Received: 17 July 2020 | Accepted: 8 June 2021

DOI: 10.1111/ijcp.14571

ORIGINAL PAPER

Infectious diseases

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Indicators and prediction models for the severity of Covid-19

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Funding information
This work was supported by the Science and Technology Project of Zhuhai (20191210E030072); and the Medical Science and Technology Research Project of Guangdong Province (A2018043)

Abstract

Objectives: Coronavirus disease 2019 (Covid-19) is outbreaking globally. We aimed to analyse the clinical characteristics, cardiac injury, electrocardiogram and computed tomography (CT) features of patients confirmed Covid-19 and explored the prediction models for the severity of Covid-19.

Methods: A retrospective and single-centre study enrolled 98 laboratory-confirmed Covid-19 patients. Clinical data, electrocardiogram and CT features were collected and analysed using Statistical Package for the Social Sciences software.

Results: There were 46 males and 52 females, with a median age of 44 years, categorised into three groups, including mild, moderate and severe/critical Covid-19. The rate of abnormal electrocardiograms in severe/critical group (79%) was significantly higher than that in the mild group (17%) ($P = .027$), which ($r = 0.392$, $P = .005$) positively related to the severity of Covid-19 (OR: 5.71, 95% CI: 0.45-3.04, $P = .008$). Age older than 60 years old, comorbidities, whether had symptoms on admission, fatigue, CT features, laboratory test results such as platelet count, lymphocyte cell count, eosinophil cell count, CD3+ cell count, CD4+ cell count, CD8+ cell count, the ratio of albumin/globulin decreased and D-dimer, C-reactive protein (CRP), B-type natriuretic peptide (BNP), cardiac troponin I (cTnI) elevated were the risk factors for the increased severity of Covid-19. The logistic model, adjusted by age, lobular involvement score and lymphocyte cell count, could be applied for assessing the severity of Covid-19 (AUC, 0.903; Sensitivity, 90.9%; Specificity, 78.1%).

Conclusions: Age >60 years old, chronic comorbidities, lymphocytopoenia and lobular involvement score were associated with the Covid-19 severity. The inflammation induced by Covid-19 caused myocardial injury with elevated BNP and cTnI level and abnormal electrocardiograms.

Abbreviations: ACE2, angiotensin-converting enzyme 2; ALT, alanine aminotransferase; ARDS, acute respiratory distress syndrome; AUC, area under curve; BNP, B-type natriuretic peptide; CDC, Center for Disease Control and Prevention; CD3+ cell, mature T lymphocyte; CD4+ cell, inducible T lymphocyte; CD8+ cell, suppressor T lymphocyte; Covid-19, Coronavirus Disease 2019; CRP, C-reactive protein; CT, computed tomography; cTnI, cardiac troponin I; ECMO, extracorporeal membrane oxygenation; IQR, interquartile range; OR, odds ratio; PCR, polymerase chain reaction; ROC, receiver operating characteristic; SPSS, Statistical Package for the Social Sciences; WHO, World Health Organization.

Jiana Huang, Jiebing Gao and Wenliang Zhu contributed equally.

1 | INTRODUCTION

In December 2019, patients of Coronavirus Disease 2019 (Covid-19) were identified. Up to 17 April 2020, it has been documented 84 149 laboratory-confirmed patients in China, and 1 994 456 patients in other countries. The World Health Organization (WHO) has announced Covid-19 is a public health emergency and adjusted the global risk level from "high" to "very high" on 28 February 2020. With the number of confirmed patients rising around the world, on March 11st, WHO characterised Covid-19 as a pandemics. With the implementation of control measures, such as isolation and quarantine, the number of Covid-19 patients tended to stabilise. In this study, we aimed to analyse the clinical characteristics and computed tomography (CT) features of patients who confirmed Covid-19 in our hospital, and firstly explored the cardiac injury and electrocardiogram characteristics induced by Covid-19, therefore found the indicators and prediction models for the severity of Covid-19.

What's known

- It is known that Covid-19 is a worldwide infectious disease, which causes complex clinical symptoms, even including induction and aggravation of cardiovascular disease, and death.
- The characteristics of individual symptom, risk factors, cumulative range of pulmonary infection and blood test indexes are the important factors affecting the prognosis.
- Earlier evaluation and treatment for reversible risk factors can improve the prognosis.

What's new

- Covid-19 confirmed patients were mainly imported, cluster, or infected by close contact, with low mortality and higher discharged rate. Progression of Covid-19 was strongly associated with the prognosis.
- The risk factors of age >60 years old, chronic comorbidities, lymphocytopoenia and lobular involvement score were malignantly associated with the Covid-19 severity, which was not parallel to the degree of fever.
- The inflammation induced by Covid-19 caused the myocardial injury with elevated BNP and cTnI level and abnormal electrocardiograms, which was firstly reported.

2 | METHODS

2.1 | Study participants and design

This research was a retrospective and single-centre study. All the patients with laboratory-confirmed Covid-19 admitted to the Fifth Affiliated Hospital of Sun Yat-sen University from 17 January to 16 February were enrolled. The Fifth Affiliated Hospital of Sun Yat-sen University is the only hospital assigned for the Zhuhai government responsible for the admission and treatment of Covid-19 patients. The final date of follow-up was 3 March, and all the patients had clinical outcomes of discharge or death.

2.2 | Data collection

The medical records of all the patients were collected. And then we recorded the demographics, history of exposure, underlying diseases, clinical manifestations, laboratory parameters, electrocardiograms, chest CT, treatments, complications, outcomes and length of hospitalisation. The laboratory parameters included blood routine, blood chemical analysis, T lymphocyte count, liver and renal function assessment, markers of myocardial injury and cardiac function. The pulmonary lobe involvement was analysed by quantitative CT analysis, and each lobe was assigned a score (Figure 1): score 0, 0% involvement; score 1, <25% involvement; score 2, 26%-49% involvement; score 3, 50%-75% involvement; and score 4, greater than 75% involvement. There was a score of 0-4 for each lobe, with a total possible score of 0-20.[1] The diagnosis was according to the WHO interim guidance, and the diagnosis and treatment criteria of Covid-19 (trial version 6) advised by the general office of the national health commission of China. The Covid-19 diagnosis was confirmed by real-time polymerase chain reaction. The degree of severity of Covid-19 was defined as following: (1) Mild: slight clinical symptoms without CT abnormality. (2) Moderate: fever, respiratory symptoms, etc, CT presented with pneumonia. (3) Severe: complied any of the following: ① anhelation, respiratory rate ≥30/min; ② at rest, oxygen saturation ≤93%; ③ PaO_2 /FiO_2 ≤ 300 mm Hg; ④ Pulmonary imaging showed that the lesion progressed more than 50% within 24-48 hours. (4) Critically severe: complied with any of the following: ① Respiratory failure and required mechanical ventilation; ② Shock; ③ Combined with other organ failure required intensive care unit. The nucleic acid detections of throat swab and stool from patients of Covid-19 were conducted by the Center for Disease Control and Prevention of Zhuhai and the Fifth Affiliated Hospital of Sun Yat-sen University.[2] According to the diagnosis and treatment criteria of Covid-19 (trial version 6), the standard for discharge and removing the isolation should be met as follows: ① Body temperature returns to normal for more than three days; ② Respiratory symptoms improved significantly; ③ Pulmonary imaging showed that acute exudative lesions were significantly absorbed and improved; ④ Negative nucleic acid test for two consecutive respiratory specimens (sampling time: at least one day apart).

2.3 | Statistical analysis

All data were analysed using Statistical Package for the Social Sciences (SPSS) version 26.0 software (SPSS Inc). Categorical variables were

described as frequency rates and percentages, and quantitative variables were described using mean (SD) or median (interquartile range, IQR) values. The Chi-square test and Fisher exact test were used for categorical variables. Quantitative variables were tested for normality using Shapiro Wilk tests. Normally distributed data were analysed by multiple independent sample T test. Otherwise, Kruskal-Wallis

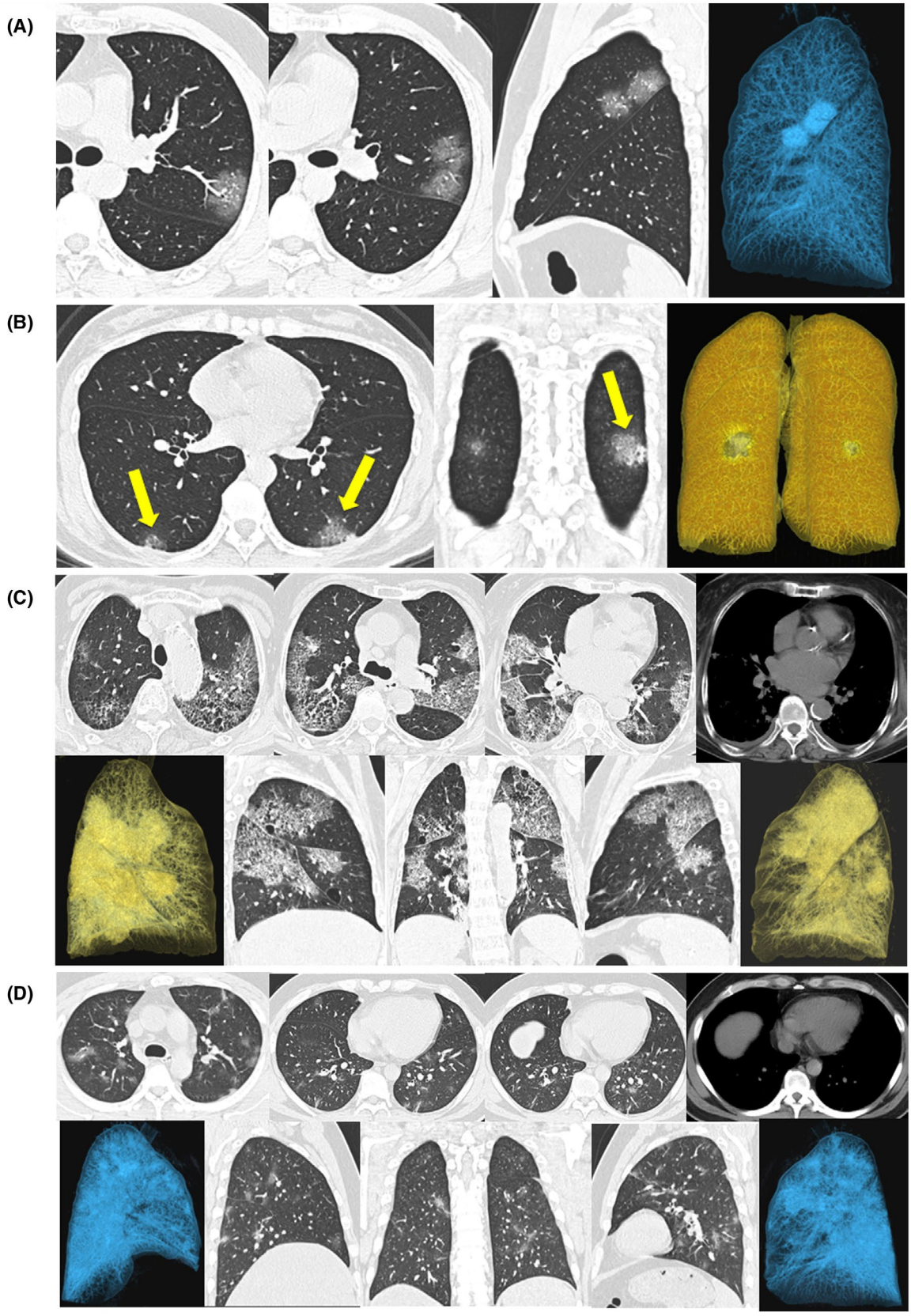

FIGURE 1 Transverse thin-section CT scan for the moderate patients of Covid-19. A, a 36-year-old male was admitted to the hospital because of cough for four days and fever for half-day and diagnosed as moderate of Covid-19. CT demonstrated pure ground-glass opacity in the left superior lobe. The lobular involvement score was one point, with the lobe involved less than 25%. B, a 36-year-old female was admitted to the hospital because of fever for 3 days, and diagnosed as moderate of Covid-19. CT revealed a subpleural confounding opacity lesion in the lower lobe of the left lung, and a patchy ground-glass opacity lesion with blurred boundaries in the lower lobe of the right lung (yellow arrows). The lobular score was one each in the left inferior lobe and the right inferior lobe, respectively, because of the involved area less than 25%. C, An 80-year-old female was admitted to the hospital because of diarrhoea, dyspnoea, anorexia, fatigue and muscular soreness, no fever or cough and diagnosed as severe of Covid-19. CT on admission showed diffuse lesions, mainly ground-glass opacity accompanied by partial consolidation, crazy-paving pattern in bilateral lungs, which were chiefly distributed under the pleura. The total lobular involvement score was 11, with two in the left superior lobe, two in the left inferior lobe, two in the right superior lobe, two in the right medial lobe and three in the right inferior lobe. The patient was also with atherosclerosis of aorta and coronary artery and a small amount of effusion in bilateral pleura. D, a 36-year-old male was admitted to the hospital because of generalised fatigue, muscular soreness for four days, and fever for three days, and diagnosed as severe of Covid-19. CT on admission indicated diffused irregular mixed patchy and ground-glass opacity lesions in bilateral lungs. The total lobular involvement score was 14, with three in the left superior lobe, three in the left inferior lobe, three in the right superior lobe, two in the right medial lobe, and three in the right inferior lobe

H test was used to compare multiple independent samples, which did not follow the normal distribution. The risk factors (including the clinical and CT features) and correlation coefficient of the severity of Covid-19 were evaluated by the spearman correlation and univariate logistic analysis. The apparent risk factors acquired were analysed and adjusted by logistic regression analysis, and then the diagnostic models were obtained to distinguish between the moderate and severe/critical of Covid-19. Receive operating characteristic (ROC) analysis was used to determine the value of clinical and CT features in distinguishing the moderated and severe/critical types of Covid-19 and found the corresponding cut-off value. *P* values < .05 were considered as statistically significant.

3 | RESULTS

3.1 | Clinical characteristics and manifestations

In our study, all of 98 Covid-19 confirmed patients were investigated. There were 12 mild, 64 moderate, 19 severe, and three critically severe patients with a median age of 44 (33-62) years, of whom 46 (47%) patients were male, and 52 (53%) patients were female (*P* = .381). For the convenience of statistics, severe and critical patients were categorised as severe/critical. There was an obvious difference in age among the three groups (*P* < .001), as shown in Table 1. Age of severe/critical (63 [50-68]) patients was significantly older than moderate (42 [33-59]) and mild (29 [15-42]) patients. On the other hand, in the 61-80 year-old group, the incidence of severe/critical patients (59%) was apparently higher than moderate (20%) and mild (0%) patients (*P* < .001). And there were no severe/critical patients observed in the 0- to 20-year-old group (*P* = .047). Notably, 77% of patients were clustering occurrences. The median of the incubation period was five days. Five patients had an incubation period exceeding 14 days, the longest of which was 27 days.

90 (92%) and 91 (93%) of patients did not have a history of smoking and alcohol, respectively. Thirty (31%) patients have comorbidities of hypertension (19%), diabetes (7%), pulmonary disease (7%), heart disease (6%), chronic kidney disease (2%), thyroid disorder (8%) and malignancy (4%). There were significant differences in whether had commodities on admission between severe/critical patients (55%) and moderate patients (27%) (*P* = .010).

We noticed that only 82 (83%) patients displayed symptoms on admission. And there was a remarkable difference in whether had symptoms between severe/critical (96%) and mild (58%) patients (*P* = .022). The most common symptom was fever (58%), with 42% of low fever (37.3℃-38℃), 15% of moderate fever (38.1℃-39℃), and 1% of high fever (39.1℃-41℃). Forty-two per cent of mid, 55% of moderate, and 77% of severe/critical patients of Covid-19 exhibited fever. Some severe/critical patients did not have a fever (Table 1). Besides, patients who displayed fatigue in severe/critical group (32%) were much more than in the moderate group (8%) (*P* = .009).

3.2 | Laboratory findings

The details were shown in Table 2. The platelet count, lymphocyte cell count, eosinophil cell count, basophil cell count of the severe/critical group were significantly lower than that of the moderate and mild groups, respectively. Fifty per cent and 68% of severe/critical patients had lymphocyte count, and eosinophil count decreased. In terms of T lymphocyte count, mature T lymphocyte (CD3+), inducible T lymphocyte (CD4+) and suppressor T lymphocyte (CD8+) cell counts were apparently reduced in the severe/critical group. Forty-two per cent of patients in the mild group showed elevated alanine aminotransferase (ALT). The values of albumin and ratio of albumin/globulin in the liver function test were clearly decreased in the severe/critical group. Besides, 32% and 77% of severe/critical patients showed significantly increased D-dimer and C-reactive protein (CRP). For the markers of cardiac function and myocardial injury during hospitalisation (Table 3), B-type natriuretic peptide (BNP) was remarkably increased in the severe/critical group (1076 pg/mL) compared with the moderate (77 pg/mL) and the mild (66 pg/mL) group (*P* < .001). Percentages of patients with elevated cardiac troponin I (cTnI) in the severe/critical group (27%) were distinctly higher than those in the moderate group (2%) (*P* = .002).

TABLE 1 Baseline characteristics and clinical outcomes of Covid-19

	Median (IQR) or No. (%)				
	Total (N = 98)	Mild (N = 12)	Moderate (N = 64)	Severe/critical (N = 22)	*P* value
Age (years)	44.0 (33.0-62.3)	29.0 (15.0-42.3)[a]	42.0 (33.0-59.0)[b]	63.0 (50.0-67.5)[ab]	<.001
0-20	10 (10)	3 (25)	7 (11)	0 (0)	.047
21-40	34 (35)	6 (50)	24 (38)	4 (18)	.128
41-60	28 (29)	3 (25)	20 (31)	5 (23)	.716
61-80	26 (27)	0 (0)[a]	13 (20)[b]	13 (59)[ab]	<.001
Sex					.381
Male	46 (47)	6 (50)	27 (42)	13 (59)	–
Female	52 (53)	6 (50)	37 (58)	9 (41)	–
Exposure					
Imported patients	78 (80)	10 (83)	49 (77)	19 (86)	.748
Contact with confirmed patient	18 (18)	3 (25)	11 (17)	4 (18)	.174
Clusters	75 (77)	6 (50)	52 (81)	17 (77)	.064
Smoking history					.353
Never	90 (92)	10 (83)	60 (94)	20 (91)	–
Former	2 (2)	0 (0)	1 (2)	1 (5)	–
Current	6 (6)	2 (17)	3 (5)	1 (5)	–
Alcohol history					.451
Never	91 (93)	11 (92)	60 (94)	20 (91)	–
Former	1 (1)	1 (8)	4 (6)	1 (5)	–
Current	6 (6)	0 (0)	0 (0)	1 (5)	–
Comorbidities	30 (31)	1 (8)	17 (27)[a]	12 (55)[a]	.010
Hypertension	19 (19)	1 (8)	10 (16)	8 (36)	.082
Diabetes	7 (7)	0 (0)	3 (5)	4 (18)	.095
Pulmonary disease	7 (7)	0 (0)	3 (5)	4 (18)	.095
Heart disease	6 (6)	0 (0)	2 (3)	4 (18)	.051
Chronic kidney disease	2 (2)	0 (0)	1 (2)	1 (5)	.576
Thyroid disorder	8 (8)	0 (0)	6 (9)	2 (9)	.740
Malignancy	4 (4)	0 (0)	3 (5)	1 (5)	1.000
Symptoms before admission	82 (84)	7 (58)[a]	53 (84)	21 (96)[a]	.022
Incubation period (days)	5 (2.0-8.0)	7.0 (2.0-11.0)	5.0 (2.0-8.5)	4.0 (2-8)	.783
Maximum (days)	27	21	25	27	–
More than 14 days	5 (5)	1 (8)	2 (3)	2 (9)	–
Fever	57 (58)	5 (42)	35 (55)	17 (77)	.084
37.3℃-38℃	41 (42)	4 (33)	25 (39)	12 (55)	–
38.1℃-39℃	15 (15)	1 (8)	9 (14)	5 (23)	–
39.1℃-41℃	1 (1)	0 (0)	1 (2)	0 (0)	–
Chill	5 (5)	0 (0)	3 (5)	2 (9)	.632
Cough	50 (51)	3 (25)	35 (55)	12 (55)	.157
Rhinorrhoea	13 (13)	1 (8)	10 (16)	2 (9)	.822
Nasal congestion	9 (9)	1 (8)	6 (9)	2 (9)	1.000
Sputum production	29 (30)	1 (8)	23 (36)	5 (23)	.114
Pharyngeal discomfort/pain	23 (24)	0 (0)	17 (27)	6 (27)	.123
Chest distress	7 (7)	0 (0)	6 (9)	1 (5)	.600
Dyspnoea	5 (5)	0 (0)	3 (5)	2 (9)	.632

(Continues)

TABLE 1 (Continued)

	Median (IQR) or No. (%)				
	Total (N = 98)	Mild (N = 12)	Moderate (N = 64)	Severe/critical (N = 22)	*P* value
Dizziness	6 (6)	0 (0)	6 (9)	0 (0)	.345
Headache	8 (8)	0 (0)	6 (9)	2 (9)	.740
Nausea	5 (5)	0 (0)	5 (8)	0 (0)	.490
Diarrhoea	6 (6)	1 (8)	3 (5)	2 (9)	.542
Myalgia/arthralgia	14 (14)	1 (8)	7 (11)	6 (27)	.163
Fatigue	12 (12)	1 (8)	4 (6)[a]	7 (32)[a]	.009
Mental state					
Anxiety	17 (17)	2 (17)	12 (19)	3 (14)	.921
Depression	7 (7)	0 (0)	6 (9)	1 (5)	.600
Complications	15 (15)	1 (8)	4 (6)[a]	10 (46)[a]	<.001
Acute respiratory distress syndrome	8 (8)	0 (0)	0 (0)[a]	8 (36)[a]	<.001
Septic shock	3 (3)	0 (0)	0 (0)[a]	3 (14)[a]	.021
Pneumothorax/hydrothorax	2 (2)	0 (0)	0 (0)	2 (9)	.062
Abnormal liver function	4 (4)	1 (8)	2 (3)	1 (5)	.570
Viral myocarditis	1 (1)	0 (0)	0 (0)	1 (5)	.347
Viral esophagitis	1 (1)	0 (0)	0 (0)	1 (5)	.347
Hypokalaemia	3 (3)	0 (0)	1 (2)	2 (9)	.164
Hyperkalaemia	1 (1)	0 (0)	0 (0)	1 (5)	.347
Hyponatraemia	2 (2)	0 (0)	0 (0)	2 (9)	.062
Hypoproteinaemia	2 (2)	0 (0)	0 (0)	2 (9)	.062
Mild anaemia	3 (3)	0 (0)	1 (2)	2 (9)	.164
Granulocytopoenia	1 (1)	0 (0)	0 (0)	1 (5)	.347
Three series decreased	1 (1)	0 (0)	1 (2)	0 (0)	1.000
Treatment outcomes					.357
Discharged	97 (99)	12 (100)	64 (100)	21 (96)	–
Dead	1 (1)	0 (0)	0 (0)	1 (5)	–
Total hospitalised duration, median (IQR)	18.0 (14.0-23.0)	14.0 (9.0-27.5)	17.0 (14.0-22.8)	20.5 (17.3-25.3)	.178

Note: a and b, there were statistical significances between groups

3.3 | Electrocardiograph findings

There were 49 patients performed electrocardiograph examinations during hospitalisation (Table 3). The rate of abnormal electrocardiographs in severe/critical group (79%) was significantly higher than that in the mild group (17%) ($P = .027$). The characteristics of abnormal electrocardiographs in moderate and severe/critical patients included abnormal q/Q wave, aberrant r wave, abnormal changes of T wave and low voltage of limb lead. Furthermore, severe/critical patients were usually associated with ST-segment changes, sinus tachycardia and obvious sinus bradycardia with frequent ventricular premature beats. In the present study, the only patient who died in critical condition was associated with significant sinus bradycardia, frequent ventricular premature beats and significant horizontal depression of ST-segment.

3.4 | CT findings

Mild patients were diagnosed with no pneumonia finding in CT images. Therefore, we only compared the difference in CT findings between the moderate and severe/critical group on admission (Table 4). The lobular involvement score in the severe/critical group (10.5 [5.8-12.0]) was apparently higher than that in the moderate group (2.0 [1.0-5.0]) ($P < .001$). In the moderate group, the right lower lobes and the left lower lobes of the lung were usually involved (Figure 1B), while in the severe/critical group, the right upper, middle, lower lobes and the left upper and lower lobes were commonly involved (Figure 1C,D). In addition, there were distinct differences in the numbers of lobes involvement between the moderate (2 [1-4]) and severe/critical group (5 [4-5]) ($P < .001$). Incidences of more than two lobes involvement (86% vs 38%, $P < .001$), bilateral

TABLE 2 The laboratory examinations in patients of Covid-19

		Median (IQR) or No (%)				
	Normal Range	Total (N = 98)	Mild (N = 12)	Moderate (N = 64)	Severe/critical (N = 22)	*P* value
Blood routine						
White blood cell count, $\times 10^9$/L	3.5-9.5	5.19 (4.06-6.61)	6.18 (4.65-7.38)	5.19 (3.99-6.60)	4.74 (3.54-6.27)	.121
Increased		5 (5)	1 (8)	4 (6)	0 (0)	.490
Decreased		24 (25)	1 (8)	16 (25)	7 (32)	.310
Haemoglobin, g/L	130-175	139.0 (126.0-151.0)	150.0 (136.5-162.5)	137.0 (126.0-145.0)	135.0 (119.5-154.8)	.062
Increased		1 (1)	0 (0)	1 (2)	0 (0)	1.000
Decreased		17 (17)	0 (0)	11 (17)	6 (27)	.120
Platelet count	125-350	192.0 (164.0-247.5)	240.5 (188.3-311.0)[a]	198.0 (179.3-276.0)[b]	149.0 (131.8-175.0)[ab]	<.001
Increased		7 (7)	2 (17)	5 (8)	0 (0)	.132
Decreased		7 (7)	0 (0)	3 (5)	4 (18)	.095
Lymphocyte cell count, $\times 10^9$/L	1.1-3.2	1.60 (1.12-2.10)	2.25 (1.65-3.05)[a]	1.70 (1.23-2.21)[b]	1.15 (0.89-1.53)[ab]	<.001
Increased		7 (7)	2 (17)	5 (8)	0 (0)	.132
Decreased		23 (24)	1 (8)	11 (17)[a]	11 (50)[a]	.003
Neutrophil cell count, $\times 10^9$/L	1.8-6.3	2.85 (2.11-3.87)	3.00 (2.22-4.09)	2.76 (2.09-3.65)	3.01 (2.03-4.07)	.726
Increased		5 (5)	0 (0)	4 (6)	1 (5)	1.000
Decreased		14 (14)	0 (0)	9 (14)	5 (23)	.185
Monocyte cell count, $\times 10^9$/L	0.1-0.6	0.49 (0.38-0.67)	0.53 (0.41-0.83)	0.50 (0.39-0.61)	0.45 (0.33-0.68)	.420
Increased		30 (31)	6 (50)	16 (25)	8 (36)	.181
Eosinophil cell count, $\times 10^9$/L	0.02-0.52	0.020 (0.000-0.800)	0.090 (0.040-0.205)[ab]	0.030 (0.000-0.078)[ac]	0.01 (0.00-0.03)[bc]	<.001
Decreased		41 (42)	1 (8)[a]	25 (39)[b]	15 (68)[ab]	.002
Basophil cell count, $\times 10^9$/L	0-0.06	0.01 (0.00-0.20)	0.025 (0.010-0.040)[a]	0.010 (0.003-0.020)[b]	0.00 (0.00-0.01)[ab]	<.001
Increased		1 (1)	1 (8)	0 (0)	0 (0)	.122
Procalcitonin, ng/mL	0-0.5					
>0.5		2 (2)	0 (0)	2 (3)	0 (0)	1.000
T lymphocyte count						
CD3+ cell count, /μL	955-2860	1057.0 (730.5-1400.3)	1419.0 (1101.0-1763.0)[a]	1086.0 (829.0-1440.0)[b]	651.0 (400.0-933.5)[ab]	<.001
Increased		1 (1)	1 (8)	0 (0)	0 (0)	.122
Decreased		37 (38)	1 (8)[a]	20 (31)[b]	16 (73)[ab]	<.001
CD4+ cell count, /μL	550-1440	566.0 (428.3-754.0)	747.0 (616.0-952.0)[a]	571.5 (467.3-786.5)[b]	322.0 (195.5-562.0)[ab]	<.001
Increased		1 (1)	1 (8)	0 (0)	0 (0)	.122
Decreased		42 (43)	2 (17)[a]	24 (38)[b]	16 (73)[ab]	.002
CD8+ cell count, /μL	320-1250	337.5 (230.8-505.5)	526.0 (483.0-762.0)[a]	376.0 (275.0-505.5)[b]	207.0 (100.0-302.5)[ab]	<.001

(Continues)

TABLE 2 (Continued)

	Normal Range	Median (IQR) or No (%)				
		Total (N = 98)	Mild (N = 12)	Moderate (N = 64)	Severe/critical (N = 22)	*P* value
Increased		1 (1)	1 (8)	0 (0)	0 (0)	.122
Decreased		38 (39)	1 (8)[a]	21 (33)[b]	16 (73)[ab]	<.001
Liver function						
Alanine aminotransferase (ALT), U/L	7-40	16.5 (10.9-29.1)	20.0 (10.6-50.2)	15.5 (9.7-26.5)	19.6 (14.2-29.1)	.223
Increased		14 (14)	5 (42)[a]	6 (9)[a]	3 (14)	.020
Decreased		5 (5)	2 (17)	2 (3)	1 (5)	.138
Aspartate aminotransferase (AST), U/L	13-35	21.0 (15.2-29.2)	23.4 (14.1-29.1)	19.4 (14.5-27.3)	24.4 (20.0-32.6)	.106
Increased		10 (10)	2 (17)	4 (6)	4 (18)	.145
Decreased		11 (11)	1 (8)	9 (14)	1 (5)	.635
AST/ALT	–	1.20 (0.91-1.60)	0.92 (0.59-1.46)	1.22 (0.96-1.68)	1.22 (0.94-1.56)	.362
Total bilirubin, μmol/L	3-24	8.23 (5.56-10.64)	8.62 (5.32-10.89)	7.16 (5.19-10.40)	8.64 (6.9-11.7)	.177
Decreased		2 (2)	0 (0)	1 (2)	1 (5)	.576
Direct bilirubin, μmol/L	0-8	3.05 (2.27-4.30)	3.33 (2.24-4.06)	3.00 (2.19-4.15)	3.58 (2.83-5.82)	.146
Increased		1 (1)	0 ()	1 (2)	0 (0)	1.000
Indirect bilirubin, μmol/L	–	4.50 (2.97-6.41)	5.28 (3.08-6.89)	4.11 (2.91-6.42)	5.43 (3.97-6.34)	.343
Total protein, g/L	65-85	69.20 (66.46-72.70)	69.1 (66.2-74.3)	70.0 (67.7-73.0)	67.0 (62.7-71.6)	.055
Increased		1 (1)	0 (0)	1 (2)	0 (0)	1.000
Decreased		16 (16)	2 (17)	8 (13)	6 (27)	.299
Albumin, g/L	40-55	39.90 (37.40-42.73)	42.5 (39.0-43.7)[a]	40.4 (38.5-43.0)[b]	36.6 (35.8-39.9)[ab]	<.001
Decreased		51 (52)	4 (33)	30 (47)[a]	17 (77)[a]	.019
Globulin, g/L	–	29.33 (26.81-31.58)	29.3 (24.5-30.5)	29.1 (26.9-31.6)	30.5 (26.3-32.8)	.548
Albumin/globulin	1.2-2.4	1.37 (1.21-1.53)	1.43 (1.36-1.76)[a]	1.37 (1.25-1.58)[b]	1.21 (1.11-1.41)[ab]	.006
Decreased		22 (22)	1 (8)	10 (16)[a]	11 (50)[a]	.003
Total bile acid	–	5.41 (3.36-8.92)	7.45 (4.30-13.84)	5.24 (3.32-9.01)	5.50 (3.13-7.29)	.351
Increased		16 (16)	3 (25)	10 (16)	3 (14)	.710
Kidney function						
Urea, mmol/L	3.6-9.5	3.75 (2.90-4.40)	3.35 (3.05-4.43)	3.45 (2.63-4.25)	4.10 (3.73-4.70)	.053
Increased		2 (2)	0 (0)	1 (2)	1 (5)	.576
Decreased		19 (19)	1 (8)	16 (25)	2 (9)	.214
Creatinine, μmol/L	57-111	58.70 (49.85-72.20)	70.3 (53.6-76.5)	55.7 (47.8-69.3)[a]	67.9 (56.5-76.4)[a]	.023
Increased		10 (10)	2 (17)	5 (8)	3 (14)	.407
Decreased		8 (8)	1 (8)	7 (11)	0 (0)	.262

(Continues)

TABLE 2 (Continued)

		Median (IQR) or No (%)				
	Normal Range	Total (N = 98)	Mild (N = 12)	Moderate (N = 64)	Severe/critical (N = 22)	*P* value
Uric acid, μmol/L	180-450	277.0 (239.5-345.0)	324.0 (262.8-363.5)	269.0 (236.5-357.8)	285.5 (234.5-330.5)	.494
Increased		23 (24)	3 (25)	16 (25)	4 (18)	.802
Decreased		1 (1)	0 (0)	1 (2)	0 (0)	1.000
Urea/Creatinine	–	58.90 (47.37-73.14)	51.03 (41.67-64.75)	59.71 (48.65-73.66)	63.6 (48.9-71.1)	.350
Biochemistry						
Lactic dehydrogenase, U/L	120-250	167.5 (140.5-201.3)	148.5 (123.3-174.8)[a]	162.5 (134.0-197.5)[b]	193.5 (156.3-229.5)[ab]	.003
Increased		11 (11)	0 (0)	6 (9)	5 (23)	.128
Decreased		4 (4)	1 (8)	3 (5)	0 (0)	.423
α-Hydroxybutyric dehydrogenase, U/L	72-182	128.0 (107.0-155.0)	122.5 (104.8-138.3)	125.0 (104.5-155.0)	141.5 (121.8-188.0)	.051
Increased		14 (14)	1 (8)	7 (11)	6 (27)	.163
Decreased		2 (2)	0 (0)	1 (2)	1 (2)	.576
Creatine kinase, U/L	26-192	68.0 (50.8-92.5)	71.0 (47.5-90.0)	68.0 (52.0-91.0)	76.5 (48.5-111.8)	.733
Increased		3 (3)	0 (0)	2 (3)	1 (5)	1.000
Decreased		3 (3)	0 (0)	2 (3)	1 (5)	1.000
D-dimer, ng/mL	0-243	100.0 (51.0-156.0)	118.0 (28.0-166.0)	83.0 (43.8-127.3)[a]	164.5 (101.3-319.8)[a]	.001
Increased		13 (13)	1 (8)	5 (8)[a]	7 (32)[a]	.026
C-reactive protein, mg/L	0.068-8.2	3.935 (0.598-14.910)	0.555 (0.073-1.363)[a]	2.700 (0.575-7.878)[b]	24.295 (7.900-39.860)[ab]	<.001
Increased		33 (34)	1 (8)[a]	15 (23.4)[b]	17 (77)[ab]	<.001
Decreased		4 (4)	3 (25)[a]	0 (0)[a]	1 (5)	.001

Note: a, b and c, there were statistical significances between groups

involvement (87% vs 45%, $P < .001$), ground-glass opacity (87% vs 61%, $P < .001$), mixed ground-glass opacity and patchy shadows (91% vs 58%, $P < .001$), and hydrothorax (27% vs 2%, $P = .001$) in the severe/critical group was conspicuously higher than that in moderate group. There were no significant differences in the conditions of tuberculosis and emphysema between the two groups. No obvious enlargement of lymph nodes or pulmonary fibrosis was found.

3.5 | Risk factors and prediction models

Table 5 showed the risk factors and correlation coefficient of the severity of Covid-19, which were evaluated by the spearman correlation and univariate logistic analysis. BNP ($r = 0.648$, $P < .001$), lobular involvement score ($r = 0.647$, $P < .001$), lobe numbers ($r = 0.607$, $P < .001$), incidence of more than two lobes involvement ($r = 0.52$, $P < .001$), CRP ($r = 0.505$, $P < .001$), mixed ground glass and patch shadow presentation ($r = 0.5$, $P < .001$), bilateral lung involvement ($r = 0.495$, $P < .001$), age ($r = 0.463$, $P < .001$), ground glass shadow presentation ($r = 0.46$, $P < .001$), abnormal electrocardiogram presentation ($r = 0.392$, $P = .005$), cTnI ($r = 0.376$, $P < .001$), hydrothorax ($r = 0.371$, $P < .001$), lactic dehydrogenase ($r = 0.342$, $P = .001$) and whether had comorbidities ($r = 0.305$, $P = .002$) were positively correlated with the severity of Covid-19. On the other hand, CD8+ cell count ($r = -0.525$, $P < .001$), CD3+ cell count ($r = -0.512$, $P < .001$), platelet count ($r = -0.463$, $P < .001$), lymphocyte cell count ($r = -0.457$, $P < .001$), CD4+ cell count ($r = -0.437$, $P < .001$), basophil cell count ($r = -0.428$, $P < .001$), eosinophil cell count ($r = -0.402$, $P < .001$), albumin ($r = -0.379$, $P < .001$), and the ratio of albumin/globulin ($r = -0.321$, $P = .001$) were negatively correlated with the severity of Covid-19.

The above factors were analysed and adjusted by logistic regression analysis, and then three diagnostic models were obtained to distinguish between severe/critical and moderate of Covid-19. Model 1: $Logit\ (P) = -2.942 + 0.311\ X$, ($X$ = Lobular involvement score); ROC curve: area under curve (AUC), 0.832 (95%CI: 0.725-0.939,

TABLE 3 Myocardial injury associated with Covid-19 during hospitalisation

	Normal range	Total	Mild	Moderate	Severe/critical	*P* value
Myocardial injury marker		Median (IQR) or No (%)				
B-type natriuretic peptide (BNP) (pg/mL)	0-125	119.0 (54.0-392.0)	66.0 (28.8-76.5)[a]	77.0 (49.5-176.5)[b]	1076.0 (247.8-2577.5)[ab]	<.001
Increased		40 (42)	1 (8)[a]	18 (29)[b]	21 (96)[ab]	<.001
Cardiac troponin I (cTnI)	0-0.0229					
N > 0.0229, No. (%)		7 (7)	0 (0.0)	1 (2)[a]	6 (27)[a]	.002
Creatine kinase-MB (CK-MB) (U/L)	0-25	17.4 (14.5-23.1)	17.3 (13.5-23.1)	17.8 (15.4-23.4)	16.7 (13.3-22.5)	.707
Increased		17 (18)	2 (17)	11 (18)	4 (18)	1.000
Electrocardiograph (ECG) presentation		N = 49	N = 6	N = 29	N = 14	
Abnormal ECG		25 (51.0)	1 (17)[a]	13 (45)	11 (79)[a]	.027
Sinus tachycardia		1 (2)	0 (0)	0 (0)	1 (7)	.408
Sinus bradycardia		2 (4)	0 (0)	0 (0)	2 (14)	.162
Ventricular premature beat		1 (2)	0 (0)	0 (0)	1 (7)	.408
Left deviation		2 (4)	0 (0)	2 (7)	0 (0)	1.000
Right deviation		1 (2)	0 (0)	1 (3)	0 (0)	1.000
Abnormal q/Q wave		10 (20)	1 (17)	6 (21)	3 (21)	1.000
Abnormal r wave		14 (29)	1 (17)	6 (21)	7 (50)	.137
Low voltage of limb lead		2 (4)	0 (0)	1 (3)	1 (7)	1.000
R wave increases poorly in chest lead		1 (2)	0 (0)	1 (3)	0 (0)	1.000
ST-segment elevation		1 (2)	0 (0)	0 (0)	1 (7)	.408
ST-segment depression		1 (2)	0 (0)	0 (0)	1 (7)	.408
T wave changes		5 (10)	0 (0)	2 (7)	3 (21)	.374

Note: a and b, there were statistical significances between groups

$P < .001$); cut-off, 0.43; sensitivity, 68.2%; specificity, 90.6%. Model 2: *Logit (P)* = −5.905 + 0.059 X_1 + 0.285 X_2, (X_1 = Age, X_2 = Lobular involvement score); ROC curve: AUC, 0.876 (95%CI: 0.800-0.952, $P < .001$); cut-off, 0.19; sensitivity, 86.4%; specificity, 78.1%. Model 3: *Logit (P)* = −3.504 + 0.53 X_1 + 0.266 X_2-1.428 X_3 (X_1 = Age; X_2 = Lobular involvement score; and X_3 = Lymphocyte cell count); ROC curve: AUC, 0.903 (95%CI: 0.838-0.967, $P < .001$); cut-off value, 0.18; sensitivity, 90.9%; specificity, 78.1% (Figure 2).

3.6 | Treatments

The therapeutic regimens were shown in Table 6. Antiviral medications included lopinavir (60%), chloroquine (55%), abidor (41%), oseltamivir (29%) and recombinant human interferon (16%). Antibacterial infections contained moxifloxacin (49%), levofloxacin (21%), ceftriaxone sodium (19%), cefoperazone and sulbactam sodium (11%), and linezolid (12%), while meropenem and vancomycin were mainly used in critically ill patients. Human immunoglobulin (54%), human blood albumin (51%), thymalfasin (42%), vitamin C (34%) and gamma globulin (12%) were used to improve patients' immunity. Trimetazidine hydrochloride (39%), coenzyme Q (37%) and dipyridamole (16%) were prescribed for improving myocardial nutrition and metabolism. In addition, antifungal drugs are mainly used to treat critically ill patients. Some severe/critical patients were treated with respiratory humidification (36%) and noninvasive assisted ventilation (55%), while extracorporeal membrane oxygenation (ECMO), tracheotomy, intubation and ventilator assisted breathing were mainly used for the treatment of critically ill patients. One moderate patient required noninvasive ventilation because of the underlying disease of the previous bronchiectasis.

The outcomes and complications of these patients were shown in Table 1. Ninety-seven patients were discharged, and one patient was dead. The total hospitalised duration was 18 (14-23) days. Fifteen (15%) patients have complications, including acute respiratory distress syndrome (8%), septic shock (3%), pneumothorax/hydrothorax (2%), abnormal liver function (4%), viral myocarditis (1%), viral esophagitis (1%), hypokalaemia (3%), hyperkalaemia (1%), hyponatraemia

TABLE 4 Evaluation of CT presentations of patients infected with Covid-19

	Median (IQR) or No. (%)				
	Total	Mild	Moderate	Severe/critical	*P* value
Radiologic findings					
Lobular involvement score	2.0 (0.0-7.0)	0.0 (0.0-0.0)	2.0 (1.0-5.0)	10.5 (5.8-12.0)	<.001
Right side					
Superior score	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	2.0 (1.0-3.0)	<.001
Superior involvement	41 (42)	0 (0)	23 (36)	18 (82)	<.001
Medial score	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	1.5 (0.8-2.0)	<.001
Medial involvement	34 (35)	0 (0)	17 (27)	17 (77)	<.001
Inferior score	1.0 (0.0-2.0)	0.0 (0.0-0.0)	1.0 (0.0-2.0)	2.0 (1.0-3.0)	<.001
Inferior involvement	54 (55)	0 (0)	36 (56)	18 (82)	.041
Left side					
Superior score	0.0 (0.0-1.3)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	2.0 (1.0-2.0)	<.001
Superior involvement	46 (47)	0 (0)	26 (41)	20 (91)	<.001
Inferior score	1.0 (0.0-2.0)	0.0 (0.0-0.0)	1.0 (0.0-2.0)	2.0 (1.0-3.0)	<.001
Inferior involvement	58 (59)	0 (0)	38 (59)	20 (91)	.008
Number of lobes	2.0 (0.0-5.0)	0.0 (0.0-0.0)	2.0 (1.0-4.0)	5.0 (4.0-5.0)	<.001
More than two lobes	43 (44)	0 (0)	24 (38)	19 (86)	<.001
Bilateral involvement	48 (49)	0 (0)	29 (45)	19 (86)	.001
Ground glass opacity	58 (59)	0 (0)	39 (61)	19 (86)	.028
Patchy shadows	11 (11)	0 (0)	6 (9)	5 (23)	.212
Mixed ground glass opacity+ patchy shadows	57 (58)	0 (0)	37 (58)	20 (91)	.005
Hydrothorax	7 (7)	0 (0)	1 (2)	6 (27)	.001
Enlargement of lymph nodes	0 (0)	0 (0)	0 (0)	0 (0)	–
Tuberculosis	2 (2)	0 (0)	1 (2)	1 (5)	1.000
Emphysema	9 (9)	0 (0)	6 (9)	3 (14)	.873
Pulmonary fibrosis	0 (0)	0 (0)	0 (0)	0 (0)	–

Note: Only the moderate and severe/critical groups were compared.

(2%), hypoproteinaemia (2%), mild anaemia (3%), granulocytopoenia (1%), three series (red blood cells, white blood cells and platelets) decreased (1%). There were conspicuous differences in whether had complications (6% vs 46%, $P < .001$), acute respiratory distress syndrome (ARDS) (0% vs 36%, $P < .001$) and septic shock (0% vs 14%, $P = .021$) between the moderate and the severe/critical group. It was worth mentioning that ARDS, septic shock, pneumothorax/pleural effusion, viral myocarditis, viral esophagitis, hypoproteinaemia and granulocytopoenia occurred only in severe/critical patients, and the incidences of ARDS (0% vs 36%, $P < .001$) and septic shock (0% vs 14%, $P = .021$) was significantly higher than that of moderate patients. On the other hand, 17% and 7% of patients presented anxiety and depression during hospitalisation, respectively.

4 | DISCUSSION

The main findings for this cohort were as follows: Covid-19 confirmed patients were mainly imported, cluster, or infected by close contact. The apparent risk factors of age >60 years, chronic comorbidities, lymphocytopoenia and lobular involvement score were malignantly associated with the severity of Covid-19, which was not parallel to the degree of fever. The inflammation induced by Covid-19 caused the myocardial injury, which was demonstrated by elevated BNP and cTnI level, and abnormal electrocardiograms. The valid logistic model, adjusted by the risk factors of age, lymphocytopoenia, and lobular involvement score, was firstly reported and applied for evaluating the severity of Covid-19, verified by the ROC curve.

Zhuhai, close to Macau, is a famous seaside-tourism city, of which the epidemiological characteristics were different from that in Beijing.[3] The median incubation period was five days, consistent with the previous reports.[4] There were 5% of patients with the incubation period exceeding 14 days, and the most prolonged period was 27 days, suggesting that a longer duration of medical observation or active monitoring of quarantining contractors may be needed. The previous research showed that Covid-19 was more likely to infect older adult males with chronic comorbidities.[5] More details were analysed in our study and showed that age and chronic comorbidities,

TABLE 5 The correlation and univariate logistic analysis of risk factors and CT score for evaluating the severity of Covid-19

	Spearman Correlation		Logistic regression		
Risk factors	r_s	*P*	**OR**	**95%CI**	*P*
Age	0.463	<0.001	–	–	–
Age>60-year-old	–	–	7.885	1.048-3.081	<.001
Comorbidities	0.305	0.002	4.104	0.479-2.344	.003
Hypertension	0.229	0.023	3.304	0.165-2.225	.023
Diabetes	0.228	0.024	5.714	0.172-3.314	.030
Pulmonary disease	0.228	0.024	5.714	0.172-3.314	.030
Heart diseases	0.254	0.012	8.491	0.367-3.910	.018
Symptoms	0.263	0.009	4.943	0.417-2.779	.008
Fever	0.216	0.032	2.638	0.092-1.848	.030
Fatigue	0.265	0.008	5.697	0.496-2.985	.006
Platelet	−0.463	<0.001	–	–	–
Decreased	–	–	5.714	0.172-3.314	.030
Lymphocyte cell count	−0.457	<0.001	–	–	–
Decreased	–	–	5.104	0.632-2.628	.001
Eosinophil cell count	−0.402	<0.001	–	–	–
Decreased	–	–	4.909	0.656-2.526	.001
CD3+ cell count	−0.512	<0.001	–	–	–
Decreased	–	–	7.345	0.955-3.032	<.001
CD4+ cell count	−0.437	<0.001	–	–	–
Decreased	–	–	4.993	0.630-2.586	.001
CD8+ cell count	−0.525	<0.001	–	–	–
Decreased	–	–	7.050	0.919-2.986	<.001
Albumin	−0.379	<0.001	–	–	–
Decreased	–	–	3.401	0.332-2.117	.007
Albumin/globulin	−0.321	0.001	–	–	–
Decreased	–	–	5.557	0.700-2.729	.001
Creatinine	0.103	0.312	–	–	–
Increased	–	–	–	–	–
Lactic dehydrogenase	0.342	0.001	–	–	–
Increased	–	–	3.834	0.080-2.608	.037
α-Hydroxybutyric dehydrogenase	0.237	0.019	–	–	–
D-dimer	0.299	0.003	–	–	–
Increased	–	–	4.683	0.349-2.739	.011
C-reactive protein	0.505	<0.001	–	–	–
Increased	–	–	11.496	1.378-3.506	<.001
B-type natriuretic peptide	0.648	<0.001	27.440	1.770-4.854	<.001
Cardiac troponin I	0.376	<0.001	25.330	1.043-5.420	.004
Abnormal ECGs	0.392	0.005	5.709	0.448-3.036	.008
Lobular involvement score	0.647	<0.001	–	–	–
Lobular involvement score >6	–	–	15.120	1.610-3.822	<.001
Lobe numbers	0.607	<0.001	–	–	–
More than two lobes	0.520	<0.001	17.975	1.604-4.174	<.001
Bilateral lung involvement	0.495	<0.001	15.425	1.463-4.009	<.001
Ground glass shadow	0.460	<0.001	–	–	–

(Continues)

TABLE 5 (Continued)

	Spearman Correlation		Logistic regression		
Risk factors	r_s	*P*	OR	95%CI	*P*
Patch shadow	0.217	0.032	3.834	0.080-2.608	<.001
Both ground glass shadow and patch shadow	0.500	<0.001	21.889	1.582-4.590	<.001
Hydrothorax	0.371	<0.001	28.361	1.157-5.533	.003

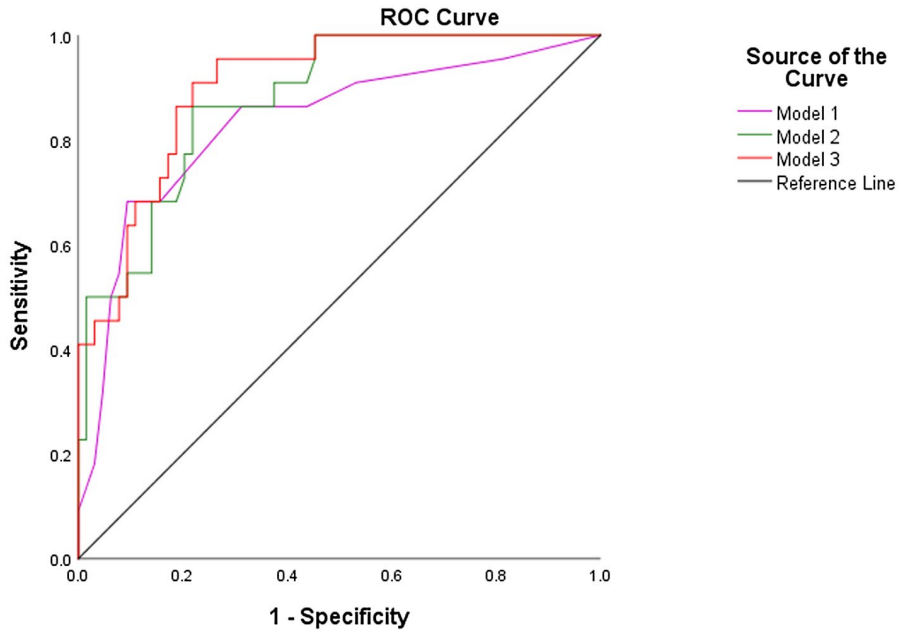

FIGURE 2 The ROC curves for the three logistic models. Model 1: *Logit (P)* = −2.942 + 0.311*X*, (*X* = Lobular involvement score); ROC curve: AUC, 0.832 (95%CI: 0.725-0.939, *P* < .001); cut-off, 0.43; sensitivity, 68.2%; specificity, 90.6%. Model 2: *Logit (P)* = −5.905 + 0.059X_1 + 0.285X_2, (X_1 = Age, X_2 = Lobular involvement score); ROC curve: AUC, 0.876 (95%CI: 0.800-0.952, *P* < .001); cut-off, 0.19; sensitivity, 86.4%; specificity, 78.1%. Model 3: *Logit (P)* = −3.504 + 0.53 X_1 + 0.266 X_2-1.428X_3 (X_1 = Age; X_2 = Lobular involvement score; and X_3 = lymphocyte cell count); ROC curve: AUC, 0.903 (95%CI: 0.838-0.967, *P* < .001); cut-off value, 0.18; sensitivity, 90.9%; specificity, 78.1%

including hypertension, diabetes, pulmonary and heart diseases, were important risk factors associated with the severity of Covid-19. Especially, age older than 60 years and chronic diseases would obviously increase the risk of severity by 7.9 and 3.3-fold. Hypertension was one of the most common comorbidities in our study and previous research.[6]

The typical main symptoms of Covid-19 include fever, cough, sputum production, pharyngeal discomfort/pain, rhinorrhoea, myalgia/arthralgia and fatigue. The gastrointestinal symptoms, such as nausea and diarrhoea,[6] might be attributed to the potential gastrointestinal infection of Covid-19, reported by our centre.[7] One other thing to note was that although fever was the typical symptom of Covid-19,[8] only 84% of patients exhibited clinical symptoms on admission in our study, which was different from the data reported before.[9] Remarkably, our centre has reported that viral load in the asymptomatic patient was similar to that in symptomatic patients.[2] Besides, the degree of fever before admission was not parallel to the severity. Therefore the severity of Covid-19 could not be assessed by whether or not the fever was present or degrees of fever. Moreover, we found that only 58% of patients presented with fever, although part of the patients in the severe/critical group did not have a fever. It was noted that most of the patients with fever in severe/critical group were low-grade. Notably, patients with symptoms [odds ratio (OR): 4.94], particularly fever (OR: 2.64) and fatigue (OR: 5.70) tended to develop more severe pneumonia.

According to the previous study, the lymphocyte cell count of the non-survivor was significantly lower than that of survivor patients of Covid-19.[9] Our study also illustrated that the severity of Covid-19 was negatively correlated to the degree of lymphocytopoenia. In addition, consistent with previous researches,[4-6] the values of platelet, eosinophil count, basophil count, CD3+ cell count, CD4+ cell count, CD8+ cell count, albumin, and albumin/globulin were negatively correlated with the severity of Covid-19. In contrast, the values of creatinine, lactic dehydrogenase, α-hydroxybutyric dehydrogenase, D-dimer and CRP were positively correlated with the severity of Covid-19. The reasons for the above phenomena may be as follows: Firstly, Covid-19 may not only consume many immune cells[5] but also induce immunosuppression by elevating secretion of T-helper-2 cytokines,[10] which associated with the severity of Covid-19. Secondly, there were significant inflammatory reactions in infected patients,

TABLE 6 The details of therapy strategies of Covid-19

Therapies	No. (%)				*P* value
	Total	Mild	Moderate	Severe/critical	
Antiviral drugs					
Oseltamivir	28 (29)	2 (17)	16 (25)	10 (46)	.116
Lopinavir/ritonavir	59 (60)	3 (25)[ab]	40 (63)[b]	16 (73)[a]	.020
Chloroquine	54 (55)	7 (54)	38 (59)	9 (41)	.314
Ribavirin	2 (2)	0 (0)	0 (0)	2 (9)	.062
Arbidol	40 (41)	3 (25)	30 (47)	7 (32)	.228
Recombinant human Interferon α	16 (16)	1 (8)	9 (14)	6 (27)	.350
Antibacterial drugs					
Moxifloxacin	48 (49)	2 (17)[a]	26 (41)[b]	20 (91)[ab]	<.001
Levofloxacin	21 (21)	2 (17)	15 (23)	4 (18)	.935
Piperacillin and tazobactam sodium	6 (6)	0 (0)	2 (3)	4 (18)	.051
Cefoperazone and sulbactam sodium	11 (11)	0 (0)	2 (3)[a]	9 (41)[a]	<.001
Ceftazidime and avibactam sodium	1 (1)	0 (0)	0 (0)	1 (5)	.347
Cefprozil	1 (1)	0 (0)	1 (2)	0 (0)	1.000
Ceftriaxone	19 (19)	0 (0)	15 (23)	4 (18)	.184
Polymyxin B	1 (1)	0 (0)	0 (0)	1 (5)	.347
Linezolid	12 (12)	0 (0)	5 (8)[a]	7 (32)[a]	.009
Meropenem	3 (3)	0 (0)	0 (0)[a]	3 (14)[a]	.021
Vancomycin	2 (2)	0 (0)	0 (0)	2 (9)	.062
Teicoplanin	1 (1)	0 (0)	0 (0)	1 (5)	.347
Voriconazole	3 (3)	0 (0)	0 (0)[a]	3 (14)[a]	.021
Fluconazole	4 (4)	0 (0)	1 (2)	3 (14)	.070
Improve immunity					
Vitamin C	31 (32)	3 (25)	20 (31)	8 (36)	.850
Thymalfasin	41 (42)	2 (17)	28 (44)	11 (50)	.148
γ-globulin	12 (12)	1 (8)	6 (9)	5 (23)	.229
Human immunoglobulin	53 (54)	4 (33)	32 (50)	17 (77)	.026
Human albumin	50 (51)	3 (25)[a]	25 (39)[b]	0 (0)[ab]	<.001
Caspofungin	3 (3)	0 (0)	0 (0)[a]	3 (14)[a]	.021
Glucocorticoid drug					
Methylprednisolone	6 (6)	0 (0)	4 (6)	2 (9)	.681
Myocardial nutrition					
Creatine phosphate sodium	5 (5)	0 (0)	1 (2)[a]	4 (18)[a]	.023
Trimetazidine	38 (39)	2 (17)	25 (39)	11 (50)	.162
Coenzyme Q10	36 (37)	1 (8)	25 (39)	10 (46)	.081
Dipyridamole	16 (16)	3 (25)	12 (19)	1 (5)	.156
Other therapies					
Extracorporeal membrane oxygenation	1 (1)	0 (0)	0 (0)	1 (5)	.347
High flow breathing humidification therapy instrument	8 (8)	0 (0)	0 (0)[a]	8 (36)[a]	<.001
Noninvasive ventilation	13 (13)	0 (0)[a]	1 (2)[b]	12 (55)[ab]	<.001
Tracheal intubation	2 (2)	0 (0)	0 (0)	2 (9)	.062
Mechanical ventilation	2 (2)	0 (0)	0 (0)	2 (9)	.062
Tracheotomy	1 (1)	0 (0)	0 (0)	1 (5)	.347

Note: a and b, there were statistical significances between groups.

especially in severe patients, who were prone to cytokine storms because of activated T-helper-1 cell responses.[10] Thirdly, according to the previous reports,[11,12] liver dysfunction occultly induced by liver inflammation related to Covid-19 slightly affected albumin synthesis. Myocardial injury was observed in moderate and especially severe/critical patients, with the apparent elevated BNP and cTnI, as well as the increased incidence of abnormal electrocardiograms. Similar to the severe acute respiratory syndrome coronavirus, Covid-19 could downregulate the angiotensin-converting enzyme 2 (ACE2) of myocardial tissue, which therefore mediated myocardial inflammation and damage.[13-15]

Initial CT scans for lungs played a crucial role in the discrimination in the moderate and severe/critical Covid-19. Increasing numbers, extent and density of ground glass shadow on CT indicated disease progression.[16,17] We found that the values of lobular involvement score, lobe numbers and the percentage of more than two lobes involvement, bilateral lung involvement, ground glass shadow, both ground glass shadow, and patch shadow were strongly and positively correlated with the severity of Covid-19. Recent research showed that the CT score was associated with the severity of Covid-19, of which AUC, sensitivity and specificity of the ROC curve were 0.87, 80.0% and 82.8%, respectively.[18] Different from this study, we firstly reported that the logistic model, including risk factors of age, lobular involvement score and lymphocyte cell counts, was used for assessing the severity of pneumonia of Covid-19, with the largest AUC of 0.903 and highest sensitivity of 90.9%, and the specificity of 78.1%. This model may be more suitable for clinical application. Additionally, different from previous report,[19] our study showed that not only the inferior lobes but also superior and medial lobes of the lung would be involved in moderate patients of Covid-19. Most of the severe/critical patients in our study presented mixed ground glass and patchy shadow, involving in the bilateral lung, more than two lobes, and any lobes.

There were some limitations in our study. Firstly, the clinical prognosis, including complete pneumonia absorption and negative nucleic acid detection, requires long-term follow-up. Secondly, it was not excluded that the abnormal electrocardiograms had existed before infection of Covid-19 in some patients. Thirdly, it was needed to evaluate further the effect of the logistic model on the long-term prognosis of Covid-19. Fourthly, CT score might be underestimated because of multiple, diffuse patchy and absorption of lesions on admission.

5 | CONCLUSION

Covid-19 confirmed patients were mainly imported, cluster, or infected by close contact, with low mortality and higher discharged rate. The risk factors of age >60 years old, chronic comorbidities, lymphocytopoenia, and lobular involvement score were malignantly associated with the Covid-19 severity, which was not parallel to the degree of fever. The inflammation induced by Covid-19 caused the myocardial injury with elevated BNP and cTnI level and abnormal electrocardiograms. Progression of Covid-19 was strongly associated with the prognosis. Therefore, early diagnosis, identification and management of these patients with indicators to develop severe or critically Covid-19 collectively play essential roles in the reduction of mortality.

ACKNOWLEDGEMENTS

None.

DISCLOSURES

The authors of this study declare that they each have no conflict of interest.

AUTHOR CONTRIBUTIONS

YBL, ZQZ and XFL designed the study, as well as contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content and approved the final version of the manuscript. JNH, YBL, JBG and WLZ contributed equally and were responsible for statistical analysis, data interpretation, tables and manuscript drafting. RLF, QRL, XMC and JMH assisted in clinical data collection and analyses. ZQZ, JBG and ZY contributed to the CT quantitative analyses and figures.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

DATA AVAILABILITY STATEMENT

The data used in this study is not publicly available, but it might be available from the corresponding author upon reasonable request and permission from relevant Chinese Authorities.

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How to cite this article: Huang J, Gao J, Zhu W, et al. Indicators and prediction models for the severity of Covid-19. *Int J Clin Pract*. 2021;75:e14571. https://doi.org/10.1111/ijcp.14571