19 in Wuhan, which mainly manifested as an increase in high-sensitivity cardiac troponin I (hs-cTnI) levels (>28 pg/mL).⁵ In another report of 138 patients with COVID-19 in Wuhan, 36 patients with severe symptoms were treated in the ICU.² The levels of biomarkers of myocardial injury were significantly higher in patients treated in the ICU than in

those not treated in the ICU (median creatine kinase (CK)-MB level 18 U/l versus 14 U/l, $P < 0.001$; hs-cTnI level 11.0 pg/mL versus 5.1 pg/mL, $P = 0.004$), suggesting that patients with severe symptoms often have complications involving acute myocardial injury.⁵ Cardiac injury occurred in 19.7% of patients during hospitalization,⁶ and it was one independent risk factor for in-hospital mortality. Troponin elevation in COVID-19 patients was an important stratification biomarker.⁷ However, it is still unclear how myocardial injury at admission affects in-hospital mortality. This study observed the outcome of a group of critically ill patients, paying particular attention to the impact of myocardial injury on patient prognosis at admission. Focus on the changes of clinical indicators, identify high-risk patients in time, and give active treatment to effectively control the condition and win opportunities for patients to recover. Analyze the clinical data of these patients and screen early warning indicators.

Methods

This study complied with the Declaration of Helsinki. All patients were confirmed 2019-nCoV infection by real-time RT-PCR and were admitted to a designated hospital (West Campus of Union Hospital, Huazhong University of Science and Technology) in Wuhan. We prospectively collected and analyzed data. Data were obtained from electronic medical records including clinical charts, nursing records, laboratory findings, and chest x-rays were from Feb 8, 2020, to April 7, 2020.

Researchers directly communicated with patients or their families to ascertain epidemiological and symptom data. According to the patient's admission situation, the patients were divided into Severe group and critical group. The Severe group diagnostic standard meets one of the following conditions, $RR \geq 30$ 次/min or $SPO_2 < 90\%$ or $P/F < 300$ mmHg. The diagnostic criteria for critical group are to meet one of the following conditions, respiratory failure requires respiratory support or circulatory failure or other organ damage according to the COVID-19 pneumonia diagnosis and treatment plan, trial version 7 (Published by China National Health Commission). The Acute Physiology and Chronic Health Evaluation (APACHE II)⁸ score, CURB-65 Pneumonia Severity Score, Sequential Organ Failure Assessment (SOFA) Score and pneumonia severity index (PSI) score were made within 24 hours of admission. Cardiac injury was diagnosed if serum levels of cardiac biomarkers, hs-cTnI were above >28 pg/mL, or new abnormalities were shown in electrocardiography and echocardiography.⁵ All patients were screened for clinical chest pain symptoms and electrocardiogram changes to rule out acute myocardial infarction. Acute kidney injury was identified and classified on the basis of the highest serum creatinine level or urine output criteria according to the kidney disease improving global outcomes classification.⁹ The length of hospital stays, survival to discharge and death and were compared between two groups. The short-term outcomes were defined as mortality in hospital.

This study was approved by the National Health Commission of China and Ethics Commission of Union Hospital in Wuhan (2020-0177). Written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

Statistical Analysis

Continuous variables were expressed as median (IQR, Median, 25th-75th) and compared with the Mann-Whitney U -test; Categorical variables were summarized as counts and percentages and compared by χ^2 test or Fisher's exact test between Severe and Critical groups. Univariate regression was used to analyze the correlation between each variable and the patient's discharge survival. Logistic stepwise regression was used to screen the above independent variables to establish a logistic regression model. The sensitivity, specificity, and area under ROC were used to evaluate the performance of the selected variables. A two-sided α of less than 0.05 was considered statistically significant. Statistical analyses were done using the SPSS software, version 13.0, unless otherwise indicated.

Results

General Information

A total of 128 patients were collected during this observation period, of which 100 patients met the diagnostic criteria of severe patients with COVID-19 during 2020.02.08–2020.04.07 according to COVID-19 pneumonia diagnosis and treatment plan, trial version 7 (Published by China National Health Commission), severe patients required oxygen inhalation to maintain $SPO_2 > 93\%$. The average age of 100 patients was 65 years (IQR, 26–97). There were 51 males (51%) and 49 females (49%). The combined underlying diseases were 31 (31%) diabetes, 46 (46%) hypertension, 10

(10%) coronary heart disease, 14 (14%) stroke, and 10 (10%) chronic obstructive pulmonary disease. The main clinical manifestations were fever in 76 (76%), dry cough in 48 (48%), shortness of breath in 46 (46%), diarrhea in 4 (4%) and fatigue (9%).

Epidemiological History

All patients live in Wuhan, 69 of them have a clear history of contact with infected persons, 15 (15%) have family-associated infection, 4 have been diagnosed with new coronary disease due to other diseases, and 12 have no Clear contact history. All patients were diagnosed with a positive throat swab nucleic acid test.

Chest High-Resolution CT Examination

8 people (8%) with small patch shadows or infiltration shadows; 13 (13%) with multiple small patch shadows and lung interstitial changes; 81 people with multiple ground glass shadows and infiltration shadows on both lungs (81%); 24 patients with lung consolidation (24%); 6 patients with pleural effusion (6%).

Treatment

Antiviral treatment, Abidor 0.2 Tid, until the nucleic acid test is negative; patients with anorexia and poor nutritional status are given nutritional support treatment, mainly enteral nutrition; treatment for basic diseases, such as controlling hypertension and controlling blood sugar, Anti-myocardial ischemia treatment, etc.

Respiratory Support Treatment Strategy

According to the patient's admission SPO₂, blood gas analysis results, giving suck oxygen or non-invasive ventilation or tracheal intubation with lung protective ventilation strategy, the detail decision process is shown in [Figure 1](#).

Clinical Outcomes

There were 76 patients in Severe group, 24 patients in Critical group, the male/female ratios of the two groups is 39/12 and 35/14, $\chi^2 = 0.330$, $p = 0.566$. The incidence of Critical group with diabetes was 13/26, which was significantly higher than that of Severe group, 18/74, $\chi^2 = 5.930$, $p = 0.015$. There was no difference between the two groups with hypertension, chronic obstructive pulmonary disease (COPD), Stroke, Coronary heart disease (CHD) and tumors diseases as shown in [Table 1](#). There was a higher incidence of shortness breath in Critical group than in Severe group ([Table 1](#)).

The age of patients was 65 years (IQR, 55–71) in Severe group, 63 years (IQR, 56–69.5) in Critical group, $p=0.865$. The diagnosis time by PCR were 6 days (IQR, 4–9) in Severe group and 6 days (IQR, 5–7), $p=0.813$.

The temperature, blood pressure and Pulse rate were no differences between two groups. The respiratory rates were 22 times (IQR, 20–27) in Severe group lower than 31 times (IQR, 24–38) in Critical group, $p<0.001$. The Pulse oxygen

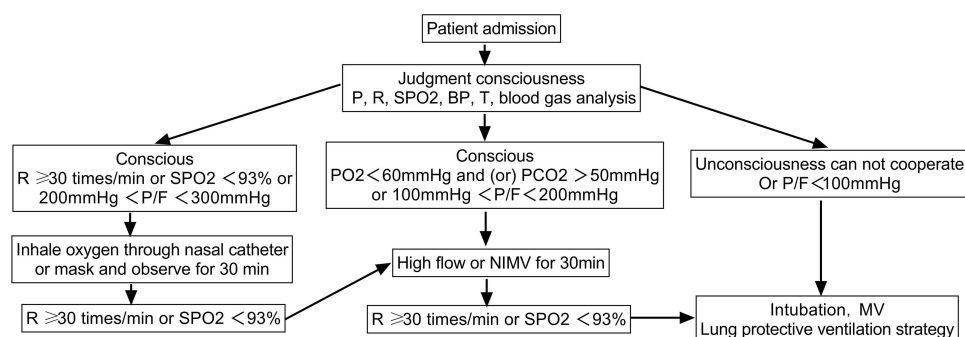


Figure 1 Oxygen therapy decision flow chart.

Abbreviations: P, pulse; R, respire; Spo₂, pulse oxygen saturation; T, temperature; BP, blood pressure; P/F, partial pressure of oxygen/fraction of inspired oxygen; MV, mechanical ventilation.

Table 1 Severe Group and Critical Group Complicated with Basic Diseases

	T2DM	HBP	COPD	Stroke	CHB	Tumor
Severe	18/74	30/74	7/74	12/74	7/74	4/74
Critical	13/26	16/26	3/26	2/26	3/26	2/26
χ^2	5.930	3.415	0.092	1.161	0.092	0.178
p	0.015	0.065	0.712	0.281	0.761	0.673
	Fever	Dry Cough	Diarrhea	Short of Breath	Fatigue	
Severe	51/74	35/74	3/74	26/74	7/74	
Critical	22/26	13/26	1/26	17/26	2/26	
χ^2	2.155	0.056	0.02	7.183	0.073	
p	0.142	0.812	0.963	0.007	0.787	

Abbreviations: T2DM, type 2 diabetes mellitus; HBP, high blood pressure; COPD, chronic obstructive pulmonary disease; CHD, coronary heart disease.

saturation (SPO₂, %) and PO₂/FiO₂ were significantly lower in Critical group than in Severe group (Table 2). The patients in Critical group need higher Oxygen flow to maintain the SPO₂ over 93%.

The incidence of Lymphopenia was 16/74 (21.6%) in Severe group and 18/26 (69.2%) in Critical group, $p < 0.001$. The incidence of cardiac injury was also very higher in Critical group 14/26 (52.9%) than 7/76 (9.9%) in Severe group, $p < 0.001$. The main laboratory test results of the two groups of patients on admission are shown in Table 2. There were a lot of biochemical markers significantly different between two groups, such as BUN, LDH, CPR, Total protein, albumin, pre-albumin, HCT, Lymphocyte, PLT, hs-cTnI, Myoglobin, BNP, D-Dimer and IL-6, Table 2.

At the time of admission, the patients' scores of CURB 65, APACH2, SOFA, and PSI, all showed that the Critical group was significantly higher than the Severe group, Table 2.

Table 2 The Vital Signs and Main Laboratory Test Results of the Two Groups of Patients on Admission

Group	Severe	Critical	P value
	Median (25th, 75th)	Median (25th, 75th)	
RR-times/minute	22 (20, 27)	31 (24, 38)	<0.001
SPO ₂ -%	91 (89, 98)	85 (75, 88)	<0.001
P/F-mmHg	294 (249, 420)	87 (52, 194)	<0.001
Oxygen flow-liter/minute	3 (2, 5)	10 (6, 10)	<0.001
Temperature-°C	37.1 (36.5, 38.5)	37.4 (36.6, 38.5)	0.838
Pulse rate-times/minute	90 (80, 104)	98 (87, 108)	0.605
SBP-mmHg	135.5 (126, 150)	132 (120, 150)	0.703
DBP-mmHg	75 (68, 80)	77 (67, 85)	0.780
Na-mmol/liter	139 (137, 141)	138 (136, 141)	0.663
K -mmol/liter	4.1 (3.8, 4.5)	4.2 (3.9, 4.5)	0.135
TBIL -mmol/liter	10.7 (7.6, 14.6)	13.0 (8.8, 18.9)	0.110
Cr-umol/liter	71.3 (59.5, 88.2)	74.2 (57.3, 149.1)	0.459
BUN-mmol/liter	5.5 (4.3, 7.9)	7.7 (5.3, 22.8)	0.021
LDH-unit/liter	209 (167, 300)	383 (292, 552)	<0.001
CRP-mg/liter	8.1 (3.3, 41.2)	102.7 (34.7, 133.4)	<0.001
TCO ₂ -mmol/liter	27 (24, 29)	26 (22, 29)	0.185
Glucose-mmol/liter	5.9 (5.2, 7.0)	6.9 (6.0, 9.3)	0.146
TP- gram/liter	65.2 (61.5, 68.6)	59.3 (56.8, 62.1)	0.006
ALB-gram/liter	33.9 (29.2, 39.8)	30.7 (28.0, 33.1)	0.004
pre-ALB-mg/liter	221.7 (137.8, 282.1)	123.5 (60.6, 209.2)	0.001

(Continued)

Table 2 (Continued).

Group	Severe	Critical	P value
	Median (25th, 75th)	Median (25th, 75th)	
HCT-%	36.1 (33.0, 39.1)	31.3 (27.4, 36.8)	0.021
WBC-10 ⁹ /liter	6.6 (4.9, 9.4)	7.5 (5.7, 9.8)	0.781
Neutrophil-10 ⁹ /liter	4.5 (3.1, 6.7)	7.0 (4.8, 10.1)	0.116
Lym-10 ⁹ /liter	1.32 (0.89, 1.70)	0.66 (0.48, 0.81)	<0.001
PLT-10 ⁹ /liter	251 (188, 334)	162 (98, 206)	<0.001
hs-cTnI-ng/liter	3.9 (1.7, 9.2)	51.6 (7.5, 215.3)	<0.001
Myoglobin -ng/mL	38.5 (29.9, 80.0)	101.1 (36.9, 491.0)	0.001
CK-MB-unit/liter	0.9 (0.6, 1.3)	2.1 (1.1, 6.8)	0.145
BNP-pg/mL	26.0 (15.0, 66.3)	142.0 (40.2, 448.1)	0.001
HBAC1-%	5.6 (5.2, 6.2)	6.5 (5.8, 7.6)	0.159
D-Dimer -mg/liter	0.7 (0.4, 2.0)	3.3 (1.1, 6.7)	<0.001
Fib-gram/liter	4.1 (3.5, 5.1)	4.5 (3.6, 6.3)	0.201
IL-6-pg/mL	4.8 (3.0, 11.8)	45.0 (8.2, 235.6)	<0.001
PCT-ng/mL	0.06 (0.04, 0.11)	0.25 (0.11, 0.64)	0.172
CURB 65	1 (0, 2)	2 (1, 3)	<0.001
APACH2	10 (7.5, 14)	17 (12, 23)	<0.001
SOFA	2 (1, 3)	7 (5, 11)	<0.001
PSI	40 (20, 62.5)	85 (50, 100)	<0.001

Abbreviations: RR, respiration rate; Spo2, pulse oxygen saturation; P/F, partial pressure of oxygen/fraction of inspired oxygen; SBP, systolic blood pressure; DBP, diastolic blood pressure; Na, sodium concentration; K, potassium concentration; TBIL, total bilirubin; Cr, creatinine; Bun, blood urea nitrogen; LDH, lactate dehydrogenase; CPR, C reaction protein; TCO2, total carbon dioxide; Glu, glucose; TP, total protein; ALB, albumin; pre-ALB, pre albumin; Hct, hematocrit; WBC, white blood cell; Lym, lymphocyte; PLT, platelet; hs-TnI, high sensitivity troponin I; CK-MB, creatine kinase MB; BNP, brain natriuretic peptide; HBAC1, hemoglobin A1c; Fib, fibrinogen; IL-6, interleukin-6; PCT, procalcitonin; CURB65, confusion status, level of urea, rate of respiration, blood pressure level, and age; APACH2, Acute Physiology and Chronic Health Evaluation 2; SOFA, Sequential Organ Failure Assessment; PSI, pneumonia severity index.

All patients in the Severe group were cured and discharged, 26 patients in the Critical group used non-invasive mask ventilation, and 12 of them underwent tracheal intubation and mechanical ventilation. 14 people in the Critical group died, and the remaining patients were discharged. The length of hospital stay was 38 days (IQR, 23–46) in Severe group, 18.5 days (IQR, 3.75–54) in Critical group, $p=0.078$. Differences between clinical and laboratory tests in the Critical group, the survivor and non-survivor are shown in Table 3.

Table 3 Differences Between Clinical and Laboratory Tests Between Survivor and Non-Survivor in the Critical Group at Admission

	Survivor (12)	Non-Survivor (14)	P value
	Median (25th, 75th)	Median (25th, 75th)	
Age (year)	62 (55, 71)	64 (60, 71)	0.7888
Hospital stay (day)	55 (39, 62)	4 (1.66, 14.5)	<0.001
Diagnose time (day)	6 (5, 7)	6.5 (5, 7)	0.860
RR-times/minute	30 (24, 38)	31 (24, 38)	0.940
SPO2-%	86 (81, 90)	82 (65, 85)	0.067
P/F-mmHg	195 (137, 270)	52 (48, 73)	<0.001
Oxygen flow-liter/minute	8 (4.25, 10)	10 (8, 10)	0.129
Temperature-°C	38.0 (36.9, 38.7)	37.1 (36.4, 38.1)	0.218
Pulse-times/minute	98 (87, 108)	94 (86, 109)	0.643
SBP-mmHg	126 (120, 147)	142 (111, 173)	0.580

(Continued)

Table 3 (Continued).

	Survivor (12)	Non-Survivor (14)	P value
	Median (25th, 75th)	Median (25th, 75th)	
DBP-mmHg	76 (69, 84)	79 (65, 89)	0.936
Na-mmol/liter	139 (137, 141)	136 (135, 142)	0.199
K -mmol/liter	4.1 (3.8, 4.4)	4.4 (3.9, 6.9)	0.040
TBIL -mmol/liter	13 (9.4, 18.3)	13 (6.5, 21.6)	0.988
Cr-umol/liter	67.8 (56.4, 74.7)	142.5 (61.1, 1686)	0.053
BUN-mmol/liter	6.5 (5.8, 8.7)	22.3 (3.8, 46.4)	0.123
LDH-unit/liter	301 (246, 469)	470 (320, 568)	0.283
CRP-mg/liter	70.6 (32.3, 129.8)	133.3 (54.7, 134.2)	0.153
TCO2-mmol/liter	27.3 (24, 29.2)	23.2 (12.5, 28.6)	0.140
Glucose-mmol/liter	6.3 (5.53, 8.7)	7.35 (6.18, 9.49)	0.679
TP- gram/liter	61.4 (58.8, 62.6)	57.5 (55.4, 59.8)	0.062
ALB-gram/liter	31.7 (29.2, 33.5)	29.7 (24.8, 33)	0.199
pre-ALB-mg/liter	126 (81.4, 271.2)	119.5 (58, 197)	0.406
HCT-%	36 (31, 40.4)	28.6 (27.1, 31.5)	0.071
WBC-109/liter	7.4 (6.0, 10.6)	7.7 (4.3, 9.1)	0.826
N-109/liter	5.8 (4.8, 9.8)	7.0 (5.3, 11.9)	0.309
Lym-109/liter	0.80 (0.64, 0.99)	0.53 (0.24, 0.69)	0.123
PLT-109/liter	193 (108, 264)	147 (76, 203)	0.203
hs-cTnI -ng/liter	12 (6, 53)	200 (51, 972)	0.004
Myo-ng/mL	87 (36, 120)	290 (155, 1029)	0.1
CK-MB-unit/liter	1.7 (0.9, 3.3)	4.6 (1.5, 10.3)	0.135
BNP-pg/mL	58.5 (36.8, 277.4)	720.1 (119, 2232.2)	0.1
HBAC1-%	6.4 (5.7, 7.9)	6.8 (6.8, 6.8)	0.923
D-Dimer -mg/liter	5.24 (1.84, 8.00)	2.02 (0.73, 4.49)	0.118
Fib-gram/liter	4.95 (1.98, 6.25)	4.32 (3.70, 6.33)	0.836
IL-6-pg/mL	27.4 (7.5, 200.7)	1851.8 (56.6, 1200)	0.114
PCT- ng/mL	0.24(0.07, 0.67)	0.37 (0.17, 0.94)	0.489
CURB 65	2 (1, 2.75)	2 (1, 3.3)	0.608
APACH2	13 (12, 21.5)	18 (14.5, 26)	0.093
SOFA	7 (3, 10.75)	7.5 (5.75, 12)	0.186
PSI	80 (50, 97.5)	85 (40, 100)	0.795

Abbreviations: RR, respiration rate; Spo2, pulse oxygen saturation; P/F, partial pressure of oxygen/fraction of inspired oxygen; SBP, systolic blood pressure; DBP, diastolic blood pressure; Na, sodium concentration; K, potassium concentration; TBIL, total bilirubin; Cr, creatinine; Bun, blood urea nitrogen; LDH, lactate dehydrogenase; CPR, C reaction protein; TCO2, total carbon dioxide; Glu, glucose; TP, total protein; ALB, albumin; pre-ALB, pre albumin; Hct, hematocrit; WBC, white blood cell; Lym, lymphocyte; PLT, platelet; hs-TnI, high sensitivity troponin I; CK-MB, creatine kinase MB; BNP, brain natriuretic peptide; HBAC1, hemoglobin A1c; Fib, fibrinogen; IL-6, interleukin-6; PCT, procalcitonin.

Screening of Prognostic Indicators

Univariate regression analysis showed that oxygen flow when patients were admitted to hospital, PO2/FiO2, SOFA and hs-cTnI were closely related to short-term outcome, [Table 4](#). PO2/FiO2 predicted the survival of patients discharge, Sensitivity 90.7% and Specificity 100% at Cutoff value of 153 mmHg. Logistic Stepwise regression showed that oxygen flow at admission, hs-cTnI and SOFA scores at admission can predict the patient's death from discharge. The corresponding ROC of hs-cTnI, oxygen flow and SOFA for patient death prediction is 0.949, 0.906 and 0.652. hs-cTnI at 47.8 ng/liter predicted death, sensitivity 92.8%, specificity 92.9%; Oxygen flow at 5.5 liter/minute predicted death sensitivity 100%, specificity 77.9%; SOFA score at 5 predicted death sensitivity 100%, specificity 73.8%.

Table 4 Oxygen Flow When Patients Were Admitted to Hospital, PO₂/FiO₂, SOFA and hs-cTnI Were Closely Related to Short-Term Outcome

Coefficients ^a								
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	1.185	0.058		20.299	0.000	1.069	1.301
	Oxygen	-0.067	0.010	-0.573	-6.699	0.000	-0.087	-0.047
2	(Constant)	1.165	0.057		20.451	0.000	1.052	1.278
	Oxygen	-0.060	0.010	-0.516	-6.040	0.000	-0.080	-0.041
	hs-cTnI	0.000	0.000	-0.229	-2.685	0.009	0.000	0.000
3	(Constant)	1.159	0.056		20.741	0.000	1.048	1.270
	Oxygen	-0.041	0.013	-0.347	-3.051	0.003	-0.067	-0.014
	hs-cTnI	0.000	0.000	-0.244	-2.909	0.005	0.000	0.000
	SOFA	-0.023	0.010	-0.243	-2.190	0.031	-0.044	-0.002

Note: ^aDependent Variable: Survival.

Discussion

The cases included in this study met the diagnostic criteria for critically ill patients according to COVID-19 pneumonia diagnosis and treatment plan, trial version 7 (Published by China National Health Commission), and 26 of them met the diagnostic criteria for critical illness. The critically ill patients suffered from respiratory failure when they were admitted to the hospital and needed assisted ventilation. 14 people used non-invasive ventilation, and 12 people were promptly given intubation after non-invasive ventilation failure, and mechanical ventilation was performed according to the lung protective strategy. 14 patients in the Critical group died. Existing evidences show that the elderly patients with some chronic diseases have a poor prognosis, and these patients are most likely to develop into critically ill pneumonia.¹⁰ The present study, 67% of patients in this series are older than 60 years old, 46/74 (62.2%) in Severe group, 19/26 (73%) in Critical group, $p=0.444$. The incidence of diabetes in critical group (13/26, 50%) is significantly higher than that in Severe group (18/74, 24.3%). According to a recent report,¹¹ diabetes should be considered as a risk factor for a rapid progression and bad prognosis of COVID-19.

Shortness of breath in clinical manifestations is an important indicator of the critical condition of the patient.¹² In the present study, the incidence of shortness of breath in Severe group was significantly lower than that of in Critical group. Non-survivor 11 of 14 patients had shortness of breath, and 32 of 86 survivor had shortness of breath, $p=0.004$. In this study, we found that inhaled oxygen flow also indicates poor prognosis, 3 liter/min (IQR, 2–5) in Severe group, 10 liter/min (IQR, 6–10) in Critical group, $p<0.001$. Multivariate regression analysis shows that oxygen flow is highly correlated with patient prognosis, ROC 0.906, Oxygen flow at 5.5 liter/minute predicted death sensitivity 100%, specificity 77.9%. The ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (P/F) predicted the survival of patients discharge, Sensitivity 90.7% and Specificity 100% at Cutoff value of 153 mmHg.

In this study, results were found similar to other studies,^{1,2,5} critical patients have a higher proportion of Lymphopenia, D-dimer, LDH and CPR increased, total protein, albumin, and pre-albumin decreased. However, univariate regression analysis showed that these variables have no significant correlation with the prognosis of patients. COVID-19 is a systemic disease that has caused lung injury as the main manifestation of systemic diseases and the incidence of multiple organ injury is relatively high in critical patients.^{13–15} This series of patients has a higher frequency of organ injury, kidney injury 8/72 (11%) in Severe group, 7/22 (31.8%) in Critical; liver injury 9/72 (12.5%) in Severe group, 7/22 (31.8%) in Critical group; myocardial injury 7/71 (9.9%) in Severe group, 9/17 (52.9%) in Critical, $p<0.001$. Stepwise regression analysis showed that myocardial injury marker hs-cTnI was closely related to the prognosis of patients, hs-cTnI at 47.8 ng/liter predicted death, ROC 0.949, sensitivity 92.8%, specificity 92.9%. In addition to the comparison of single indicators in this study, we also used the commonly used scoring system to evaluate the patients,

such as APACH2, CURB 65, SOFA and PSI scores. These scoring methods can reflect the severity of the covid-19 disease, the scores in critical group were significantly higher than in severe group. Stepwise regression analysis showed that only the SOFA score could predict the death of patients on discharge, ROC was 0.652, SOFA score at 5 predicted death sensitivity 100%, specificity 73.8%. Compared with other indicators, hs-cTnI has a higher ROC, sensitivity and specificity for the prediction of short-term death of patients, hs-cTnI can be used as an important reference index for patients with poor prognosis. We also tested other myocardial biomarkers, such as Myoglobin, CK-MB and BNP, multivariate logistic regression analysis showed that these variables cannot predict the death of patients, the hs-cTnI had superiority to Myoglobin, CK-MB, BNP for prognosis of covid-19 patient due to its myocardial specificity. This also implies that we should pay more attention to myocardial damage during the treatment of covid-19 pneumonia, it may be an independent predictor for adverse outcomes.¹⁶ The impact of covid-19 on the cardiovascular system, especially myocardial injury and hemodynamics, needs further observation and research.

This study has the following limitations: the first is a single center, and the included patients are mainly severe patients over 60 years old. To fully understand the occurrence of myocardial injury in covid-19 patients, it is necessary to expand the observation population, but most of the mild patients no hospital observation is required, and it is difficult to know about the incidence of myocardial injury in total covid-19 patients. Second, the observation time of patients in this study is relatively short; Third, the sample size of this group of patients is too small, so used all-cause mortality as short-term outcome. Studies with a larger number of samples have also been published,⁶ the systematic observation of the impact of myocardial injury on in hospital mortality can better reflect the value of hs-cTnI as a risk stratification.

In summary, our cohort study demonstrated that inhaled oxygen flow, SOFA score, and myocardial injury at admission in critically ill COVID-19 patients were important indicators for predicting short-term death of patients, the hs-cTnI can be as a risk stratification, which may provide a simple method for the physicians to identify high-risk patients and give reasonable treatment in time.

Acknowledgments

We gratefully acknowledge all the health-care workers on the front line of West campus of Union Hospital, Huazhong University of Science and Technology and the First Affiliated Hospital of Sun Yat-sen University and all the patients involved in the study. This study was supported by funding from the Shenzhen Science and technology R&D Fund (Grant No. JCYJ20160608142215491) and Guangdong Province Basic and Applied Basic Research Fund Project (Grant No. 2020A1515010120 and 2020A1515110919). The funders had no role in the study design, data collection, analysis, decision to publish, or the preparation of the manuscript.

Disclosure

The declare no conflicts of interests.

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