The correlation between severity scores in computed tomography lung scans and viral load in the severity of novel coronavirus 2019 progression

Zheng Liu MD1 | Qian Wang MD1 | Jing Li MD1 | Jiaqi Liu MM2 | Hui Wang MD1 | Cuijiao Jia MD1 | Leiqian Xu MD1 | Xueyan Wang MS3

1Department of Respiratory Medicine, The Petroleum Clinical Medical College of Hebei Medical University, Langfang, Hebei, China
2Schulich School of Medical and Dentistry-Honour Specialization in Interdisciplinary Medical Science and Major in Pharmacology, Western University, London, Ontario, Canada
3Department of medical statistics, Maternal and Child Health Hospital, Langfang, Hebei, China

Correspondence
Zheng Liu, Department of Respiratory Medicine, The Petroleum Clinical Medical College of Hebei Medical University, No. 51 of Xinkai Road, Guangyang District, Langfang, Hebei 065000. China. Email: zhengl06drsun@163.com

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Abstract
Background: This study aimed to find the correlation between severe computed tomography (CT) lung scores and nasopharyngeal viral load (Ct value) in the severity of COVID-19 disease progression.

Method: In this study, 37 patients diagnosed with COVID-19 were categorized into severely ill and not severely ill samples. Their Ct values, epidemiological data, lung CT, and laboratory test results were collected three times, respectively, on the first day of their hospital admission, 3–5 days thereafter, and prior to hospital discharge. Among the 37 patients, 8 progressed from not severely ill to severely ill; we also paid attention and observed changes in clinical parameters of COVID-19 patients who entered our city from other cities (imported cases) and the infected local residents who contacted these imported patients (non-imported cases).

Results: Among the 37 patients, the Ct values and lung severity scores (LSSs) were similar in imported and non-imported cases (F = 0.59 and 2.56; p = 0.45 and 0.12, respectively) but the proportion of severely ill imported patients was significantly higher compared with non-imported patients (F = 7.77; p = 0.01). Additionally, 21.6% of patients’ illness worsened; lymphocyte counts and Ct values were significantly lowered, and C-reactive protein and LSS significantly increased during COVID-19 disease progression. Furthermore, LSS negatively correlated with lymphocyte and mononuclear cell counts, as well as Ct values (Pearson’s rank = −0.763, −0.824, and −0.588; p = 0.028, 0.012, and 0.003, respectively).

Conclusion: In the severity of COVID-19 disease progression, nasopharyngeal viral load and lung CT severity were closely related, and LSS negatively correlated with lymphocyte and mononuclear cell counts, as well as Ct values.

KEYWORDS
COVID-19, severe CT lung scores, viral load

1 | INTRODUCTION

The spread of the novel coronavirus disease 2019 (COVID-19) virus currently remains widespread worldwide. Suspected cases can be
confirmed following positive nucleic acid testing for the 2019 novel coronavirus (SARS-CoV-2) in sputum via a throat swab, as well as lower respiratory tract secretion using real-time fluorescence polymerase chain reaction (RT-PCR). Fluorescence RT-PCR is considered an important indicator of viral load\(^1,2\) as it is used to detect the cycle threshold (Ct) values of largely coronavirus-expressed genes. A low Ct value represents a high viral load. Hence, the Guidelines on the Novel Coronavirus-Infected Pneumonia Diagnosis and Treatment (2020) recommends using it in this regard.\(^3\) A study\(^7\) has suggested that a correlation existed between the viral load, disease progression, and the spread of COVID-19. Chen\(^5\) found that a change in Ct values was likely to make a COVID-19 patient with mild symptoms to develop into a severe case as part of the disease’s progression. Specifically, based on Chen’s results, five patients’ Ct values showed a decreasing tendency, while two other patients had higher Ct values before or during disease severity progression.

A time window exists to help prevent patients infected with COVID-19 from deteriorating by providing clinical interventions. Changes are observable via computed tomography (CT) imaging as it serves as an important tool for evaluating the severity of COVID-19.\(^6,7\) The CT lung scan results of patients may vary over time. For example, ground-glass opacity (GGO) is often observed at the initial stage, a crazy-paving pattern at the progressive stage and consolidation at the peak stage, as well as at the recovery stage when consolidation is gradually absorbed and fibrotic changes arise.\(^8-11\) Therefore, the dynamics of chest CT scans represent a means for evaluating COVID-19 conditions.

The aggravation of clinical symptoms is another important indicator of disease progression. Commonly observed symptoms of COVID-19 include fever, cough, myalgia, fatigue, pneumonia, and dyspnea, while some patients experience a headache, diarrhea, hemoptysis, a runny nose, and expectoration.\(^12\) These symptoms, along with a decrease in the oxygenation index (OI), indicate that the disease has worsened.

Treating severely ill cases of COVID-19 has become a major focus of research. Nonetheless, few studies have made a distinction between non-severely ill and severely ill patients with COVID-19 pneumonia in terms of clinical, laboratory, viral load, and radiological contexts. This study aimed to explore the correlation between viral load, lung severity score (LSS), and CT lung scans in the severity of COVID-19 progression to provide clinicians with a theoretical reference for the early diagnosis of critically ill patients.

## 2 | MATERIALS AND METHOD

### 2.1 | Study population

In this retrospective study, patients with COVID-19 were admitted to the Petroleum Clinical Medical College of Hebei Medical University, which was designated to treat COVID-19 patients, from January 24, 2020 to February 26, 2020. All 37 patients were diagnosed with COVID-19, based on the positive real-time RT-PCR test results using oropharyngeal swab samples. These samples underwent RT-PCR using the ORF1ab and N genes Da An gene DA0992-Detection Kit for 2019-nCoV (Da An Gene Co., Ltd., Sun Yat-sen University, Guangzhou, China). This study used the Ct value of the N gene as a reference. The Ct value was inversely correlated with the ribonucleic acid (RNA) copy number of the virus.\(^1\) A Ct value <35 was considered to indicate a positive COVID-19 result. For the transcription-mediated amplification (TMA), the result was considered positive when the relative light unit was above 850.

### 2.2 | Data collection and definitions

The data extracted from patient records included age, sex, epidemiology, comorbid conditions, symptoms at onset, the time from the onset of symptoms to hospital admission, vital signs on admission, laboratory test results during hospitalization, high-resolution CT imaging findings, virus clearance time, and clinical outcomes. For epidemiological factors, the record included the field “Wuhan imported,” which was defined as travel to Wuhan city, Hubei (also labeled “imported case”). Conversely, we defined patients who had been in contact with recent travelers from Wuhan city as non-imported cases.

According to the Guidelines on the Novel Coronavirus Infected Pneumonia Diagnosis and Treatment (7th ed., 2020),\(^13\) we classified the severity of the participants’ disease as follows: (1) a mildly ill group, in which patients exhibited mild clinical symptoms and no imaging manifestations of pneumonia; (2) a moderately ill group, in which patients had a fever and respiratory symptoms, and signs of pneumonia were observed in imaging; (3) a severely ill group, in patients exhibited dyspnea, a respiratory rate ≥30 breaths/min, oxygen saturation (SpO2) ≤93% at a resting state, or arterial partial pressure of oxygen/oxygen concentration (FiO2) ≤300 mm Hg; pulmonary imaging showed marked lesion progression >50% within 24–48 h; (4) a critically ill group, in which patients who had any of the following symptoms had to be admitted to the intensive care unit: respiratory failure and requiring mechanical ventilation, or shock combined with the failure of other organs. Patients who were severely and critically ill were labeled “severely ill patients,” while mildly/moderately ill patients were defined as “not severely ill patients.”

### 2.3 | Lung severity score analysis

Classification of the chest HRCT severity was primarily based on the invasion range and morphological characteristics of lesions as follows: CT-1, GGO in ≤25% of the lung parenchyma; CT-2, GGO in 26%–50% of the lung parenchyma; CT-3, GGO and consolidation in 51%–75% of the lung parenchyma; CT-4, GGO and consolidation in ≥76% of the lung parenchyma. The extent of lesions in each lung lobe was evaluated applying a score ranging from 0 to 4. A summation of the scores from all five lobes provided the total CT severity score ranging from 0 to 20 (see Figure 1).\(^14,15\)
2.4 | The frequency of computed tomography scanning and nucleic acid testing

This study was divided into three periods, that is, “admission,” “follow-up/exacerbation,” and “predischarge” periods. All patients received their first high-resolution CT scan on hospital admission. During the follow-up period (3–5 days) thereafter, depending on the severity of their clinical symptoms and FiO2 (≤300 mm Hg), patients received a second round of CT scans. When symptoms were completely relieved and nucleic acid results were negative after two consecutive tests, another lung CT scan was conducted. The scanning scope was set between the superior aperture of the thorax and the posterior costophrenic angle with a slice interval of 1 mm and a slice thickness of 1.25 mm. All CT images were analyzed by two senior radiologists. The nucleic acid test for COVID-19 was also divided into three periods, with the first period being nucleic acid (RT-PCR) for patients diagnosed with COVID-19 before admission. The results are reviewed by the municipal CDC on the same day and the diagnosis was confirmed unanimously. The second nucleic acid test was performed on the same day as the disease progression and the second lung CT. The third nucleic acid test was performed before discharge. These were done using RT-PCR and the CT values were obtained.

2.5 | Statistical analysis

The SPSS Statistics 21.0 (IBM) software program was used for analysis in this study. Continuous data were expressed as the mean and standard deviation or as a percentage, and categorical data were expressed as a frequency. The distributions and imaging manifestations during admission, follow-up, exacerbation, and predischarge periods were analyzed using a $\chi^2$ or Fisher’s exact tests. The comparison of the two samples was completed by a t-test of independent samples. Correlations were analyzed using the Pearson correlation coefficient. The absolute values of the correlation coefficients (r) were graded as 0.15–0.24 (very low), 0.25–0.49 (low), 0.50–0.69 (moderate), 0.70–0.89 (high), and 0.90–1.00 (very high). A p-value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Demographics, and epidemiological and clinical data

The 37 patients included in this study were enrolled and analyzed retrospectively (15 females and 22 males, mean age 42.14 ± 14.98 years; range, 19–83 years). Some of the 37 patients were accompanied by a previous medical history, which included chronic hepatitis B virus infection (35.14%, 13/37), hypertension (18.92%, 7/37), heart disease, and chronic lung structure destruction disease (each 5.41%, 2/37), and diabetes mellitus, kidney disease, and obesity (each 2.7%, 1/37). The 37 patients were divided into 29 (78.4%) non-severe and 8 (21.6%) severe cases; the latter group included older members and had more men than women ($p = 0.01$). When comparing severe with non-severe cases, the former had significantly higher blood neutrophil counts, C-reactive protein, and procalcitonin (PCT) ($p < 0.01$) levels. There was no statistical difference concerning viral load between the two groups ($F = 0.59$, $p = 0.45, 0.12$, respectively.) but the disease severity was significantly higher among imported compared with non-imported cases ($F = 7.77; p = 0.01$) (see Figure 2 and Table 1).

There were no statistical difference in the Ct value and lung CT severity score between imported and non-imported cases ($F = 0.59$, $2.56; p = 0.45, 0.12$, respectively.) but the disease severity was significantly higher among imported compared with non-imported cases ($F = 7.77; p = 0.01$) (see Figure 2 and Table 1).

3.2 | Computed tomography image characteristics

Among the included cases, 91.9% (34/37) showed CT chest abnormalities. Common imaging manifestations of CT lung scans include GGO, consolidation, bronchial–vascular thickening, intralobular septal thickening, and interlobular septal thickening. At admission periods, multisite (76.3%), multiple lesions (63.2%), GGO (47.4%), consolidation opacity (23.7%), and GGO and consolidation opacity (91.9%) were characteristics that accompanied the thickening of bronchial vascular bundles (44.7%). At the follow-up or exacerbation periods, lung CT

FIGURE 1 High-resolution computed scan: (A) ground-glass opacities and consolidations; (B) ground-glass opacities
showed significantly increased consolidation opacity (23.7%–50%) and intralobular septal thickening (2.6%–18.4%). Lung CT images taken before hospital discharge showed interlobular septal thickening (31.6%). We scored lung CT images at three stages, that is, 4.86 ± 4.81, 4.66 ± 4.31, and 2.86 ± 3.06 (t = 5.45, 5.81, and 5.04, respectively, for all of these values, p < 0.01) (see Table 2).

TABLE 1  Demographic, epidemiological characteristics, comorbidities, viral load, and clinical and laboratory findings of patients with no-severe and severe confirmed COVID-19 at admission

| Characteristics                              | Characteristics | All patients | No-severe cases | Severe cases | F values | p values |
|----------------------------------------------|----------------|-------------|----------------|-------------|----------|----------|
| Age (years)                                  | 42.14 ± 14.98  | 40.66 ± 2.37| 47.50 ± 7.42  | 7.22        | 0.01     |
| Sex                                          |                |             |                |             | 6.69     | 0.01     |
| Men                                          | 22 (59.46%)    | 16 (43.24%) | 6 (16.22%)     |             |          |
| Women                                        | 15 (40.54%)    | 13 (35.14%) | 2 (5.41%)      |             |          |
| Epidemiological                              |                |             |                |             | 7.71     | 0.01     |
| Imported case                                | 11 (29.7%)     | 5 (13.5%)   | 6 (16.2%)      |             |          |
| Non-imported case                           | 26 (70.3%)     | 23 (62.2%)  | 3 (8.1%)       |             |          |
| Comorbid conditions                          |                |             |                |             | 17.23    | <0.01    |
| Hypertension                                 | 7 (18.92%)     | 5 (13.51%)  | 2 (5.41%)      |             |          |
| Diabetes                                     | 1 (2.70%)      | 0           | 1 (2.70%)      |             |          |
| Coronary heart disease                       | 2 (5.41%)      | 1 (2.70%)   | 1 (2.70%)      |             |          |
| Chronic hepatitis B virus infection          | 13 (35.14%)    | 11 (29.73%) | 2 (5.41%)      |             |          |
| Chronic lung structure destruction disease   | 2 (5.41%)      | 1 (2.70%)   | 1 (2.70%)      |             |          |
| Kidney disease                               | 1 (2.70%)      | 0           | 1 (2.70%)      |             |          |
| Obesity                                      | 1 (2.70%)      | 0           | 1 (2.70%)      |             |          |
| Laboratory data                              |                |             |                |             |          |
| Neutrophil count (×10⁹/L)                    | 4.03 ± 3.98    | 3.03 ± 0.27 | 7.66 ± 3.81    | 12.98       | <0.01    |
| Lymphocyte count (×10⁹/L)                    | 1.58 ± 0.71    | 1.63 ± 0.11 | 1.38 ± 0.38    | 1.45        | 0.24     |
| Monocyte count (×10⁹/L)                      | 0.49 ± 0.22    | 0.53 ± 0.04 | 0.37 ± 0.07    | 0.77        | 0.39     |
| C-reactive protein (mg/L)                    | 32.71 ± 40.75  | 21.18 ± 2.46| 74.50 ± 26.52  | 16.88       | <0.01    |
| Procalcitonin levels (ng/ml)                 | 0.67 ± 2.76    | 0.22 ± 0.01 | 2.28 ± 0.15    | 20.69       | <0.01    |
| Ct values                                    | 30.24 ± 2.97   | 30.76 ± 0.51| 28.38 ± 1.10   | 0.29        | 0.59     |
| Other                                        |                |             |                |             |          |
| Time from illness onset to hospital admission (days) | 4.70 ± 3.91    | 5.0 ± 0.80  | 3.63 ± 0.67    | 5.33        | 0.03     |
| Days in hospital                            | 12.92 ± 5.44   | 11.03 ± 0.43| 28.38 ± 1.10   | 13.99       | 0.01     |

Note: Chronic lung structure destruction disease: TB, bronchiectasis or chronic obstructive pulmonary disease.

FIGURE 2  Epidemiological analysis. Both the viral load (Ct value) (A) and lung CT severity scores (B) of the imported case were equivalent to that non-imported cases (F = 0.59, 2.56, p = 0.45, 0.12, respectively)
3.3 Changes in the cycle threshold value of viral ribonucleic acid, lung severity scores, and inflammatory factors during the progression of severe coronavirus 2019 cases

We conducted a comparative review of the Ct value of viral RNA and LSS, neutrophil and lymphocyte count, PCT, and CRP in eight patients with severe COVID-19 pneumonia during three periods. In the process of disease deterioration, these median of neutrophil, lymphocyte, and monocyte count, PCT, and Ct values were significantly lower than the same corresponding parameters at hospitalization, while LSS were significantly higher. The lymphocyte count of convalescent patients before discharge was still lower compared with hospitalized patients (see Table 3).

3.4 The correlation between the cycle threshold value and lung severity scores and inflammatory indexes and hospitalization length in eight patients during disease exacerbation

When the patient's symptoms worsened and/or SpO2 ≤93% at a resting state, we re-performed nucleic acid tests via throat swab, lung CT, and laboratory tests, and analyzed the correlation between these data. The results showed that LSS negatively correlated with lymphocyte count, mononuclear cell count, and Ct value (Pearson's rank = −0.763, −0.824, and −0.588; \( p = 0.028, 0.012, \) and \( 0.003, \) respectively). The Ct value of nucleic acid detection during this period was negatively related to CRP \( (r = −0.452; p = 0.002) \) and did not correlate with lymphocyte, mononuclear cell, or neutrophil counts, PCT, or the length of

**TABLE 2** Changes of lung CT during hospitalization

| CT findings                  | Admission periods | Follow-up or exacerbation periods | Predischarge periods |
|------------------------------|-------------------|----------------------------------|----------------------|
| Lesion distribution          |                   |                                  |                      |
| Single lesion                | 5 (13.2%)         | 7 (18.4%)                        | 8 (21.1%)            |
| Multiple lesions             | 29 (76.3%)        | 29 (76.3%)                       | 24 (63.2%)           |
| Unilateral                   | 10 (26.3%)        | 11 (28.9%)                       | 11 (28.9%)           |
| Bilateral                    | 24 (63.2%)        | 25 (65.8%)                       | 21 (55.3%)           |
| No abnormality               | 3 (7.9%)          | 1 (2.6%)                         | 5 (13.2%)            |
| Lesion density               |                   |                                  |                      |
| Ground-glass opacity         | 18 (47.4%)        | 11 (28.9%)                       | 18 (47.4%)           |
| Consolidation                | 9 (23.7%)         | 19 (50%)                         | 3 (7.9%)             |
| Ground-glass opacity and consolidation | 7 (18.4%) | 3 (7.9%)                  | 0                    |
| None                         | 3 (7.9%)          | 4 (10.5%)                        | 16 (42.1%)           |
| Accompanying abnormality     |                   |                                  |                      |
| Interlobular septal thickening| 4 (10.5%)         | 4 (10.5%)                        | 12 (31.6%)           |
| Intralobular septal thickening| 1 (2.6%)          | 7 (18.4%)                        | 9 (23.7%)            |
| Bronchovascular thickening   | 17 (44.7%)        | 12 (31.6%)                       | 4 (10.5%)            |
| Bilateral pleural Thickening | 3 (7.9%)          | 3 (7.9%)                         | 2 (5.3%)             |
| LSS                          | 4.86 ± 4.81       | 4.66 ± 4.31                      | 2.86 ± 3.06          |

**TABLE 3** Correlation analysis of viral load, LSS, and inflammatory factor during the process of disease progression

| Characteristic parameter | Admission periods | follow-up exacerbation periods | Predischarge periods | \( p \) values |
|--------------------------|-------------------|--------------------------------|----------------------|----------------|
| Neutrophil count (10^9 /L) | 8.45 (6.01–32.80) | 4.04 \( ^a \) (2.73–5.74) | 7.04 (3.20–9.62) | 0.04           |
| Lymphocyte count (10^9 /L) | 1.47 (0.50–3.92)  | 0.65 \( ^a,b \) (0.09–2.04) | 1.01 \( ^a \) (0.61–1.45) | 0.01           |
| Monocyte count (10^9 /L)  | 0.36 (0.13–0.72)  | 0.18 \( ^a,b \) (0.04–0.78) | 0.50 \( ^a \) (0.18–0.76) | 0.01           |
| C-reactive protein (mg/L) | 66.15 (5.72–230.00) | 64.90 \( ^a,b \) (11.90–799.00) | 13.35 \( ^a \) (5.00–40.00) | <0.01          |
| Procalcitonin levels (ng/ml) | 0.21 (0.11–0.53) | 0.10 \( ^a \) (0.11–0.53) | 0.20 (0.10–7.00) | 0.02           |
| LSS (median)              | 11.50 (1.00–16.00) | 17.50 \( ^a,b \) (7.00–19.00) | 7.00 \( ^a \) (3.00–18.00) | <0.01          |
| Ct values (median)        | 29.00 (24.00–33.00) | 26.00 \( ^a,b \) (22.00–33.00) | 37.50 \( ^a \) (29.00–40.00) | <0.01          |

\( ^a \) Compared to “admission.”

\( ^b \) Compared to “predischarge.”
hospital stay \( (r = 0.056\), 0.204, 0.267, –0.076, and –0.057; p = 0.709, 0.170, 0.073, 0.616, and 0.893, respectively) (see Figure 3A–C).

### 3.5 The correlation between cycle threshold value, lung severity score, inflammatory indexes, and hospitalization length in non-severe patients

In patients with non-severe COVID-19, Ct value showed no correlation with neutrophil, lymphocyte, or monocyte counts, PCT, CRP, or LSS \( (r = –0.346, 0.158, –0.055, 0.020, –0.150, \) and \( 0.041; p = 0.066, 0.414, 0.778, 0.917, 0.940, \) and 0.831, respectively), nor with the length of stay during disease follow-up \( (r = –0.255; p = 0.183) \). The LSS correlated with CRP and age \( (r = 0.606 \) and 0.586; \( p < 0.001 \), respectively) (see Figure 4A,B).

### 4 DISCUSSION

The ongoing COVID-19 pandemic is causing severe global morbidity and mortality. Early identified risk factors of COVID-19 severity are key to reducing mortality. The diagnosis of COVID-19 is based on nucleic acid tests of the virus’ RNA using nasopharyngeal swabs and the Ct values of RT-PCR assays. \(^1^6\) Whether there is a correlation between viral load and disease severity has not been clarified. In addition to clinical symptoms, signs and monitoring indicators, such as OI, many scholars depend on lung CT imaging, lymphocyte count, CRP, proinflammatory cytokines (such as tumor necrosis factor alpha, interleukin (IL)-1α, and IL-1β), Th2-type cytokines (IL-4, 5, and 13), specific inflammatory chemokines (CXCL1/GRO-α and CXCL12/SDF-1α), and growth factors (leukemia inhibitory factor, vascular endothelial growth factor, stem cell growth factor, and granulocyte colony-stimulating factor) as indicators for judging disease progression. \(^17\)

### 4.1 The cycle threshold value and coronavirus 2019 progression

In prior analysis during the SARS-CoV-1 outbreak, viral load in nasopharynx swabs had been associated with disease severity and increased mortality. \(^18\) However, there were also clear and stark differences between SARS-CoV-1 and 2. Whether the degree of SARS-CoV-2 viral load within the respiratory tract can predict disease outcomes must be established. Our data showed that the viral load of the nasopharyngeal specimen in imported cases were similar to those of non-imported cases, and there was no statistical difference in viral load between non-severely and severely ill patients \( (p = 0.59) \). This result suggested that viral load would not reduce the transmission from imported patients to closely contacted patients. However, the proportion of imported severely ill patients was higher compared with non-imported patients \( (F = 7.77; p = 0.01) \). One important reason is that an increase in the proportion of severely ill patients among imported patients should be related to viral load. In this study, the virus specimens were derived from the upper airway. It is widely

![Figure 3](image3.png)

**Figure 3** (A–C) respectively showed that lung CT score (LSS) is negative correlation to and lymphocyte count, monocyte count, and Ct value during the progression of COVID-19 \( (r = –0.763, –0.824, \) and –0.588; \( p = 0.028, 0.012, \) and 0.003, respectively)

![Figure 4](image4.png)

**Figure 4** (A, B) show that Lung CT score were correlated with CRP and age, respectively \( (r = 0.606, 0.586, p < 0.001, \) respectively) in the no-severe patients.
acknowledged that severely ill patients often show more obvious lung damage. Therefore, for viral load in severely ill patients, doctors may need to evaluate the viral load in both upper and lower airways.

A study reported that COVID-19 patients had detectable SARS-CoV-2 RNA at the time of initial sample collection, with 50% showing detectable SARS-CoV-2 RNA by nasopharyngeal swab, 67% by oropharyngeal swab, and 85% by sputum testing. Although the levels of SARS-CoV-2 viral load were significantly associated with each of the different respiratory specimen types, severely ill patients had significantly lower Ct values (the samples from the lower respiratory tract) compared with mild/moderate cases on admission. This meant that there was a higher viral load in the lower respiratory tract. Another study showed that plasma viremia was generally associated with increased disease severity. Our data also showed that the viral load in the nasopharynx was significantly increased in the disease progression from non-severely to severely ill patients (p < 0.01). These results indicated that the dynamic monitoring of viral load changes, whether in the upper/lower respiratory tracts, as well as plasma viral load, were all important for evaluating disease progression.

4.2 Lung severity score and coronavirus 2019 disease progression

Changes in lung CT images were instrumental in evaluating whether the disease would worsen. Lung CT images may vary in different stages. In our study, most patients had multiple sites and multiple lesions. GGO was first observed at inpatient admission. Consolidation opacity developed 3–5 days thereafter. Prior to hospital discharge, consolidation opacity absorption or residual interlobular septal thickening manifested. This study noted a significant increase in LSS during the progression of COVID-19 from non-severe to severe cases. This also meant that in CT images, GGO and consolidation opacity during the exacerbation period (LSS 17.50 (7–19)) were more commonly observed than among admission period CT scans (LSS 11.50 (1–16); p < 0.001) and predischarge period CT imaging (LSS 7.00 (3–18); p < 0.01). Compared with the admission period, in addition to an increased LSS and viral load (a decreased Ct value) also increased (p < 0.01), while lymphocyte and monocyte count both decreased significantly (p = 0.01) in the exacerbation period.

4.3 Correlation between cycle threshold value, lung severity score, and inflammatory factors

A study conducted in the United States showed that higher plasma viral loads were significantly associated with several inflammation markers and disease severity, with lower absolute lymphocyte counts (r = −0.31; p = 0.008), and higher levels of both CRP (r = 0.40; p = 0.0003) and IL-6 (r = 0.50; p = 0.0001). Significant associations were also detected between nasopharyngeal and sputum viral loads and these three markers. In our non-severely ill COVID-19 patients, neither the Ct value derived at the inpatient admission period nor the Ct value recorded at follow-up periods were related to neutrophil, lymphocyte, or monocyte counts, PCT, CRP, or LSS (r = −0.346, 0.158, −0.055, 0.020, −0.150, 0.041, −0.249, 0.129, −0.116, 0.095, 0.048, and 0.153, respectively, all values were p < 0.05). However, LSS correlated with CRP and age (r = 0.606 and 0.586; p < 0.001 and p < 0.001, respectively.) This showed that the worsening conditions indicated by the imaging results in non-severely ill patients were mainly related to combined bacterial infections.

Among our severely ill COVID-19 patients, the Ct value was negatively related to CRP and LSS (r = −0.452 and −0.588; p = 0.002 and p = 0.003, respectively) but did not correlate with lymphocyte, mononuclear cell, and neutrophil counts, PCT, and the length of hospital stay (r = 0.056, 0.204, 0.267, −0.076, and −0.057, respectively; all values were p > 0.05). This suggested that an increased viral load and CRP were associated with increased lung inflammation. Different from the correlation between lymphocyte count decline and Ct value reported in the literature, one of the reasons for the difference in results may have been that the patients we observed were non-severely ill patients who subsequently became severely ill patients, not patients with acute respiratory distress syndrome (ARDS). When the severity of the disease progressed, lymphocyte counts decreased but no statistical correlation was observed between lymphocyte counts and Ct values. The results also showed that LSS negatively correlated with lymphocyte and mononuclear cell counts. (Pearson’s rank = −0.763 and −0.824; p = 0.028 and p = 0.012, respectively). At this stage, both viral infection and inflammatory factors will be involved in lung inflammation, and corresponding treatment strategies should be adopted to avoid the occurrence of Cytokine storm and the development of ARDS in patients.

In summary, this study found that when the severity of COVID-19 progressed, nasopharyngeal viral load and lung CT severity were closely related, and LSS negatively correlated with lymphocyte and mononuclear cell counts, as well as Ct values. Therefore, it is advised that by closely monitoring these indicators, early intervention measures can be taken to reduce the occurrence of mortality.

CONFLICT OF INTEREST
The authors declare no potential conflict of interest.

ETHICS APPROVAL
This study was conducted with approval from the Ethics Committee of The Petroleum Clinical Medical College of Hebei Medical University (KYLL-2020-06). This study was conducted in accordance with the declaration of Helsinki. The consent from the patient for the publication of the case was obtained.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID
Zheng Liu https://orcid.org/0000-0001-7143-4242
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