Original Article

Electrocardiographic findings over time and their prognostic value in patients with COVID-19

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Background: The objective of this study was to carry out a retrospective analysis of the progression of electrocardiographic (ECG) findings over time, based on biomarkers for myocardial injuries in patients with coronavirus disease 2019 (COVID-19). Also, the ECG observations were assessed for possible prognostic use.

Methods: Diagnostic criteria provided by the Coronavirus Pneumonia Diagnosis and Treatment Program of the Chinese National Health Commission were used. We conducted a retrospective analysis of 31 COVID-19 cases diagnosed as positive by high-throughput sequencing of nasopharyngeal nucleic acid test and admitted to Sichuan Province Public Health Clinical Medical Center, Sichuan Province, China. Based on changes in biomarkers, the 31 participants were divided into a non-myocardial injury group (A) and a myocardial injury group (B). Our study observed the dynamic changes and new abnormal changes of the ECG during the hospitalization of patients.

Results: The results summarized in the 4 following points: (I) the time sequence changes for ST and T indicated that the absolute ST-segment depression and T-wave inversion values in group B were larger. (II) The heart rate (HR) and RV5 values in group B were higher, the QTC value for group B was lower. (III) The sensitivity of ST-segment depression for the diagnosis of myocardial injury was 32.60% and the specificity was 90.50%. The sensitivity of T-wave inversion was 41.30% and the specificity was 85.10%. (IV) Lactate dehydrogenase (LDH) is a major factor affecting patient's death.

Conclusions: If abnormal ST-T, increased heart rate, shortened QTC interval, and high ventricular voltage are observed in a COVID-19 patient, it may infer that myocardial damage has occurred. Using ECG as a point of reference for change can compensate for the time limitation of myocardial enzyme index. Regardless of the stage of disease development, ECG can reflect myocardial damage. Particularly in the 8–12 days after hospitalization, almost all myocardial enzymes cannot be applied. The ST-depression and T-wave inversion had diagnostic significance with relatively high sensitivity and specificity for myocardial injury. Assessment of LDH and biomarkers in combination with ECG can more accurately reflect myocardial injury, and facilitate prompt clinical diagnosis and treatment.

Keywords: COVID-19; electrocardiogram; myocardial injury; biomarker

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Introduction

The novel coronavirus disease 2019 (COVID-19) has rapidly developed into a severe global pandemic. On 11 February 2020, the International Committee on Taxonomy of Viruses announced the official name of this new type of coronavirus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is understood that myocardial infection of humans by SARS-CoV-2 depends on the virus binding to ACE-2 receptors. The destruction of ACE-2 can result in age-related cardiomyopathy, cardiac dysfunction, and heart failure (1). Hypoxemia, systemic inflammation, immune system abnormalities, and electrolyte abnormalities caused by COVID-19 are all likely to cause damage to myocardial cells, which result in a more than threefold increase in mortality (2). Oudit *et al.* (3) detected SARS-CoV-2 viral RNA in autopsy samples of heart from COVID-19 patients and described pronounced infiltration of macrophages in the myocardial samples. At present, the seventh edition of the new Chinese Coronavirus Pneumonia Diagnosis and Treatment Program has indicated that myocardial cell degeneration and necrosis, partial vascular endothelial shedding, intimal inflammation, and thrombosis have been reported in COVID-19 patients and can result in myocardial and coronary artery damage.

Several biomarkers have been used to identify myocardial injury and cardiac complications. Tsung (4) found that most creatine kinase (CK) activity was present in skeletal and cardiac muscle, as well as other organs. Ischemic necrosis, inflammation of the lungs and other organs, trauma, surgery, and the use of antibiotics and dexamethasone can lead to elevated peripheral blood CK-myocardial band (MB). In peripheral blood, CK-MB increases in 4–6 h, reaches its highest concentration within 24 h, and returns to normal within 3 days, which may result in misdiagnosis or a missed diagnosis. Fan *et al.* (5) demonstrated that cardiac troponin I (cTnI) could be used as a routine indicator for acute myocardial infarction (AMI). The drawback is that the increase in cTnI only persists for approximately 2 weeks. Thus, it is difficult to distinguish whether increased cTnI levels are caused by an actual myocardial infarction (6). The guidelines (7) state that high sensitivity (hs)-cTnI or T and N-terminal pro b-type natriuretic peptide (NT-proBNP), and electrocardiogram (ECG) should be assessed in patients with highly suspected myocardial injury but with undiagnosed symptoms or signs. Any observed dynamic changes might help monitor the course of the disease and assist in making an accurate diagnosis. A recent study (8) reported that abnormal ECG changes occurred in COVID 19 patients. The innovation of this study, were to explore the relationship between dynamic ECG changes and biomarkers of myocardial injuries, the sensitivity and specificity of the ECG changes required for the detection of myocardial injuries and determine a prognosis for patients with COVID-19. We present the following article in accordance with the STARD reporting checklist (available at https://dx.doi.org/10.21037/apm-21-3188).

Methods

This was a retrospective study of medical record samples, wherein we compared the ECG and myocardial enzyme markers to explore myocardial injury. It only involved collection of the clinical patient data, did not interfere with the patient's treatment plan, did not present any risk to the patient, strictly followed the protection of patient privacy, and all data were anonymized before the start of the study. The study was approved by the Human Body Research Institution Committee of Sichuan Provincial People's Hospital [No.: Lun Shen (Research) No. 220 (2020)] and the Human Body Research Institution Committee of Sichuan Public Health Clinical Medicine Center [No.: Shen (Research) No. 150 (2020)]. Individual consent for this retrospective analysis was waived. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). As we were unable to determine whether patients who had been diagnosed with the COVID-19 virus had pre-existing heart disease which may cause abnormal ECG, our study observed the dynamic and new abnormal changes of the ECG during the hospitalization of participants. Clinical information and index test and reference standard results were available to the assessors of the reference standard.

Study cohort

The eligibility criteria were as follows: according to the diagnostic criteria developed by the Coronavirus Pneumonia Diagnosis and Treatment Program of the National Health Commission (9), a positive high-throughput sequencing of nasopharyngeal nucleic acid test or real-time reverse transcriptase polymerase chain reaction (RT-PCR) test on a nasopharyngeal swab sample was considered a confirmed case of COVID-19. From 1 January 2020 to 1 March 2020, 31 consecutive patients confirmed as infected with COVID-19 were admitted to the Public Health Clinical Medical Center of Chengdu City, Sichuan Province, China. The 31 consecutive patient cohort consisted of 17 males and 14 females, with an average age of 52±16 years.

Laboratory test and biomarker classification

Myocardial enzyme instruments (Hitachi-LABO SPECT008AS; Hitachi, Tokyo, Japan) and reagents Mike Biological Co., Ltd., Chengdu, China and Roche e602; Roche, Basel, Switzerland) were used. The laboratory myocardial injury indicators, such as CK-MB, CK, hs-TNT and LDH were tested. Engel's (10) study demonstrated that the sensitivity of troponin T at the first visit, 3 hours and 6 hours after the visit were 79.7%, 95.7% and 98.4%, respectively. Using a combination of troponin T and CK-MB relative index, the sensitivity increased to 90.6%. The sensitivity at 3 hours and 6 hours was increased to 97.9% and 100%, respectively. Therefore, we grouped the participants into the myocardial injury group (group B): CK-MB greater than 14 pg/mL or hs-TnT greater than 24 IU/L (n=11), and the non-myocardial injury group (group A): CK-MB and hs-TnT were normal (n=20).

ECG examination

The analysis was conducted on a total of 31 participants, 4 times per participant, for a total of 124 ECG data readings. Barman's (11) research showed that ST depression, T-wave inversion, and ST-T changes on admission ECG are closely associated with the severity of COVID-19 infection. We therefore observed the dynamic changes and new abnormal changes of the ECG during the hospitalization of participants. We selected the 12-lead conventional ECG [RAGE-12 full-function digital electrocardiograph (Xiamen Nalong Technology Co. Ltd., Fujian, China)] at the following time points: the first ECG conducted after admission was designated time 1; the second ECG taken on the third day; the third ECG performed on the eighth day; and the fourth ECG conducted on the twelfth day of admission. The test was arranged in this way is based on the findings of previous peer research. It adopted a calibration voltage of 10 mm/mv, paper speed 25 mm/s, filter frequency 35 Hz, and was collected 10 s after the baseline was stabilized. The following parameters were recorded: (I) heart rate, the time interval from the start of the P wave to the end (P wave duration), the time interval from the start of the P wave to the start of the Q wave (PR duration), the time interval from the start of the Q wave to the end of the S wave (QRS duration), the time interval from the start of the Q wave to the end of the T wave (QT duration), QT after heart rate correction (QTC duration); (II) P wave amplitude (P voltage), Q wave amplitude (Q voltage), Amplitude of R wave in lead V5 (Rv5), Amplitude of S wave in lead V1 (Sv1); (III) special parameters: Bimodal P wave, ST depression or elevation, PR elevation or depression, J-point elevation, T wave inversion. The diagnosis of ECG is according to the *AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part IV* (12).

Statistical analysis

Statistical analyses were performed using the software SPSS 22.0 (IBM Corp., Armonk, NY, USA). The positive rate, chi-square test (χ^2), and *t*-test were used to assess the ECG parameters. Using a repeated-measures analysis of variance, the receiver operating characteristic (ROC) curve was used to quantitatively evaluate the diagnostic capability and value of ST-segment depression and T-wave inversion for the presence and degree of myocardial injury in COVID-19 patients. Logistic regression was used to screen for risk factors and make predictions based on the regression models. A P-value of <0.05 indicated statistical significance. Due to the impact of the epidemic, the number of patients is determined according to the actual admission of patients.

Results

General clinical data

There was statistical significance in respiratory rate, systolic blood pressure, and mortality between groups A and B (*Table 1*).

Table 1 Baseline characteristics of patients with COVID-19

Characteristic	Group A (n=20)	Group B (n=11)	t/χ^2	P value
Gender (male)	10	7	0.533	0.707
Gender (female)	10	4		
Contact history, n (%)	17 (85.00)	10 (90.91)	0.22	0.639
Heart rate (HR)	48.8±15.6	58±16.6	–1.546	0.133
Temperature	37.2±0.7	37.7±0.9	–1.954	0.06
Respiratory rate	20±0.9	23.7±5.1	–3.18	0.003*
Systolic blood pressure (mmHg)	124.5±14.8	142.4±17.6	–3.02	0.005*
Diastolic blood pressure (mmHg)	78.6±8.4	82.8±18	–0.895	0.378
High blood pressure, n (%)	2 (10.00)	2 (18.18)	0.423	0.516
Diabetes, n (%)	3 (15.00)	3 (27.27)	0.685	0.408
Lung disease, n (%)	2 (10.00)	2 (18.18)	0.423	0.516
Coronary heart disease, n (%)	1 (5.00)	1 (9.09)	0.197	0.657
Immune diseases, n (%)	1 (5.00)	1 (9.09)	0.197	0.657
Length of hospitalization (day)	26.3±14.8	22.4±11.8	0.76	0.454
Death	0	3 (27.27)	6.039	0.015*

Myocardial injury group (group B); non-myocardial injury group (group A). *P<0.05.

ECG examination

Analysis of the global characteristics of ECG in group A and group B.

The analysis was conducted on a total of 31 participants, 4 times per participant, for a total of 124 ECG data readings. Select the 12-lead conventional ECG at the corresponding time: the first ECG conducted after admission was designated time 1. The second ECG was taken on the third day. The third ECG was performed on the eighth day, and the fourth ECG was conducted on the twelfth day.

(I) The ECG characteristics of myocardial injury group B (n=11 participants/total of 44 ECG data) were sorted in descending order from high to low: left atrium overload, bimodal P wave, ST depression, T wave inversion, J-point elevation, and arrhythmia. (II) The ECG characteristics of non-myocardial injury group A (n=20 participants/total of 80 ECG data) were sorted in descending order from high to low: left atrium overload, bimodal P wave, J-point elevation, ST segment depression, T wave inversion, and atrioventricular or bundle branch block. (III) The predominant ECG features were left atrium overload, bimodal P-wave, ST-segment depression, T-wave inversion, and J-point elevation. In group B, the proportion of the bimodal P-wave, ST-segment depression, and T wave inversion were higher than in group A. The ST-segment depression (P=0.025) and T-wave inversion (P=0.012) between groups A and B were significantly different.

Analysis the abnormal rate in group A and B over time.

The results showed that there was no statistically significant in the abnormality rate between Group A and Group B at each time point (P>0.05) (*Table 2*). Analysis of the dynamic changes of ECG parameters in groups A and B at each time point revealed that the heart rate (HR) in group B was higher than group A at time points 1, 3, and 4. The HR in group B showed a trend to increase over time. The QT value for group B was lower than group A at time points 3 and 4. The QTC value for group B was lower than group A at time point 4. The QTC in group B showed a trend to decrease over time. The RV5 and RV5 + SV1 values in group B were higher than group A at time points 2 and 4. The SV1 in group B showed a trend to increase over time while SV1 for group A remained stable (*Table 3*).

Analysis of the ST and T in group A and B over time

In group A, only the 8th, 9th, 11th, and 14th patients had T

Table 2 Abnormal rate of ECG in group A and B at different time points

T	Group	ST	T	Q wave	Block	Bimodal P	J point	Low voltage	Arrhythmia	PTFV1	Af	VT
T1	A	4 (20%)	3 (15%)	2 (10%)	3 (15%)	5 (25%)	5 (25%)	0 (0%)	2 (10%)	9 (45%)	0 (0%)	0 (0%)
	B	3 (27.27%)	3 (27.27%)	2 (18.18%)	1 (9.09%)	5 (45.54%)	3 (27.27%)	1 (9.09%)	2 (18.18%)	6 (54.55%)	0 (0%)	0 (0%)
T2	A	3 (15%)	4 (20%)	2 (10%)	3 (15%)	7 (35%)	5 (25%)	0 (0%)	0 (0%)	8 (40%)	0 (0%)	0 (0%)
	B	4 (36.36%)	3 (27.27%)	2 (18.18%)	1 (9.09%)	4 (36.36%)	3 (27.27%)	1 (9.09%)	0 (0%)	6 (54.55%)	0 (0%)	0 (0%)
T3	A	3 (15%)	2 (10%)	2 (10%)	2 (10%)	5 (25%)	5 (25%)	0 (0%)	4 (20%)	9 (45%)	0 (0%)	0 (0%)
	B	5 (45.45%)	3 (27.27%)	2 (18.18%)	1 (9.09%)	5 (45.45%)	3 (27.27%)	1 (9.09%)	3 (27.27%)	6 (54.55%)	1 (9.1%)	0 (0%)
T4	A	3 (15%)	2 (10%)	2 (10%)	2 (10%)	3 (15%)	5 (25%)	0 (0%)	1 (5%)	9 (45%)	0 (0%)	0 (0%)
	B	4 (36.36%)	3 (27.27%)	2 (18.18%)	1 (9.09%)	6 (54.54%)	3 (27.27%)	1 (9.09%)	3 (27.27%)	5 (45.45%)	1 (9.09%)	1 (9.09%)

Myocardial injury group (group B); non-myocardial injury group (group A). Block: Atrial ventricular block. Low voltage: Low voltage in limb leads or chest leads. Jpoint: J point up. Arrhythmia: Arrhythmia that occurs in the atria or ventricles. PTFV1, terminal potential of lead V1; Bimodal P, bimodal P wave; Af, atrial fibrillation; VT, ventricular tachycardia; ST, ST segment changes; T, T wave change; Q wave, abnormal Q wave.

Table 3 ECG parameters between group A and group B at different time points

T	Group	HR	P duration	PR duration	QRS duration	QTC duration	QT duration	RV5	SV1	Rv5+Sv1	P voltage
T1	A	77.35±11.37	101.30±8.29	158.85±20.37	94.5±10.28	433.4±35.35	385.00±38.23	1.17±0.27	0.62±0.31	1.79±0.48	0.14±0.05
	B	88.73±17.82●	103.91±10.56	155.36±18.79	94.73±16.91	427.36±28.89	357.73±41.84	1.38±0.63	0.73±0.39	2.12±0.57	0.11±0.04
T2	A	74.45±10.67	103.35±7.81	155.5±24.24	90.55±9.03	417.65±21.86	379.30±27.06	1.16±0.32	0.60±0.33	1.76±0.49	0.13±0.04
	B	81.36±17.43	102.64±9.62	145.45±46.02	88.36±8.30	423.64±22.40	369.36±41.79	1.63±0.56●	0.70±0.34	2.33±0.81●	0.12±0.03
T3	A	73.00±12.20	106.16±7.78	154.11±15.14	93.58±13.44	423.32±27.99	384.53±21.21	1.22±0.30	0.61±0.36	1.83±0.51	0.13±0.03
	B	90.09±18.35●	105.64±11.12	152.73±16.98	86.73±6.84	422.82±30.79	349.18±51.06●	1.29±0.37	0.86±0.44	2.15±0.56	0.11±0.01
T4	A	77.50±13.19	101.83±7.70	153.83±17.54	84.5±25.89	424.75±28.43	373.58±22.76	1.21±0.44	0.62±0.03	1.83±0.53	0.13±0.03
	B	95.30±21.90●	100.4±14.49	144.40±12.09	83.90±2.81	381.50±38.62●	310.40±16.73●	1.65±0.12●	0.95±0.47	2.60±0.59●	0.12±0.02

Myocardial injury group (group B); non-myocardial injury group (group A). ● $P<0.05$. P duration: the time interval from the start of the P wave to the end. PR duration: the time interval from the start of the P wave to the start of the Q wave. QRS duration: the time interval from the start of the Q wave to the end of the S wave. QT duration: the time interval from the start of the Q wave to the end of the T wave. QTC duration: QT after heart rate correction. RV5, R wave voltage in lead V5; SV1, S wave voltage in lead V1; Rv5+Sv1, the sum of V5 and SV1; HR, heart rate.

wave inversion, with a maximum of 0.2 mv; in group B, only the 6th, 7th, and 8th patients had T wave inversion, with a maximum of 0.5 mv.

In group A, only the 6th, 11th, 14th, 18th, and 19th patients had ST-segment depression, with a maximum of 0.1 mv; in group B, only the 4th, 6th, 8th, 9th, 10th, and 11th patients had ST-segment depression, with a maximum of 0.2 mv.

Diagnostic significance of ST segment depression and T wave inversion

There was a significant difference in abnormal changes for the ST-segment (χ^2=7.82, P=0.005) and T-wave (χ^2=10.576, P=0.001) between the 2 groups, regardless of the time point (*Table 4*). The repeated measures data for the ST-T and the positive rate of the ST-segment and T-wave data were significantly higher in group A compared to group B. The sensitivity of ST-segment depression for the diagnosis of myocardial injury was 32.60%, and the specificity was 90.50%, which was statistically significant (P=0.033) in the diagnosis of myocardial injury. The sensitivity of T-wave inversion in diagnosing myocardial injury was 41.30%, and the specificity was 85.10%, which also was statistically significant (P=0.015) in the diagnosis of myocardial injury (*Table 5*).

Table 4 The positive rate of ST and T

Variables	Group A (n=20)	Group B (n=11)	χ^2	P value
ST				
Negative	67 (88.2)	31 (67.4)	7.82	0.005
Positive	9 (11.8)	15 (32.6)		
T				
Negative	63 (85.1)	11 (14.9)	10.576	0.001
Positive	27 (58.7)	19 (41.3)		

Myocardial injury (group B); non-myocardial injury (group A). ST, ST segment changes. T, T wave change.

Analysis of factors affecting the prognosis of patients with COVID-19

Taking the outcome of the 31 participants (28 survived and 3 died) as the dependent variable Y (Y=1, death; Y=0, survival); the ST segment depression, the inverted T wave, LDH, CK-MB, and hs-TnT were used as X1-X5. Logistics regression analysis showed that: LDH is a major factor affecting patient's death, and finally the model equation was established as (χ^2=8.013, P=0.005) (*Table 6*):

$$Logit\{P(y=1)\} = -9.189 + 0.023 * LDH \quad [1]$$

Correlation between ECG parameters and myocardial enzymes:

BNP is negatively correlated with P wave and R wave amplitude (r=–0.488 and r=–0.546), Myoglobin is positively

Table 5 Significance of ST and T in the diagnosis of myocardial injury

Variables	Sensitivity%	Specificity%	ROC	Standard error	P value	95% CI	
						Lower	Upper
ST	32.60	90.50	0.616	0.055	0.033	0.509	0.723
T	41.30	85.10	0.632	0.054	0.015	0.526	0.738

ROC, receiver operating characteristic; CI, confidence interval; ST, ST segment changes; T, T wave change.

Table 6 Factors affecting prognosis

Variables	Regression B	Standard error	Wald	P value	OR	95% CI for OR	
						Lower	Upper
LDH	0.023	0.016	2.064	0.151	1.023	0.992	1.055
Constant	–9.189	5.223	3.095	0.079	0.000		

CI, confidence interval; OR, odds ratio; LDH, lactate dehydrogenase.

correlated with R wave amplitude (r=0.381), CK-MB is positively correlated with HR and R wave amplitude (r=0.0.427 and r=0.367), and negatively correlated with QT duration (r=-0.465), LDH is negatively correlated with QT duration (r=-0.401), and positively correlated with R wave amplitude and ST segment changes (r=0.445 and r=0.585).

Discussion

Cardiac injury and acute myocarditis are currently recognized complications of acute viral infections. A recent report by the National Health Commission of China (13) reported that cardiomyocyte necrosis and monocyte infiltration were found in myocardial autopsy specimens. The report showed that myocarditis may be an important cause of acute heart injury in COVID-19 patients. In clinical, COVID-19 myocarditis may only manifest as mild chest tightness or palpitations, which cannot be distinguished from other causes. One of the characteristics of the ECG is: instantaneous changes, so dynamic observation of the changes of the ECG helps to discover the existence and severity of myocardial damage in time. As the disease progresses, myocarditis may also develop into conduction block, tachyarrhythmia, and impaired left ventricular function, all of which urgently need electrocardiogram for timely diagnosis. If the dynamic changes of the ECG were found at the early stage of myocardial cell injury, the prognosis of cardiac complications may be able to significantly improved through clinical intervention. We should strengthen prevention according to WHO and CDC guidelines: More extensive use of telemedicine tools for daily monitoring, initial visits and regular 12-lead ECG, serum high-sensitivity troponin, NT-proBNP, echocardiography to assess blood flow dynamics, strain function, cardiac electrophysiology.

Previous studies (14) have reported that the mortality rate resulting from COVID-19 infections in critically ill patients with myocardial injury is 59.6%. In this study, the mortality rate was 9.7%. Regardless of the presence or absence of myocardial injury, the ECG changes in COVID-19 patients primarily included ST-segment depression, T-wave inversion, left atrial overload, bimodal P-wave, J-point elevation, and arrhythmia. The SARS-CoV-2 virus not only can bind to the ACE-2 receptor to directly damage the myocardium and microvessels (15) but also cause apoptosis and necrosis of myocardial cells through immune injury and induction of a cytokine storm (16).

In this study, patients with myocardial injury whose systolic blood pressure increased (142.4±17.6 mmHg) were thought to exhibit down-regulation of ACE-2, which blocked angiotensin vasodilation and produced natriuretic and diuretic effects. Early studies by Babapoor-Farrokhran (17) have shown that ACE-2 plays a vital role in the pathogenesis of SARS-CoV-2, and ACE-2 expression was significantly reduced in the above mentioned category of patients. A cohort study (13) by the Chinese Center for Disease Control and Prevention (CDC) showed that the prevalence of hypertension in the whole group was 12.8%, and the final death rate was 39.7%. Hypertension increases the odds ratio (OR) for deaths of COVID-19 patients by 3.05 (95% CI: 1.57–5.92). Hypertension appeared to be associated with more severe disease, higher risk of acute respiratory distress syndrome (ARDS), and increased mortality.

The basic HR in group B always was higher compared to group A. The HR has been recognized as a predictor of morbidity and mortality in the general population. An increased HR is associated with an increased chance for the occurrence of myocardial damage. Patients whose HR was higher than 90 bpm also had a greater chance of dying within 30 days. The HR is considered a critical factor in the balance between supply and demand in the myocardium (18). Hypoxia and symptoms of infection-induced toxicity during pneumonia can cause an increased HR. Also, increased excitation of sympathetic nerves and excessive activation of the renin-angiotensin-aldosterone system and preload were shown to have occurred due to increased HR. Subsequently, the diastolic period was shortened, the coronary supply was insufficient, the myocardial oxygen consumption was increased, the diastolic function was reduced, filling of left ventricular was limited, the left atrium became enlarged, and pulmonary congestion developed.

Early research (19) found that an increase in R-wave voltage is a specific characteristic of left ventricular hypertrophy, which predicts adverse cardiovascular events related to myocardial remodeling, as well as electrical, biochemical, and mechanical changes. Recent studies (20) have shown that left ventricular voltage is related to serum troponin levels, and an increased R-wave voltage is significantly associated with myocardial injury. This study also demonstrated that the R-wave voltage in group B was higher than group A, which may have been due to decreased ATP hydrolysis and inhibition of calcium reabsorption in cells, all of which resulted in a delay in stretching myofibrils. Lampert's (21) study found that the dynamic QRS voltage reduction is an independent predictor of death

during COVID-19 infection, while our study found that the R wave voltage of group B showed a dynamic change state of high and low during the development of the disease. This reversibility of R wave voltage may be related to the improvement of heart function after drug treatment. Isobe's (22) studies have also confirmed this; although our study did not directly find that the R wave voltage of group B was significantly reduced, we found that the voltage of the S in lead V1 showed an increasing trend. As we know, when the thickness of the lung tissue around the left ventricle increases, the surrounding area increases or the resistance increases (such as fibrosis, inflammation, emphysema, etc.), the voltage of the left ventricular surface attenuation increases, the positive potential on the corresponding electrode on the left ventricular surface decreases, while the negative potential increases relatively, so the S wave increases, that is to say, the deep S wave of lead V1 at this time actually reflects the isolated right ventricular depolarization potential which loss the left ventricular confrontation. Therefore, the heavier the attenuation of the left ventricular surface voltage, the deeper S on the right ventricular surface lead, which reflects that the lung symptoms of patients in group B are more severe and the prognosis is worse, which also confirmed by the diffuse inflammation and consolidation fibrosis found in the chest CT of the patients in group B.

Graettinger *et al.*'s research (23) showed that the bimodal P wave in lead V1 is associated with increased systolic blood pressure, increased left ventricular mass, and increased stroke volume. The double-peak P wave can predict the parameters that affect the size of the left atrium, especially the quality of the left ventricle. The terminal potential of lead V1. (PTFV1) is considered a good predictor of atrial fibrillation and a reflection of left atrial overload (24). A PTFV1 value that is greater than 40 ms/mv is independently associated with ischemic stroke (25). In this study, both group A and B patients showed bimodal P-wave abnormalities, indicating that COVID-19 affected atrial structure and function. However, this finding needs additional investigation with cardiovascular ultrasound.

The QTC is a heart rate-corrected QT interval. A prolonged QTC reflects prolonged electrical contraction. High-dose chloroquine, a supportive treatment for COVID-19, is likely to cause a QTC greater than 500 ms (26). However, this study did not find that the QT and QTC were prolonged. The QT in group B was shorter than that in group A. It could not be ruled out that the myocardium was affected by the short QT syndrome. The mechanism might be that the current damage changed the duration of the cardiac action, characterized by the short QT, atrial fibrillation, and sudden cardiac death (27).

The early repolarization pattern (ERP) is characterized by J-point elevation. The Matoshvili (28) study showed that a J-point elevation equal to or greater than 0.15 mV is more arrhythmogenic and induces premature ventricular beats. Rosso *et al.* (29) reported that J-point elevation is found more frequently among patients with idiopathic ventricular fibrillation (VF) than healthy controls. Hisamatsu (30) also demonstrated that J-point elevation observed with a standard 12-lead ECG was an independent predictor of cardiac death and death from coronary artery disease among middle-aged individuals.

When the subendocardial myocardium is injured, ST-depression is observed in the lead towards the epicardium, and the T-wave shows a deep inversion. In this condition, the presence of extensive ST-segment depression is usually attributed to severe endocardial ischemia caused by severe multiple vessel damage or left main coronary artery disease (31). Patients with ST-segment depression in the precordial region might exhibit a higher rate of in-hospital mortality (32). In group B, more than 54% of the cases showed significant ST-T changes, and the 3 participant deaths all occurred in group B.

An observational cohort study (33) investigated that atrial fibrillation (AF) was seen in over 15% in COVID-19 cases and more than 60% have never had AF before. The study also found that age, male sex and past history of AF are all independently related to the occurrence of atrial arrhythmia. Patients with AF have a higher rate of myocardial damage and systemic inflammation index. In our study, the incidence of arrhythmia was approximately 14%, the incidence of AF was approximately 3%. The causes of atrial arrhythmia associated with COVID-19 are diverse (34,35): changes in vascular volume, electrolyte abnormalities and metabolic disorders, drug treatment, systemic inflammation, microvascular injury and stress cardiomyopathy, Acute coronary syndrome and viral heart injury. Atrial fibrillation is a common complication that can lead to a higher risk of death. Mortality was significantly higher among patients with AF compared to patients without. AF were independently associated with 30-day mortality. Also, SARS-CoV-2 infection stimulates sympathetic nerves and triggers rapid supraventricular arrhythmia (36), which is an independent prognostic indicator for mortality of patients with sepsis (37), which might be due to the spontaneous release of calcium from

the sarcoplasmic reticulum (38,39).

Research conducted by Kishaba *et al.* (40) identified LDH as the biomarker providing the most important prognostic indication of lung injury. The latest research Yan *et al.* (41) found that LDH, lymphocytes, hs-TNT, and C-reactive protein (CRP) could predict the mortality associated with COVID-19 infections. This study selected ST, T-wave, LDH, CRP, BNP, CK, and lymphocyte level as indictors with possible prognostic value. The results demonstrated that LDH was the only indicator that correlated with patient death.

Conclusions

If abnormal ST-T, increased heart rate, shortened QTC interval, and high left ventricular voltage are observed in covid-19 patient, it may be inferred that myocardial damage has occurred. The ECG can make up for the time limitation of myocardial enzyme index. No matter what stage of disease development, ECG can reflect myocardial damage; whereas, especially in the 8–12 days after hospitalization, almost all myocardial enzymes cannot be applied at certain times. The ST-depression and T-wave inversion had diagnostic significance with relatively high sensitivity and specificity for myocardial injury. Although LDH is a major factor affecting patient death, when myocardial enzymes cannot be used to assist clinical diagnosis (due to the short-term utility of myocardial enzymes), combination with ECG can more accurately reflect myocardial injury, assisting prompt clinical diagnosis and treatment.

Limitations

This research is a retrospective analysis. First select appropriate data extractors for unified training to ensure the consistency of the extracted scores; secondly, in order to prevent selection bias, two people extract the results separately, and the other two extract independent variables blindly and independently; third, select two people to monitor data extraction, and the data extraction table is regularly checked with medical records; fourth, research plan selected the dynamic changes of the ECG during hospitalization to prevent recall bias or selection bias. Due to the special of COVID-19 prevention and control, the sample size of this study is small, but we combined with myocardial enzymology to conduct continuous dynamic tracking and observation of electrocardiogram, if the continuous ECG records show new or dynamic abnormal changes, it reflects that the myocardial injured. In the later, we will combine chest CT and cardiac ultrasound strains, and at the same time strive to obtain large sample size to make up, which will also continue to be written in subsequent articles.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Human Body Research Institution Committee of Sichuan Provincial People's Hospital [No.: Lun Shen (Research) No. 220 (2020)] and the Human Body Research Institution Committee of Sichuan Public Health Clinical Medicine Center (No.: Shen (Research) No. 150 (2020)). Individual consent for this retrospective analysis was waived. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

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