Indicators and prediction models for the severity of Covid-19

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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, lymphocytopenia 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.

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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.

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. 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.

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, lymphocytopenia 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 cTnl level and abnormal electrocardiograms, which was firstly reported.

(2) Moderate: fever, respiratory symptoms, etc. CT presented with pneumonia. (3) Severe: complied any of the following: ① anhela- tion, respiratory rate ≥30/min; ② at rest, oxygen saturation ≤93%; ③ PaO2 /FiO2 ≤ 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. 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
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 moderate 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°C-38°C), 15% of moderate fever (38.1°C-39°C), and 1% of high fever (39.1°C-41°C). 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)**        |                         |                |              |                  |                          |         |
| 0-20                   | 44.0 (33.0-62.3)        | 29.0 (15.0-42.3) | 7 (11)       | 42.0 (33.0-59.0) | 63.0 (50.0-67.5) | <.001   |
| 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)          | 13 (20)      | 13 (59)          |                          | <.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**           |                         |                |              |                  |                          | .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**      |                         |                |              |                  |                          |         |
| 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)         | 53 (84)      | 21 (96)          |                          | .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°C-38°C            | 41 (42)                 | 4 (33)         | 25 (39)      | 12 (55)          |                          |         |
| 38.1°C-39°C            | 15 (15)                 | 1 (8)          | 9 (14)       | 5 (23)           |                          |         |
| 39.1°C-41°C            | 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)
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 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/artralgia    | 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

- 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
- Granulocytopenia: 1 (1) | 0 (0) | 0 (0) | 1 (5) | .347
- Three series decreased: 1 (1) | 0 (0) | 1 (2) | 0 (0) | 1.000

Treatment outcomes

- 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

\(^a\) and \(^b\), there were statistical significances between groups

Median (IQR) or No. (%)
TABLE 2  The laboratory examinations in patients of Covid-19

|                  | Normal Range | Total (N = 98) | Mild (N = 12) | Moderate (N = 64) | Severe/critical (N = 22) | P value |
|------------------|--------------|----------------|---------------|-------------------|--------------------------|---------|
| Blood routine    |              |                |               |                   |                          |         |
| White blood cell count, ×10⁹/L | 3.5-9.5 (4.06-6.61) | 5.19 (4.65-7.38) | 6.18 (4.06-6.60) | 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 (126.0-150.0) | 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) | 198.0 (179.3-276.0) | 149.0 (131.8-175.0) | <.001   |
| Increased        | 7 (7)        | 2 (17)         | 5 (8)         | 0 (0)             | .132                      |         |
| Decreased        | 7 (7)        | 0 (0)          | 3 (5)         | 4 (18)            | .095                      |         |
| Lymphocyte cell count, ×10⁹/L | 1.1-3.2 (1.12-2.10) | 1.60 (1.65-3.05) | 2.25 (1.65-3.05) | 1.70 (1.23-2.21) | 1.15 (0.89-1.53) | <.001   |
| Increased        | 7 (7)        | 2 (17)         | 5 (8)         | 0 (0)             | 1.000                     |         |
| Decreased        | 23 (24)      | 1 (8)          | 11 (17)       | 11 (50)           | .003                      |         |
| Neutrophil cell count, ×10⁹/L | 1.8-6.3 (2.11-3.87) | 2.85 (2.22-4.09) | 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, ×10⁹/L | 0.1-0.6 (0.38-0.67) | 0.49 (0.41-0.83) | 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                      |         |
| Decreased        | 41 (42)      | 1 (8)          | 25 (39)       | 15 (68)           | .002                      |         |
| Eosinophil cell count, ×10⁹/L | 0.02-0.52 (0.00-0.800) | 0.020 (0.040-0.205) | 0.090 (0.040-0.205) | 0.030 (0.000-0.078) | 0.01 (0.00-0.03) | <.001   |
| Increased        | 0.01 (0.00-0.20) | 0.025 (0.010-0.040) | 0.010 (0.003-0.020) | 0.00 (0.00-0.01) | .122                      |         |
| Procalcitonin, ng/mL | 0-0.5 | 2 (2) | 0 (0) | 2 (3) | 0 (0) | 1.000 |
| T lymphocyte count | 955-2860 | 1057.0 (730.5-1400.3) | 1419.0 (1101.0-1763.0) | 1086.0 (829.0-1440.0) | 651.0 (400.0-933.5) | <.001   |
| CD3+ cell count, /μL | Increased | 1 (1) | 1 (8) | 0 (0) | 0 (0) | .122 |
| CD4+ cell count, /μL | Decreased | 37 (38) | 1 (8) | 20 (31) | 16 (73) | <.001 |
| CD8+ cell count, /μL | Increased | 1 (1) | 1 (8) | 0 (0) | 0 (0) | .122 |
| CD19+ cell count, /μL | Decreased | 42 (43) | 2 (17) | 24 (38) | 16 (73) | .002 |

(Continues)
| 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)       | 16 (73)          | <.001                   |        |
| Decreased    | 38 (39)                | 1 (8)          | 21 (33)     | 16 (73)          | <.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)          | 6 (9)         | 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 (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 |

| Albumin, g/L | 40-55 | 39.90 (37.40-42.73) | 42.5 (39.0-43.7) | 40.4 (38.5-43.0) | 36.6 (35.8-39.9) | <.001 |
| Decreased       | 51 (52) | 4 (33)         | 30 (47)        | 17 (77)         | .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) | 1.37 (1.25-1.58) | 1.21 (1.11-1.41) | .006 |
| Decreased       | 22 (22) | 1 (8)          | 10 (16)         | 11 (50)         | .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 |

| Creatinine, μmol/L | 57-111 | 58.70 (49.85-72.20) | 70.3 (53.6-76.5) | 55.7 (47.8-69.3) | 67.9 (56.5-76.4) | .023 |
| Increased       | 10 (10) | 2 (17)         | 5 (8)          | 3 (14)          | .407 |

(Continues)
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 (\( r = 0.392, P = .005 \)), cTnl (\( r = 0.376, P < .001 \)), 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 2 (Continued)

| Normal Range | Total (\( N = 98 \)) | Mild (\( N = 12 \)) | Moderate (\( N = 64 \)) | Severe/critical (\( N = 22 \)) | \( P \) value |
|--------------|----------------------|---------------------|------------------------|-----------------------------|--------------|
| Uric acid, \( \mu \text{mol/L} \) | 180-450 | 277.0 (239.5-345.0) | 324.0 (262.8-363.5) | 269.0 (236.5-357.8) | 285.0 (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 |

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

### Biochemistry

| Normal Range | Total (\( N = 98 \)) | Mild (\( N = 12 \)) | Moderate (\( N = 64 \)) | Severe/critical (\( N = 22 \)) | \( P \) value |
|--------------|----------------------|---------------------|------------------------|-----------------------------|--------------|
| Lactic dehydrogenase, U/L | 120-250 | 167.5 (140.5-201.3) | 148.5 (123.3-174.8) | 162.5 (134.0-197.5) | 193.5 (156.3-229.5) | .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 (82.0-166.0) | 83.0 (43.8-127.3) | 164.5 (101.3-319.8) | .001 |
| Increased | 13 (13) | 1 (8) | 5 (8) | 7 (32) | .026 |
| C-reactive protein, mg/L | 0.068-8.2 | 3.935 (0.598-14.910) | 0.555 (0.073-1.363) | 2.700 (0.575-7.878) | 24.295 (7.900-39.860) | <.001 |
| Increased | 33 (34) | 1 (8) | 15 (23.4) | 17 (77.7) | <.001 |
| Decreased | 4 (4) | 3 (25) | 0 (0) | 1 (5) | .001 |

Note: a, b and c, there were statistical significances between groups.
TABLE 3 Myocardial injury associated with Covid-19 during hospitalisation

| Myocardial injury marker | Normal range | Total | Mild | Moderate | Severe/critical | P value |
|--------------------------|--------------|-------|------|----------|-----------------|---------|
| B-type natriuretic peptide (BNP) (pg/mL) | 0-125 | Median (IQR) or No (%) | 119.0 (54.0-392.0) | 66.0 (28.8-76.5) | 77.0 (49.5-176.5) | 1076.0 (247.8-2577.5) | <.001 |
| Increased | 40 (42) | 1 (8) | 18 (29) | 21 (96) | <.001 |
| Cardiac troponin I (cTnI) | 0-0.0229 | 0.0229 | 0.0 | 0.43 | 0.032 |
| N > 0.0229, No. (%) | 7 (7) | 0 (0.0) | 1 (2) | 6 (27) | <.001 |
| 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) | <.001 |
| Increased | 17 (18) | 2 (17) | 11 (18) | 4 (18) | 1.000 |

**Electrocardiograph (ECG) presentation**

| Abnormal ECG | N = 49 | N = 6 | N = 29 | N = 14 |
|--------------|-------|------|-------|-------|
| Abnormal q/Q wave | 10 (20) | 1 (17) | 6 (21) | 3 (21) |
| Abnormal r wave | 14 (29) | 1 (17) | 6 (21) | 7 (50) |
| Low voltage of limb lead | 2 (4) | 0 (0) | 1 (3) | 1 (7) |
| R wave increases poorly in chest lead | 1 (2) | 0 (0) | 1 (3) | 0 (0) |
| ST-segment elevation | 1 (2) | 0 (0) | 0 (0) | 1 (7) |
| ST-segment depression | 1 (2) | 0 (0) | 0 (0) | 1 (7) |
| T wave changes | 5 (10) | 0 (0) | 2 (7) | 3 (21) |

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 + 0.059X1 + 0.285X2, (X1 = Age, X2 = 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 + 0.53X1 + 0.266X2 + 1.428X3, (X1 = Age; X2 = Lobular involvement score; and X3 = 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%), abidir (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 (1%), and ischaemic heart disease (1%).
(2%), hypoproteinaemia (2%), mild anaemia (3%), granulocytopenia (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 granulocytopenia 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, lymphocytopenia 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, lymphocytopenia, 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 4 Evaluation of CT presentations of patients infected with Covid-19 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|---------------|
|                            | Total (IQR) or No. (%) | Mild (0.0-0.0) | Moderate (1.0-5.0) | Severe/critical (10.5-12.0) | \( P \) 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.
TABLE 5 The correlation and univariate logistic analysis of risk factors and CT score for evaluating the severity of Covid-19

| Risk factors               | Spearman Correlation | Logistic regression |
|----------------------------|----------------------|---------------------|
|                            | $r_s$    | $P$       | 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 | .111 |
| 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   | 23.330   | 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)
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, rhinorrhea, myalgia/arthritis and fatigue. The gastrointestinal symptoms, such as nausea and diarrhea, 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, only 84% of patients exhibited clinical symptoms on admission in our study, which was different from the data reported before.8 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 lymphocytopenia. In addition, consistent with previous researches, 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 but also induce immunosuppression by elevating secretion of T-helper-2 cytokines, which associated with the severity of Covid-19. Secondly, there were significant inflammatory reactions in infected patients,

### TABLE 5 (Continued)

| Risk factors                                      | Spearman Correlation | Logistic regression |
|---------------------------------------------------|----------------------|---------------------|
|                                                   | $r_s$    | $P$    | 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    | <.0001 | 21.889   | 1.582-4.590 | <.001 |
| Hydrothorax                                       | 0.371    | <.0001 | 28.361   | 1.157-5.533 | .003  |

### FIGURE 2
The ROC curves for the three logistic models. Model 1: Logit ($P$) = $-2.942 + 0.311X$, ($X =$ 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 ($P$) = $-3.504 + 0.53X_1 + 0.266X_2 - 1.428X_3$, ($X_1 =$ 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%.
| Therapies                              | No. (%)     | Total | Mild  | Moderate | Severe/critical | P value |
|---------------------------------------|-------------|-------|-------|----------|-----------------|---------|
| **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            |         |
| Cefotaxime and sulbactam sodium       | 11 (11)     | 0 (0)| 2 (3)a| 9 (41)a  | <.001           |         |
| Ceftazidine 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    | 8 (8)       | 0 (0)| 0 (0)a| 8 (36)a  | <.001           |         |
| therapy instrument                    |             |       |       |          |                 |         |
| 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. Thirdly, according to the previous reports, 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.

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. 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. 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, 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.

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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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