

Electrocardiogram analysis of patients with different types of COVID-19

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 causes acute myocardial damage and arrhythmia in coronavirus disease 2019 (COVID-19) patients. Studying the changes of electrocardiogram is of great significance for the diagnosis of patients with COVID-19.

Methods: A retrospective analysis method was adopted to compare the electrocardiogram changes between COVID-19 critically severe and severe patients. Univariate and multivariate logistic regression were used to analyze the correlation of the levels of serum indexes and past medical history with ST-T changes and atrial fibrillation. And the correlation of ECG parameters with in-hospital death and ventilator use were investigated by using the same methods.

Results: The incidence of male, stroke, elevated cardiac troponin I (cTnI), N-terminal of the prohormone brain natriuretic peptide (NT-proBNP), d-dimer, high-sensitivity C-reactive protein (hs-CRP), hyperkalemia, and hypocalcemia in the critically ill patients was higher than that in severe patients. There were differences in ST-T changes, sinus tachycardia, atrial fibrillation, and atrial tachycardia between the two groups. Multivariate logistic regression analysis showed that elevated cTnI and NT-proBNP were the independent risk factors of ST-T changes. Elevated NT-proBNP and age were the independent risk factors of atrial fibrillation. Sinus tachycardia and atrial fibrillation were the independent risk factors of in-hospital death and ventilator use.

Conclusion: ST-T changes, sinus tachycardia, and atrial fibrillation are with great significance in the diagnosis of the severity, myocardia injury, and cardiac insufficiency of COVID-19 patients. Sinus tachycardia and atrial fibrillation could be used as independent variables predicting in-hospital death and ventilator use.

KEYWORDS

COVID-19, electrocardiogram, myocardial injury, ST-T changes

Yina Wang and Lie Chen are with equal contributions.

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1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as the new coronavirus, infects humans and causes coronavirus disease 2019 (COVID-19), a highly infectious disease. Currently, SARS-CoV-2 has caused a worldwide epidemic with more than ten million of infections, and the cumulative number of infections continues to rise (World Health Organization, 2020). In addition to causing severe damage to the respiratory system, SARS-CoV-2 also causes acute myocardial damage, resulting in arrhythmia (Dawei et al., 2020; Elissa et al., 2020; Hongde, Fenglian, Xin, & Yuan, 2020). It has been suggested that myocardial damage is an important clinical feature of COVID-19 critically ill patients (Chen et al., 2020). As one of the most used clinical examination methods, electrocardiogram (ECG) is an irreplaceable important technique for recording cardiac electrical activity. It is of great significance to study the changes of electrocardiogram in patients with COVID-19. Therefore, to understand the ECG features of distinct types of COVID-19 patients, we retrospectively analyzed the electrocardiograms of 408 critically ill and noncritical COVID-19 patients and dissected the relationship between abnormal changes in ECG and myocardial injury. Our study provides an electrocardiographic basis for the early diagnosis and treatment of COVID-19-induced myocardial injury.

2 | METHODS

2.1 | Inspection objects

COVID-19 critically ill and noncritical patients admitted to the Optics Valley Campus and the Sino-French New City Campus of Tongji Hospital, an Affiliated hospital of Tongji Medical College of Huazhong University of Science and Technology, from January 27, 2020, to March 21, 2020. The diagnosis and typing criteria were based on the World Health Organization interim guidance (World Health Organization, 2020). The study was approved by the Medical Ethics Committee of Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology (Approval Number: TJ-C20200140). This study is a retrospective study without a need for signed informed consent.

2.2 | Examination method

The twelve-channel conventional ECG collected at the first time after the patients admitted to the hospital was used and divided into normal and abnormal based on the ECG diagnosis. ECG diagnosis was performed according to the 2009 ACC, AHA, HRS ECG standardization and analysis guidelines (Borys et al., 2009; Galen et al., 2009; Jay et al., 2007; Paul et al., 2007; Pentti et al., 2009; William et al., 2009). The exclusion criteria of ST-T changes were

nonspecific ST-T changes caused by ventricular premature beats, bundle branch block, ventricular pre-excitation, and pacemaker implantation.

2.3 | Laboratory examination

After the patients were admitted to the hospital, their myocardial troponin I (cTnI), N-terminal pro-B-type natriuretic peptide (NT-proBNP), d-dimer, serum calcium, and high-sensitivity C-reactive protein (hs-CRP) levels were examined. According to the clinical laboratory manual of Tongji Hospital and reagent instructions, an elevated cTnI was defined as a cTnI level that exceeds the upper limit of the cTnI levels of 99th percentile of the population; the normal reference intervals of NT-proBNP are as follows: 5.0–97.3 ng/L for 18–44 years old, 5.0–121.0 ng/L for 45–54 years old, 5.0–198.0 ng/L for 55–64 years old, 5.0–285.0 ng/L for 65–74 years old, and 5.0–526.0 ng/L for ≥ 75 years old.

2.4 | Statistical analysis

Statistical analysis was performed using SPSS21.0 software. For statistical comparison of two groups, measured data conforming to normal distribution were analyzed using independent sample *t* test, while count data were analyzed using chi-square test. If the minimum expected value is <5 , Fisher's exact test was used. Univariate and multivariate logistic regression were used to analyze the risk factors of ST-T changes in ECG of COVID-19 patients. A *p* value $<.05$ ($p < .05$) indicates that the differences between groups are statistically significant.

3 | RESULTS

3.1 | Basic data of patients

319 cases, consisting of 152 males and 167 females aged from 22 to 92 years, were enrolled in this study. The average age of the critically severe type was greater than that of severe type ($p < .05$), and the proportion of males in the critically severe type was higher than that in the other type ($p < .05$). The proportion of stroke in the critically ill group was significantly higher than that in the severe group ($p < .05$). The incidence of elevated cTnI ($p < .001$), NT-proBNP ($p < .001$), d-dimer ($p < .001$), and hs-CRP ($p < .001$) levels and hypocalcemia ($p = .002$) in the critically ill patients was higher than that of patients with severe type (Table 1).

3.2 | ECG changes in critically severe and severe types

118 cases (37.0%) had normal ECG, and 201 (63%) had abnormal ECG. Among the critically ill patients (97 cases), 15 (15%) cases

TABLE 1 Subject characteristics

Subject	Overall	Critically severe type	Severe type	t/χ^2	<i>p</i> value
Age (years)	64.97 ± 13.15	67.23 ± 14.43	63.98 ± 12.46	2.040	.042
Male, <i>n</i> (%)	152 (47.6)	69 (71.1)	83 (37.4)	30.819	<.001
Medical history, <i>n</i> (%)					
Hypertension, <i>n</i> (%)	139 (43.6)	49 (50.5)	90 (40.5)	2.732	.098
Coronary heart disease, <i>n</i> (%)	47 (14.7)	19 (19.6)	28 (12.6)	2.614	.106
PCI or CABG, <i>n</i> (%)	10 (3.1)	6 (6.2)	4 (1.8)	/	.073
Diabetes mellitus, <i>n</i> (%)	73 (22.9)	26 (26.8)	47 (21.2)	1.214	.271
Stroke, <i>n</i> (%)	13 (4.1)	8 (8.2)	5 (2.3)	/	.026
Elevated cTnI, <i>n</i> (%)	74 (23.2)	44 (45.4)	30 (13.5)	38.429	<.001
Elevated NT-proBNP, <i>n</i> (%)	152 (47.6)	75 (77.3)	77 (34.7)	49.191	<.001
Elevated d-dimer, <i>n</i> (%)	199 (62.4)	44 (45.4)	155 (69.8)	17.209	<.001
Hypocalcemia, <i>n</i> (%)	243 (76.2)	85 (87.6)	158 (71.2)	10.075	.002
Elevated hs-CRP, <i>n</i> (%)	291 (91.2)	97 (100)	194 (87.4)	/	<.001

Abbreviations: CABG, Coronary Artery Bypass Grafting; cTnI, cardiac troponin I; hs-CRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal of the prohormone brain natriuretic peptide; PCI, Percutaneous Transluminal Coronary Intervention.

had normal ECG and 82(86.0%) cases had abnormal ECG, and the highest proportion of abnormal ECG was ST-T changes (47 cases, 48.5%), followed by sinus tachycardia (29 cases, 29.9%), atrial arrhythmia (13 cases, 13.4%), and right bundle branch block (12 cases, 12.4%). Among the patients with severe type (222 cases), 103 cases (46.4%) had normal ECG, and 119 cases (53.6%) had abnormal ECG, including ST-T changes (57 cases, 25.7%), right bundle branch block (19 cases, 8.6%), and sinus bradycardia (28 cases, 9.5%) (Table 2). There was statistical significance on ST-T change ($p < .001$), sinus tachycardia ($p < .001$), atrial fibrillation ($p = .001$), atrial tachycardia ($p = .008$), and abnormal Q-wave and poor R-wave progression ($p = .001$) between critical severe and severe types (Table 2).

3.3 | Univariate and multivariate logistic regression analysis of ST-T changes in ECG of COVID-19 patients

Univariate logistic regression analysis showed that elevated cTnI (OR = 4.345, 95% CI 2.498–7.558, $p < .001$), elevated NT-proBNP (OR = 3.559, 95% CI 2.166–5.848, $p < .001$), hyperkalemia (OR = 2.280, 95% CI 1.229–4.230, $p = .009$), elevated hs-CRP (OR = 4.430, 95% CI 1.306–15.029, $p = .017$), hypertension (OR = 1.855, 95% CI 1.156–2.978, $p = .010$), stroke (OR = 3.500, 95% CI 1.116–10.978,

$p = .032$), critically ill (OR = 2.721, 95% CI 1.652–4.483, $p < .001$), and age (OR = 1.039, 95% CI 1.018–1.060, $p < .001$) were significantly corrected with ST-T abnormal changes. Multivariate logistic regression analysis showed that elevated cTnI (OR = 2.164, 95% CI 1.135–4.124, $p = .019$) and NT-proBNP (OR = 1.939, 95% CI 1.077–3.488, $p = .027$) levels were the independent risk factors of ST-T changes in ECG (Table 3).

3.4 | Univariate and multivariate logistic regression analysis of atrial fibrillation in ECG of COVID-19 patients

Univariate logistic regression analysis showed that elevated cTnI (OR = 2.688, 95% CI 1.085–6.659, $p = .033$), elevated NT-proBNP (OR = 25.152, 95% CI 3.332–189.853, $p = .002$), stroke (OR = 4.800, 95% CI 1.213–18.990, $p = .025$), critically ill (OR = 4.140, 95% CI 1.656–10.48, $p = .002$), and age (OR = 1.133, 95% CI 1.071–1.198, $p < .001$) were significantly corrected with atrial fibrillation. Multivariate logistic regression analysis showed that elevated NT-proBNP (OR = 13.280, 95% CI 1.900–108.287, $p = .016$) and age (OR = 1.103, 95% CI 1.043–1.166, $p = .001$) were the independent risk factors of atrial fibrillation in ECG (Table 4).

	Overall, n (%)	Critically severe type, n (%)	Sever type, n (%)	χ^2	p value
Normal ECG	118 (37.0)	15 (15.5)	103 (46.4)	27.712	<.001
Abnormal ECG	201 (63.0)	82 (84.5)	119 (53.6)	27.712	<.001
ST-T change	104 (32.6)	47 (48.5)	57 (25.7)	15.939	<.001
Sinus tachycardia	40 (12.5)	29 (29.9)	11 (5.0)	38.292	<.001
Atrial arrhythmia					
Atrial fibrillation	20 (6.6)	12 (13.4)	8 (3.6)	10.539	.001
Atrial flutter	4 (1.3)	3 (3.1)	1 (0.5)	—	.085
Atrial tachycardia	4 (1.3)	4 (4.1)	0	—	.008
Atrial premature beats	15 (4.7)	8 (8.2)	7 (3.2)	5.083	.080
Bradycardia					
Sinus bradycardia	19 (6.0)	4 (4.1)	15 (6.8)	0.836	.361
First degree AVB	11 (3.4)	3 (3.1)	8 (3.6)	—	1.000
Second degree AVB	2 (0.6)	0	2 (0.9)	—	1.000
Bundle branch block					
Right bundle branch block	31 (9.7)	12 (12.4)	19 (8.6)	1.118	.290
Left bundle branch block	3 (0.9)	2 (2.1)	1 (0.5)	—	.220
Left anterior fascicular block	9 (2.8)	5 (5.2)	4 (1.8)	6.140	.137
Ventricular premature beats	10 (3.1)	4 (4.1)	6 (2.7)	2.988	.499
Low voltage	5 (1.6)	3 (3.1)	2 (0.9)	—	.180
Abnormal Q-wave and poor R-wave progression	18 (5.6)	12 (12.4)	6 (2.7)	11.852	.001
Others					
Left ventricular high voltage or hypertrophy	21 (6.6)	7 (7.2)	14 (6.3)	0.091	.763
Abnormal U wave	6 (1.9)	2 (2.1)	4 (1.8)	—	1.000
Long QT interval	4 (1.3)	1 (1.0)	3 (1.4)	—	1.000

Abbreviations: AVB, atrioventricular block; ECG, electrocardiograph.

3.5 | Univariate and multivariate logistic regression analysis of ECG parameters with in-hospital death and ventilator use of COVID-19 patients

Univariate logistic regression analysis showed that ST-T changes (OR = 2.518, 95% CI 1.357–4.674, $p = .003$), sinus tachycardia (OR = 6.545, 95% CI 3.166–13.531, $p < .001$), atrial fibrillation (OR = 3.857, 95% CI 1.506–9.879, $p = .005$), and abnormal Q-wave and poor R-wave progression (OR = 3.000, 95% CI 1.069–8.418, $p = .037$) were related to in-hospital death. Sinus tachycardia (OR = 4.804, 95% CI 2.322–9.941, $p < .001$) and atrial fibrillation (OR = 4.701, 95% CI 1.864–11.856, $p = .001$) were related to the need for ventilator. Multivariate logistic regression analyses showed that sinus tachycardia (OR = 7.932, 95% CI 3.660–17.189, $p < .001$) (OR = 6.213, 95% CI 2.920–13.222, $p < .001$) and atrial fibrillation

TABLE 2 ECG changes in critically severe type and severe type

(OR = 5.338, 95% CI 1.882–15.142, $p = .002$) (OR = 6.990, 95% CI 2.683–18.213, $p < .001$) were the independent risk factors of both the two outcome (Table 5).

4 | DISCUSSION

COVID-19 mainly causes lung injury, but it can also affect multiple organs throughout the body, including the heart, kidneys, and liver. A recent study shows that all populations are susceptible, but males, elders, and people with a history of hypertension and coronary heart disease are more likely to develop critical illness (Chen et al., 2020). Our study found that the average age of patients in the COVID-19 critically ill group was higher than that in the severe group and that the proportion of males in the critically ill group was significantly

TABLE 3 Univariate and multivariate logistic regression analysis of ST-T changes in ECG of COVID-19 patients

Factors	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR值 (95% CI)	p值	OR值 (95% CI)	p值
Elevated cTnI	4.345 (2.498, 7.558)	<.001	2.322 (1.230, 4.384)	.009
Elevated NT-proBNP	3.559 (2.166, 5.848)	<.001	1.937 (1.080, 3.475)	.027
Elevated d-dimer	1.759 (0.962, 3.216)	.066		
Hypocalcemia	0.780 (0.455, 1.338)	.367		
Elevated hs-CRP	4.430 (1.306, 15.029)	.017	1.679 (0.457, 6.167)	.435
Hypertension	1.855 (1.156, 2.978)	.010	1.468 (0.872, 2.470)	.149
CHD	1.305 (0.678, 2.510)	.425		
Diabetes	1.072 (0.618, 1.860)	.805		
Stroke	3.500 (1.116, 10.978)	.032	1.812 (0.522, 6.290)	.349
Male	1.150 (0.720, 1.837)	.559		
Critically ill	2.721 (1.652, 4.483)	<.001	1.404 (0.784, 2.515)	.253
Age	1.039 (1.018, 1.060)	<.001	1.019 (0.997, 1.042)	.084

Abbreviations: CHD, coronary heart disease; cTnI, cardiac troponin I; ECG:electrocardiogram, hs-CRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal of the prohormone brain natriuretic peptide.

TABLE 4 Univariate and multivariate logistic regression analysis of atrial fibrillation in ECG of COVID-19 patients

Factors	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR值 (95% CI)	p值	OR值 (95% CI)	p值
Elevated cTnI	2.688 (1.085, 6.659)	.033	0.597 (0.206, 1.728)	.342
Elevated NT-proBNP	25.152 (3.332, 189.853)	.002	13.280 (1.9, 108.287)	.016
Hypertension	1.795 (0.734, 4.390)	.200		
CHD	1.045 (0.295, 3.705)	.946		
Diabetes	1.037 (0.367, 2.933)	.945		
Stroke	4.800 (1.213, 18.990)	.025	2.435 (0.495, 11.972)	.273
Male	0.999 (0.412, 2.422)	.998		
Critically ill	4.140 (1.656, 10.348)	.002	2.110 (0.738, 6.031)	.164
Age	1.133 (1.071, 1.198)	<.001	1.103 (1.043, 1.166)	.001

Abbreviations: CHD, coronary heart disease; cTnI, cardiac troponin I; NT-proBNP, N-terminal of the prohormone brain natriuretic peptide.

higher than that of severe type. Moreover, many critically ill patients generally had underlying diseases such as hypertension and coronary heart disease, but only the proportion of stroke in the two groups was significantly different (Table 6).

We also found that ST-T abnormal changes were the most common ECG manifestations in COVID-19 patients, and they accounted for the highest proportion of ECG abnormalities in both critically severe and severe types. The proportion of ST-T abnormal changes in critically severe type was significantly higher than that in severe type. ST-T change may be related to hypocalcemia, coronary heart disease, hypertension, or myocardial damage caused by SARS-CoV-2. Our study also showed that elevated cTnI and NT-proBNP levels were the independent risk factors of ST-T changes. Chen et al (Chen et al., 2020) found that about 20% of COVID-19 patients may have myocardial damage and cardiac dysfunction. Wang et al. (Dawei

et al., 2020) suggested that SARS-CoV-2 infection caused myocardial injury, which was mainly manifested in the increase of myocardial injury marker cTnI or cardiac troponin T beyond the 99th percentile upper limit and a potential increase in NT-ProBNP levels, without clinical evidence of myocardial ischemia (Chaolin et al., 2020). In our study, 23.2% patients with COVID-19 had increased cTnI and 47.6% had increased NT-proBNP. And the percentage of elevated cTnI and NT-proBNP in critically severe type was higher than that in severe type, indicating that more critically ill patients suffer from myocardia damage. For the lack of ECG before onset, it is not yet demonstrated that ST-T changes are the characteristic finding on ECG of COVID patients. But ST-T abnormal changes are still important in the diagnosis of myocardia damage and the severity of COVID-19 patients.

In our study, sinus tachycardia was the second most frequent abnormal ECG change in critically ill patients and the incidence

Factors	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR值 (95% CI)	p值	OR值 (95% CI)	p值
ST-T changes	2.518 (1.357, 4.674)	.003	1.748 (0.861, 3.549)	.122
Sinus tachycardia	6.545 (3.166, 13.531)	<.001	7.932 (3.660, 17.189)	<.001
Atrial fibrillation	3.857 (1.506, 9.879)	.005	5.338 (1.882, 15.142)	.002
Atrial tachycardia	3.787 (0.616, 23.238)	.151		
Atrial flutter	0.000	.999		
Atrial premature beats	2.955 (0.964, 9.056)	.058		
Sinus bradycardia	0.292 (0.038, 2.237)	.236		
First degree AVB	1.234 (0.258, 5.892)	.792		
Second degree AVB	0.000	.999		
RBBB	1.309 (0.509, 3.369)	.576		
Ventricular premature beats	1.599 (0.322, 7.933)	.566		
Abnormal Q-wave and poor R-wave progression	3.000 (1.069, 8.418)	.037	2.746 (0.830, 9.083)	.098
Left ventricular high voltage or hypertrophy	0.000	.998		

Abbreviation: AVB, atrioventricular block.

TABLE 5 Univariate and multivariate logistic regression analysis of in-hospital death of COVID-19 patients

Factors	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR值 (95% CI)	p值	OR值 (95% CI)	p值
ST-T changes	1.623 (0.874, 3.012)	.125		
Sinus tachycardia	4.804 (2.322, 9.941)	<.001	6.213 (2.920, 13.222)	<.001
Atrial fibrillation	4.701 (1.864, 11.856)	.001	6.990 (2.683, 18.213)	<.001
Atrial tachycardia	0.000	.999		
Atrial flutter	5.562 (0.765, 40.445)	.090		
Atrial premature beats	2.878 (0.940, 8.813)	.064		
Sinus bradycardia	1.009 (0.283, 3.601)	.989		
First degree AVB	0.529 (0.066, 4.223)	.548		
Second degree AVB	0.000	.999		
RBBB	1.589 (0.647, 3.903)	.313		
Ventricular premature beats	1.560 (0.314, 7.735)	.587		
Abnormal Q-wave and poor R-wave progression	2.188 (0.744, 6.436)	.155		
Left ventricular high voltage or hypertrophy	0.254 (0.033, 1.938)	.186		

Abbreviation: AVB, atrioventricular block.

TABLE 6 Univariate and multivariate logistic regression analysis of ventilator use of COVID-19 patients

rate was higher than that in severe type, which may be related to fever, hypoxia, myocardial injury, and cardiac insufficiency. However, according to clinical observations (Zhe et al., 2020), COVID-19 patients with myocardial injury often show sinus tachycardia, especially tachycardia at night, and the acceleration of heart rate that is not commensurate with the increase of body temperature (>10 beats/°C). Some researchers also analyzed the patient's blood oxygen saturation and found that the blood oxygen saturation levels of severe patients are low, but the heart rates are consistent with other groups (Nanshan et al., 2020), showing that COVID-19 critically ill patients with sinus tachycardia are not always caused by fever and hypoxia. Our study also found that the proportion of patients with increased cTnI and NT-proBNP in the critically ill group was significantly higher than that of noncritical group, suggesting that a higher proportion of patients in the critically severe group could develop myocardial injury and cardiac insufficiency. Thus, sinus tachycardia is an important ECG feature in the diagnosis of myocardia injury and cardiac insufficiency.

There was statistical significance on atrial fibrillation between critically severe and sever types of COVID-19 patients. And atrial fibrillation was also with high proportion in abnormal ECG changes, which may be attributed to the lung damage caused by the extensive invasion of SARS-CoV-2 to the lungs, or other related damages, such as cardiac insufficiency. The univariate logistic regression analysis showed that elevated cTnI and NT-proBNP levels, stroke, critically ill, and age were related to atrial fibrillation of COVID-19 patients. Multivariate logistic regression analysis showed that elevated NT-proBNP and age were the independent risk factors of atrial fibrillation. It is well known that the incidence of atrial fibrillation increases with age. Our results suggested that cardiac insufficiency plays an important role in the occurrence of atrial fibrillation.

In our study, sinus tachycardia and atrial fibrillation were the independent risk factors of in-hospital death and ventilator use. As described above, tachycardia and atrial fibrillation were related to cardiac insufficiency and myocardia injury, which indicated that cardiac insufficiency and myocardia injury might be the main reason of death and ventilator use of COVID-19 patients. And the results further illustrated ECG examination is with great significance in predicting outcomes.

This study is still lacking the dynamic observation and analysis of the ECG of COVID-19 patients and has no ECG data of patients before admission. Thus, it remains to be verified further whether these ECG changes we found are the characteristic ECG changes in COVID-19 patients.

5 | CONCLUSION

ST-T changes, sinus tachycardia, and atrial fibrillation are powerful ECG features for diagnosing the severity, myocardia injury, and cardiac insufficiency of COVID-19 patients. A dynamic observation

of changes in ECG can provide an important basis for assessing the severity of COVID-19 patients.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Yina Wang participated in article writing, modification, data acquisition and statistical analysis; Lie Chen participated in article writing, modification, data acquisition and statistical analysis; Jingyi Wang participated in data acquisition and statistical analysis; Xingwei He participated in data acquisition and statistical analysis; Fen Huang participated in paper modification; Jing Chen participated in paper modification; Xiaoyun Yang participated in thesis topic selection, modification, finalization, data analysis.

DATA AVAILABILITY STATEMENT

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

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