Clinical Characteristics of Patients With Progressive and Non-progressive Coronavirus Disease 2019: Evidence From 365 Hospitalised Patients in Honghu and Nanchang, China

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Background: Coronavirus disease (COVID-19) has swept around the globe and led to a worldwide catastrophe. Studies examining the disease progression of patients with non-severe disease on admission are scarce but of profound importance in the early identification of patients at a high risk of deterioration.

Objectives: To elucidate the differences in clinical characteristics between patients with progressive and non-progressive COVID-19 and to determine the risk factors for disease progression.

Study design: Clinical data of 365 patients with non-severe COVID-19 from 1 January 2020 to 18 March 2020 were retrospectively collected. Patients were stratified into progressive and non-progressive disease groups. Univariate and multivariate logistic regression analyses were performed to determine the independent risk factors for disease progression.

Results: Compared with patients with non-progressive disease, those who progressed to severe COVID-19 were older and had significantly decreased lymphocyte and eosinophil counts; increased neutrophil and platelet counts; lower albumin levels; higher levels of lactate dehydrogenase, C-reactive protein (CRP), creatinine, creatinine kinase, and urea nitrogen; and longer prothrombin times. Hypertension, fever, fatigue, anorexia, bacterial coinfection, bilateral patchy shadowing, antibiotic and corticosteroid administration, and oxygen support had a significantly higher incidence among patients with progressive disease. A significantly longer duration of hospital stay was also observed in patients with progressive disease. Bilateral patchy shadowing (OR = 4.82,
with more than 2.9 million confirmed cases resulting in 204,000
deaths as of 27 April 2020. Its pathogen, severe acute respirato ry
syndrome coronavirus 2 (SARS-CoV-2), can spread rapidly
between humans, causing the number of confirmed cases to
increase quickly. The severity spectrum of COVID-19 ranges
between mild to critical, but the majority of infections have not been
severe (1–6). Eighty-one percent of confirmed cases have been
mild to moderate, including those with and without pneumonia;
14% had severe disease (dyspnoea, blood oxygen saturation ≤
93% at rest, PaO2/FiO2 ratio ≤ 300 mmHg, respiratory rate
≥ 30 breaths/min, and lung infiltrates appearing within 24–48 h in >
50% of the lung field); and 5% have presented in critical condition
(septic shock, respiratory failure, and/or multiple organ dysfunction) (7). It has been reported that mild symptoms may become severe within 5–7 days (1, 7), suggesting
that patients initially hospitalised with mild or moderate disease
are still at a risk of severe or critical illness. If the treatment of
severely ill patients lies “downstream” to the control of COVID-
19, then it is the “upstream” strategy to identify patients who are
at a risk of progressing to severe disease. Early identification of
these patients coupled with early intervention could save lives
and alleviate the burden on the health care system.

Previous studies placed huge significance on transmission
dynamics (8, 9), the clinical manifestations of COVID-19 (3, 4, 7),
characteristics of patients with severe/critical disease (6, 10),
and the differences between patients with severe and non-severe
disease (11, 12). However, studies shedding light on patients
with non-severe disease on admission and tracking their disease
progression are scarce but of profound importance. Therefore, in
this study, we tracked patients admitted with mild or moderate
COVID-19 and probed the discrepancies between progressor and
non-progressor patients to determine the risk factors for disease
progression. In this way, we hope to guide the development of
effective early predictive tools to identify patients at a high risk
for developing severe disease.

INTRODUCTION

Coronavirus disease (COVID-19) has swept around the world,
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non-progressor patients to determine the risk factors for disease
progression. In this way, we hope to guide the development of
effective early predictive tools to identify patients at a high risk
for developing severe disease.

MATERIALS AND METHODS

Study Design and Patient Cohort

This retrospective study was approved by the Medical Ethics
Committee of Nanfang Hospital of Southern Medical University.
Written informed consent from all participating patients
was obtained.

We retrospectively collected data from 690 patients with
confirmed COVID-19 diagnosed between 1 January 2020 and 18
March 2020 from hospitals in Honghu and Nanchang. Patients
were diagnosed according to the guidelines of the Diagnosis and
Treatment Protocol for Novel Coronavirus Pneumonia (Trial
Version 7) (13). SARS-CoV-2 nucleic acid tests were positive in
all participants, and all diagnostic criteria were met according
to the guidelines. After excluding patients who had incomplete
clinical data, 442 patients were retained, among whom 365
patients with mild or moderate disease were included in the final
analysis. Of the 365 patients, 285 were from the People’s Hospital
of Honghu, while 80 were from the First Affiliated Hospital of
Nanchang University.

Definition

All patients were diagnosed and typed under the guidance of the
Diagnosis and Treatment Protocol for Novel Coronavirus
Pneumonia (Trial Version 7) (13) developed by the Chinese
National Health Commission and the State Administration of
Traditional Chinese Medicine. Patients with mild symptoms and
no signs of pneumonia on imaging were regarded to have mild
disease, while fever and respiratory symptoms were indicators
of moderate disease. Patients who suffered from respiratory
distress, arterial partial pressure of oxygen (PaO2)/fraction of
inspired oxygen (FiO2) ≤ 300 mmHg, oxygen saturation ≤ 93% at
rest, or with obvious lesion progression on chest imaging
within 24–48 h of >50%, were considered to have severe disease.
When respiratory failure, shock, or other organ failure appeared,
patients were diagnosed with critical disease. In this study,
patients who maintained mild or moderate symptoms during the
entire hospital stay were assigned to the non-progressive disease
group, and those with mild or moderate disease on admission
who later progressed to a severe or critical status were assigned
to the progressive disease group.

Data Collection and Outcome Evaluation

Clinical electronic medical records, nursing records, laboratory
findings, and radiological reports for all included patients with
COVID-19 were reviewed. For each patient, detailed admission
data were collected, including demographic information, signs
and symptoms, comorbidities, imaging reports, and laboratory
test results. After admission, the treatment, disease severity

Keywords: coronavirus disease 2019, disease progression, severe acute respiratory syndrome coronavirus 2, bilateral patchy shadowing, creatinine kinase, creatinine, C-reactive protein
state, outcomes, and length of hospital stay were also recorded. The treatments were conducted before disease progression. Two researchers independently checked the electronic medical reports and recorded the daily assessment of the disease severity. The progression from non-severe to severe disease was monitored.

**Statistical Analysis**

Continuous variables are presented as mean and standard deviation (SD) while normally distributed and otherwise as medians and interquartile ranges (IQR). Categorical variables are presented as frequencies and percentages. For continuous variables, the comparisons between progressive and non-progressive disease groups were performed using the Student’s t-test or the Mann–Whitney U test, as appropriate. For categorical variables, comparisons were conducted using the Pearson's chi-square test or Fisher's exact test, as appropriate. To investigate the risk factors associated with disease progression, univariate and multivariate logistic regression models were used. In the univariate logistic regression analyses, variables with \( P < 0.05 \) were regarded as potential risk factors and included in multivariate regression analysis by a backward elimination procedure (likelihood ratio test and elimination if \( P > 0.1 \)). Statistical analyses were conducted with the SPSS software version 25.0 and R version 4.0.2. The pROC package was employed to draw the receiver operating characteristic (ROC) curves and calculate the area under the curve (AUC). All statistical tests were two-sided, and \( P < 0.05 \) was regarded as statistically significant.

**RESULTS**

By 18 March 2020, a total of 690 patients with confirmed COVID-19 were recruited, of whom 365 patients from the People's Hospital of Honghu and the First Affiliated Hospital of Nanchang University with complete medical records and who were diagnosed with mild or moderate COVID-19 on admission were included in this study.

The demographics and baseline clinical characteristics of these patients are shown in **Tables 1, 2**. The patients’ mean age was 46.8 years [SD 15.5], 74 patients (20.3%) were older than 60 years, and 176 (48.2%) were men. Only 7 (1.9%) were current smokers. Hypertension (10.7%) was the most commonly observed comorbidity, followed by diabetes mellitus (4.7%), chronic liver disease (2.5%), and cardiovascular disease (1.6%). Among these patients, 221 (60.5%) had a fever, 194 (53.2%) had a cough, 253 (69.3%) had multi-lobular infiltration, and 228 (62.5%) had bacterial co-infection. The patients’ median temperature on admission was 36.8 degrees Centigrade (IQR 36.5–37.1). As for treatment, 352 (96.4%) received antiviral therapy, 251 (68.8%) underwent antibiotic therapy, 131 (35.9%) were treated with corticosteroids, and 149 (40.8%) required oxygen support. In terms of the outcomes, 363 patients (99.5%) were ultimately discharged from the hospital, and 2 patients (0.5%) died during their hospital stay. The median length of hospital stay was 14 days (IQR 10–20).

The patients were divided into progressive and non-progressive disease groups, depending on whether their disease became severe after admission. The results of the comparisons between groups are shown in **Tables 3, 4**. Compared with patients with non-progressive disease, those who progressed to severe COVID-19 were older (59.3 years [SD 13.2] vs. 45.9 years [SD 15.3], \( P < 0.001 \)). The proportion of patients with hypertension, fever, fatigue, anorexia, bacterial co-infection, or bilateral patchy shadowing was significantly higher among patients with progressive disease. From the perspective of laboratory findings, we found significantly decreased lymphocyte

**TABLE 1** | Demographics and baseline characteristics of patients with non-severe COVID-19.

| Characteristic                  | All patients (\( n = 365 \)) |
|--------------------------------|-----------------------------|
| Age, years                     | 46.8 ± 15.5                 |
| \( \geq 60 \)                   | 74 (20.3)                   |
| Male                           | 176 (48.2)                  |
| **Laboratory findings**        |                             |
| Red blood cell count, \( \times 10^9/\text{L} \) | 4.5 (4.1–4.9)               |
| White blood cell count, \( \times 10^9/\text{L} \) | 6.0 (4.3–6.9)               |
| Lymphocyte count, \( \times 10^3/\text{L} \) | 1.5 (1.1–1.8)               |
| Neutrophil count, \( \times 10^9/\text{L} \) | 4.0 (2.5–4.7)               |
| Hemoglobin, g/dL               | 135.3 (125.0–147.0)         |
| Platelet count, \( \times 10^9/\text{L} \) | 241.4 (178.0–293.5)         |
| Albumin, g/L                   | 42.7 (38.1–44.9)            |
| Total bilirubin, \( \mu \text{mol/L} \) | 11.1 (7.3–13.4)            |
| Direct bilirubin, \( \mu \text{mol/L} \) | 3.4 (2.2–3.8)               |
| Alanine aminotransferase, U/L   | 30.6 (13.0–34.5)            |
| Prothrombin time, s            | 12.6 (11.9–13.2)            |
| Creatinine, \( \mu \text{mol/L} \) | 65.6 (60.9–74.2)           |
| Urea nitrogen, mmol/L          | 4.6 (3.3–5.1)               |
| Lactate dehydrogenase, U/L     | 219.4 (167.5–246.0)         |
| Creatinine kinase, U/L         | 94.0 (44.5–103.0)           |
| C-reactive protein, mg/L       | 16.3 (6.0–15.2)             |
| Ground-glass opacity           | 181 (49.6)                  |
| Local patchy shadowing         | 55 (15.1)                   |
| Bilateral patchy shadowing     | 200 (54.8)                  |
| Interstitial abnormalities     | 11 (3.0)                    |

Continuous variable data are presented as the mean (standard deviation) or median (interquartile ranges, IQR). Categorical variable data are presented as n (%).
TABLE 2 | Smoking history, comorbidity, signs and symptoms, treatment and clinical outcomes of patients with non-severe COVID-19.

| Characteristic                                      | All patients (n = 365) |
|-----------------------------------------------------|------------------------|
| Smoking history                                     |                        |
| Current smokers                                     | 7 (1.9)                |
| Ex-smokers                                          | 0 (0.0)                |
| Comorbidity                                         |                        |
| Hypertension                                        | 39 (10.7)              |
| Diabetes mellitus                                   | 17 (4.7)               |
| Cardiovascular disease                              | 6 (1.6)                |
| Cerebrovascular disease                             | 3 (0.8)                |
| Chronic liver disease                               | 9 (2.5)                |
| COPD                                                | 2 (0.5)                |
| Asthma                                              | 1 (0.3)                |
| Renal disease                                       | 2 (0.5)                |
| Cancer                                              | 2 (0.5)                |
| Signs and symptoms                                  |                        |
| Fever                                               | 221 (60.5)             |
| Temperature on admission (°C)                       | 36.8 (36.5–37.1)       |
| Highest temperature (°C)                            | 37.4 (36.6–38.0)       |
| <37.3                                               | 192 (52.8)             |
| 37.3–37.9                                          | 61 (16.7)              |
| 38–38.9                                             | 92 (25.2)              |
| ≥39                                                 | 20 (5.5)               |
| Cough                                               | 184 (53.2)             |
| Sputum production                                   | 52 (14.2)              |
| Nasal congestion                                    | 6 (1.6)                |
| Fatigue                                             | 77 (21.1)              |
| Headache                                            | 17 (4.7)               |
| Sore throat                                         | 37 (10.1)              |
| Shortness of breath                                 | 28 (7.7)               |
| Dyspnea                                             | 13 (3.6)               |
| Anorexia                                            | 27 (7.4)               |
| Diarrhea                                            | 15 (4.1)               |
| Nausea                                              | 13 (3.6)               |
| Myalgia or arthralgia                               | 1 (0.3)                |
| Combination of bacterial infection                  | 228 (62.5)             |
| Treatment                                           |                        |
| Antiviral therapy                                   | 352 (96.4)             |
| Antibiotic therapy                                  | 251 (68.8)             |
| Use of corticosteroid                               | 131 (35.9)             |
| Oxygen support                                      | 149 (40.8)             |
| Clinical outcomes                                   |                        |
| Discharge from hospital                             | 363 (99.5)             |
| Length of hospital stay                             | 14.0 (10.0–20.0)       |
| Death                                               | 2 (0.5)                |

Continuous variable data are presented as the mean (standard deviation) or median (interquartile ranges, IQR). Classified variable data are presented as n (%). COPD, Chronic obstructive pulmonary disease.

DISCUSSION

The majority of patients were diagnosed with mild or moderate COVID-19 upon initial hospitalization. Although they had mild symptoms on admission, they were still at a risk of illness deterioration. There is a medical need to clarify the differences between patients with progressive and non-progressive disease in order to predict which patients are at risk of exacerbation and to conduct early interventions to reduce mortality. In this study, we assessed 365 patients with mild or moderate confirmed COVID-19 on admission. Twenty-six (7.1%) patients progressed to severe or critical disease after admission and were assigned to the progressive disease group, while the others were assigned to the non-progressive disease group. We elucidated the discrepancies in the clinical characteristics between patients with progressive and non-progressive disease and investigated the independent risk factors that could influence disease deterioration, with the purpose to enhance the early identification of at-risk populations. Many studies have investigated the risk factors associated with disease severity by comparing patients with non-severe COVID-19 and those with severe COVID-19. Liu et al. (10) reported that age, fever, SpO₂, and cough were linked to severe or critical infections in patients with COVID-19. Zhou et al. (14) proposed that lymphopenia and increased CRP levels were independent risk factors for disease severity. Gong et al. (12) revealed that age, increased CRP, serum lactate dehydrogenase, the coefficient of variation of red blood cell distribution width, albumin, blood urea nitrogen, and direct bilirubin were related to severe COVID-19 and established a predictive tool to distinguish individuals
TABLE 3 | Demographics and clinical characteristics of progressive and non-progressive COVID-19 patients.

| Characteristic                      | Non-progressor patients (n = 339) | Progressor patients (n = 26) | P-value |
|-------------------------------------|-----------------------------------|------------------------------|---------|
| **Disease progression**             |                                   |                              |         |
| Age, years                          | 45.9 ± 15.3                       | 59.3 ± 13.2                  | < 0.001 |
| >60                                 | 63 (18.6)                         | 11 (42.3)                    | 0.004   |
| Male                                | 157 (46.3)                        | 19 (73.1)                    | 0.008   |
| **Laboratory findings**             |                                   |                              |         |
| Red blood cell count, ×10⁹/L        | 4.5 (4.1–4.8)                     | 4.5 (3.9–5.0)                | 0.857   |
| White blood cell count, ×10⁹/L      | 5.8 (4.3–6.8)                     | 6.1 (4.3–7.6)                | 0.352   |
| <10                                 | 323 (96.3)                        | 23 (88.5)                    | p = 0.131 |
| Lymphocyte count, ×10⁹/L            | 1.47 (1.1–1.6)                    | 0.9 (0.7–1.5)                | < 0.001 |
| <0.8                                | 29 (8.6)                          | 7 (26.9)                     | 0.001   |
| Neutrophil count, ×10⁹/L            | 3.4 (2.4–4.6)                     | 4.0 (2.7–6.5)                | 0.033   |
| >6.4                                | 25 (7.4)                          | 7 (26.9)                     | 0.001   |
| Eosinophil counts, ×10⁹/L           | 0.05 (0–0.1)                      | 0.01 (0–0.1)                 | 0.002   |
| Hemoglobin, g/dL                    | 135.0 (125.0–147.0)               | 141.0 (120.8–154.5)          | 0.445   |
| Platelet count, ×10⁹/L              | 236.0 (180.0–297.8)               | 197.0 (141.8–233.5)          | 0.004   |
| <100                                | 7 (2.1)                           | 2 (7.7)                      | 0.075   |
| Albumin, g/L                       | 42.0 (38.5–45.0)                  | 38.2 (34.3–42.8)             | 0.004   |
| Total bilirubin, μmol/L            | 9.8 (7.3–13.3)                    | 11.3 (7.2–15.4)              | 0.315   |
| >17.1                               | 38 (11.2)                         | 6 (23.1)                     | 0.108   |
| Alanine aminotransferase, U/L       | 20.0 (13.0–35.0)                  | 29.0 (17.0–35.0)             | 0.085   |
| >40                                 | 63 (18.6)                         | 3 (11.5)                     | 0.596   |
| Prothrombin time, s                | 12.5 (11.8–13.1)                  | 13.0 (12.4–13.8)             | 0.003   |
| ≥16                                 | 3 (0.9)                           | 1 (3.8)                      | 0.257   |
| Creatinine > 133μmol/L             | 6 (1.8)                           | 4 (15.4)                     | < 0.001 |
| Lactate dehydrogenase, U/L         | 199.0 (167.0–241.0)               | 248.5 (208.0–342.8)          | < 0.001 |
| >245                                | 78 (23.0)                         | 14 (53.8)                    | < 0.001 |
| Creatinine kinase, U/L             | 67.0 (44.0–95.0)                  | 108.0 (80.3–192.3)           | 0.011   |
| >120                                | 56 (16.5)                         | 11 (42.3)                    | 0.003   |
| C-reactive protein, mg/L           | 2.0 (0.5–12.3)                    | 37.7 (9.6–59.9)              | < 0.001 |
| ≥10                                 | 89 (26.3)                         | 20 (76.9)                    |         |
| **Abnormalities on chest CT**       |                                   |                              |         |
| Ground-glass opacity               | 166 (49.0)                        | 15 (57.7)                    | 0.391   |
| Local patchy shadowing             | 53 (15.6)                         | 2 (7.7)                      | 0.397   |
| Bilateral patchy shadowing         | 177 (52.2)                        | 23 (88.5)                    | < 0.001 |
| Interstitial abnormalities          | 11 (3.2)                          | 0 (0)                        | > 0.999 |

Continuous variable data are presented as the mean (standard deviation) or median (interquartile ranges, IQR). Classified variable data are presented as n (%).
TABLE 4: Smoking history, comorbidity, signs and symptoms, treatment and clinical outcomes of progressive and non-progressive COVID-19 patients.

| Characteristic                  | Non-progressor patients (n = 339) | Progressor patients (n = 26) | P-value |
|--------------------------------|-----------------------------------|------------------------------|---------|
| **Smoking history**            |                                   |                              |         |
| Current smokers                | 5 (1.5)                           | 2 (7.7)                      | 0.082   |
| Ex-smokers                     | 0 (0)                             | 0 (0)                        |         |
| **Comorbidity**                |                                   |                              |         |
| Hypertension                   | 33 (9.7)                          | 6 (23.1)                     | 0.046   |
| Cardiovascular disease         | 4 (1.2)                           | 2 (7.7)                      | 0.061   |
| Cerebrovascular disease        | 2 (0.6)                           | 1 (3.8)                      | 0.199   |
| Chronic liver disease          | 8 (2.4)                           | 1 (3.8)                      | 0.49    |
| COPD                           | 2 (0.6)                           | 0 (0)                        | > 0.999 |
| Asthma                         | 1 (0.3)                           | 0 (0)                        | > 0.999 |
| Renal disease                  | 2 (0.6)                           | 0 (0)                        | > 0.999 |
| Cancer                         | 2 (0.6)                           | 0 (0)                        | > 0.999 |
| **Signs and symptoms**         |                                   |                              |         |
| Fever                          | 198 (58.4)                        | 23 (88.5)                    | 0.003   |
| Temperature on admission (°C)  | 36.7 (36.5–37.1)                  | 37.1 (36.7–38.0)             | 0.001   |
| Highest temperature (°C)       | 37.1 (36.6–38.0)                  | 38.3 (37.7–38.6)             | < 0.001 |
| <37.3                          | 188 (55.5)                        | 4 (15.4)                     | < 0.001 |
| 37.3–37.9                      | 57 (16.8)                         | 4 (15.4)                     |         |
| 38–38.9                        | 79 (23.3)                         | 13 (50.0)                    |         |
| >39                            | 15 (4.4)                          | 5 (19.2)                     |         |
| Cough                          | 179 (52.8)                        | 15 (57.7)                    | 0.63    |
| Sputum production              | 48 (14.2)                         | 4 (15.4)                     | 0.775   |
| Nasal congestion               | 4 (1.2)                           | 2 (7.7)                      | 0.061   |
| Fatigue                        | 67 (19.8)                         | 10 (38.5)                    | 0.024   |
| Headache                       | 16 (4.7)                          | 1 (3.8)                      | > 0.999 |
| Sore throat                    | 35 (10.3)                         | 2 (7.7)                      | > 0.999 |
| Shortness of breath            | 25 (7.4)                          | 3 (11.5)                     | 0.437   |
| Dyspnea                        | 12 (3.5)                          | 1 (3.8)                      | > 0.999 |
| Anorexia                       | 22 (6.5)                          | 5 (19.2)                     | 0.033   |
| Diarrhea                       | 13 (3.8)                          | 2 (7.7)                      | 0.29    |
| Nausea                         | 12 (3.5)                          | 1 (3.8)                      | > 0.999 |
| Myalgia or arthralgia          | 1 (0.3)                           | 0 (0)                        | > 0.999 |
| Combination of bacterial infection | 205 (60.5)                  | 23 (88.5)                    | 0.005   |
| **Treatment**                  |                                   |                              |         |
| Antiviral therapy              | 326 (96.2)                        | 26 (100.0)                   | 0.611   |
| Antibiotic therapy             | 228 (67.3)                        | 23 (88.5)                    | 0.255   |
| Use of corticosteroid          | 109 (32.2)                        | 22 (84.6)                    | < 0.001 |
| Oxygen support                 | 125 (36.9)                        | 24 (92.3)                    | < 0.001 |
| **Clinical outcomes**          |                                   |                              |         |
| Discharge from hospital        | 338 (99.7)                        | 25 (96.2)                    | 0.138   |
| Length of hospital stay        | 14.0 (9.0–20.0)                   | 21.0 (16.0–27.3)             | < 0.001 |
| Death                          | 1 (0.3)                           | 1 (3.8)                      | 0.138   |

Continuous variable data are presented as the mean (standard deviation) or median (interquartile ranges, IQR). Classified variable data are presented as n (%). COPD, Chronic obstructive pulmonary disease.

Inflammatory marker and is linked to the state of infection and inflammation in patients with severe COVID-19 (21). Prior to CT findings, CRP increased at the early stage of severe COVID-19. CRP level was reported to be associated with CT scores and disease deterioration of COVID-19 (22). The predictive role of CRP for severe COVID-19 has been previously reported (22–24). Increased creatine kinase levels obtained statistical significance in the univariate analyses but lost its position in the multivariate analyses, suggesting that increased creatine kinase levels may be not an independent predictor for disease...
progression. They are often accompanied by elevated levels of creatine kinase-MB (CK-MB), one of the three forms of creatine kinase and serving as a specific indicator of myocardial injury. The underlying mechanism of how SARS-CoV-2 causes acute myocardial injury is speculated to be related to angiotensin-converting enzyme 2 (25). Interestingly, in a report involving 138 patients hospitalised with COVID-19 in Wuhan, 36 patients who presented with severe manifestations and were treated in the intensive care unit had significantly higher levels of CK-MB than those with non-severe symptoms (1), suggesting that severely ill patients were likely to suffer from acute myocardial injury.

Several limitations existed in the present study. Only 26 patients were included in the group with progressive disease. The relatively small sample size may have had some impact on the results of our study. However, the total population from which these patients were sampled was large at 690. In addition, some clinical indicators such as cytokines were not included because of data unavailability. The role of these indicators may have been underestimated. Moreover, the retrospective nature of the data collection and the risk of potential attribution bias, since the reviewers were not blinded to the final clinical status when they attributed the initial clinical status, remain intrinsic limitations of this study. However, when considering that it is extremely difficult to undertake a prospective collection of data in the context of a COVID-19 outbreak, which still poses a threat to the global community, this method seems appropriate. Additionally, since some previous studies exist in this field, the novelty of this report is limited. Despite these limitations, we still hope our study can contribute to improving the clinical management of disease and benefit patients with COVID-19, especially since so much remains unknown regarding the progression of this disease. More clinical data and further work are urgently needed to define the relevant thresholds and predictive values for the three main variables. Development of predictive tools based on these results to stratify initially hospitalised patients into groups with non-progressive and progressive disease holds great promise and calls for further comprehensive research work.

In conclusion, the patients with progressive disease were significantly different from those with non-progressive disease in terms of demographic features, clinical manifestation, laboratory findings, imaging reports, and clinical outcomes. Bilateral patchy shadowing and elevated levels of creatinine and CRP were found to be independent predictors of disease progression. We hope our study can help elucidate the pathogenic characteristics of patients with COVID-19 and help develop effective biomarkers and further therapeutic strategies for patients with COVID-19.

**DATA AVAILABILITY STATEMENT**

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

**ETHICS STATEMENT**

The studies involving human participants were reviewed and approved by the Medical Ethics Committee of Nanfang Hospital of Southern Medical University and the institutional ethics review boards of all participating hospitals. The requirement for informed consent was waived by the ethics committees.

**AUTHOR CONTRIBUTIONS**

YZ and L-sX designed the research study, analysed the data, and wrote the paper. YZ, L-sX, HongbZ, and PL contributed with literature search and tables. CH and W-FZ contributed with data analysis and writing of the paper. Q-cS, M-yS, S-sL, and W-lZ designed the research study, analysed clinical data, and wrote the paper. All authors contributed to the article and approved the submitted version.
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SUPPLEMENTARY MATERIAL
The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2020.556818/full#supplementary-material

Supplementary Figure 1 | ROC curves for assessing the predictive value of creatinine kinase, creatinine, C-reactive protein and bilateral patchy shadowing for disease progression. ROC, receiver operating characteristic curve; AUC, area under the ROC curve.