

Changes in the clinical characteristics of severe Corona Virus Disease 2019 in Jiangxi Province

Jingjing Yu

First Affiliated Hospital of Nanchang University

Tianxin Xiang

First Affiliated Hospital of Nanchang University

Xinping Xu

First Affiliated Hospital of Nanchang University

Wei Zuo

First Affiliated Hospital of Nanchang University

Congyang Zhou

First Affiliated Hospital of Nanchang University

Yu Liu

First Affiliated Hospital of Nanchang University

Yang Liu

First Affiliated Hospital of Nanchang University

Dechang Peng

First Affiliated Hospital of Nanchang University

Ning Zhang

First Affiliated Hospital of Nanchang University

Fen Liu

First Affiliated Hospital of Nanchang University

Na Cheng

First Affiliated Hospital of Nanchang University

Fei Xu

First Affiliated Hospital of Nanchang University

Siguang Xie

First Affiliated Hospital of Nanchang University

Jibin Yang

First Affiliated Hospital of Nanchang University

Yi Shao

First Affiliated Hospital of Nanchang University

Kejian Qian

First Affiliated Hospital of Nanchang University

Wei Zhang (✉ zhangweiliuxin@163.com)

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Abstract

Backgrounds: To determine the differences in clinical manifestations and biomarker levels of Corona Virus Disease 2019 (COVID-19) patients, including common patients and severe (serious and critical) patients.

Methods: A total of 89 COVID-19 patients were diagnosed and treated at the First Affiliated Hospital of Nanchang University. We clinically classified the patients and collected data.

Findings: There was a higher proportion of confirmed cases in patients with type A blood (44.8%). There were no obvious differences in number of lung lobes involved in the lesion between the patients with or without a positive nucleic acid test ($p>0.05$). There were obvious differences in contact history ($p<0.001$), duration of symptoms ($p=0.004$), and respiratory rate ($p=0.029$) between the patients with or without a positive nucleic acid test. According to the results of the nucleic acid diagnosis test, there were no obvious differences in the number of lung lobes involved in the lesion and all items of routine blood, liver, and kidney function tests between the patients with or without positive nucleic acid tests (all $p>0.05$). Between the common patients and severe patients, there were obvious differences in age ($p=0.006$), duration of symptoms ($p=0.001$), diastolic blood pressure ($p=0.046$), lymphocyte count ($p=0.0001$), neutrophil count ($p=0.019$), albumin ($p=0.002$), lactate dehydrogenase ($p=0.007$), calcium ($p=0.0001$), C-reactive protein (CRP) ($p=0.004$), erythrocyte sedimentation rate ($p=0.021$), international standard ratio ($p=0.020$), and CD3 ($p=0.001$), CD3+CD4 ($p=0.006$), and CD3+CD8 ($p=0.001$) levels. In patients infected with SARS-COV-2, the number of lung lobes involved in the lesion were positively correlated with lymphocytes ($R=0.261$, $p=0.044$); the body mass index (BMI) values were positively correlated with the number of lung lobes involved in the lesion ($R=0.320$, $P=0.034$); the age ($R=0.391$, $p<0.001$) and respiratory rate ($R=0.352$, $p=0.001$) were positively correlated with neutrophil count; and the age ($R=0.349$, $p=0.001$) and the number of lung lobes involved in the lesion ($R=0.422$, $p=0.001$) were positively correlated with CRP.

Conclusion: Patients with blood type A may be more susceptible to SARS-COV-2. The decrease in lymphocytes may indicate the aggravation of COVID-19, whereas the number of lung lobes involved in the lesion may not be a valid criterion for COVID-19 diagnosis.

Introduction

Since December 2019, several local health institutions have reported a number of patients with pneumonia of unknown cause, which may have originated from a seafood and wildlife wholesale market in Wuhan City, Hubei Province, China. With the spread of the epidemic, such cases have been found in other regions of China and other countries. At present, it has been confirmed that this type of pneumonia is caused by a new coronavirus, which the World Health Organization (WHO) initially named the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) (Xinhuanet News Report, 2020). And the pneumonia named Corona Virus Disease 2019 (COVID-19).

Prior to this discovery, six coronaviruses were known to cause human diseases, comprising 229E and nl63 of the α genus, hku1, OC43, severe acute respiratory syndrome coronavirus (SARS CoV), and Middle East respiratory syndrome coronavirus (MERS CoV) of the β genus. In normal people, 229E, nl63, hku1, and OC43 only cause common cold symptoms, while severe SARS CoV and MERS CoV can cause death (Su et al., 2016; Cui et al., 2019).

Current research shows that the new coronavirus belongs to a new type of β genus, with a capsule, round or oval particles, often polymorphous, and with a diameter of 60–140 nm. Its genetic characteristics are significantly different from those of SARS CoV and MERS CoV, and thus has been named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). At present, the homology with bat-sl-covz45 is more than 85% (National Health Office Medical Letter, 2020a).

The outbreak of the new coronavirus SARS-COV-2 poses a huge threat to global public health. With the spread of this disease, an increasing number of patients have no direct relationship with the seafood wholesale market in Wuhan City, indicating that the virus can be spread between people. At present, the Chinese government believes that the virus is mainly transmitted through respiratory droplets and contact, although the exact mechanisms of aerosol and digestive tract transmission are still unclear (National Health Office Medical Letter, 2020a).

In order to study COVID-19, we collected the data from 89 patients diagnosed in our hospital, analyzed their symptoms, signs, complications, and cytokines, and subsequently reported the results.

Methods

Subjects and study design

A total of 89 cases of COVID-19 were diagnosed and treated at the First Affiliated Hospital of Nanchang University, including 56 common patients, 22 severe patients (including serious patients and critical patients), and 11 suspected patients (Figure 1).

The purpose of this study is to determine the differences in clinical manifestations, typing, and biomarker levels in common and severe COVID-19 patients. This study was carried out according to the Declaration of Helsinki, and the plan was approved by the ethics committee of the First Affiliated Hospital of Nanchang University (ethics No.: 2020013). All methods were carried out to the extent permitted by relevant guidelines and regulations. The inclusion criteria of COVID-19 patients meet any of the following: (1) real-time fluorescent reverse transcription-polymerase chain reaction (RT-PCR) detection of new coronavirus nucleic acid isolated from respiratory or blood samples; (2) virus gene sequences from respiratory or blood samples that are highly homologous with the known new coronavirus. All procedures were repeated more than twice, with an interval of more than 24 hours.

Figure 1

Clinical classification

(1) Common patients: with fever, respiratory tract and other symptoms, pneumonia confirmed via imaging.

(2) Severe patients: comply with any of the following: (1) respiratory distress, respiratory rate ≥ 30 times / min; (2) in the resting state, oxygen saturation $\leq 93\%$; (3) arterial partial pressure of oxygen (PaO_2) / concentration of oxygen (FiO_2) ≤ 300 mmHg (1 mmHg = 0.133 kpa).

(3) Critical patients: those who meet one of the following conditions: (A) respiratory failure and require mechanical ventilation; (B) shock; (C) other organ failure requiring intensive care unit (ICU) monitoring and treatment.

Data collection

All subjects provided their informed consent before participating in the study. Body mass index (BMI), incubation period, temperature, pulse frequency, systolic blood pressure, diastolic blood pressure, and other clinical data were obtained through detailed physical examination and medical history inquiry. Routine blood tests and tests for liver function, kidney function, inflammatory index, coagulation function, and lymphocyte count were performed in the laboratory.

Statistical analysis

The chi-square test and *t*-test were used to compare the basic clinical characteristics of the two groups, such as age, gender, and clinical classification. Then, the levels of various cytokines, electrolyte and blood gas analysis results, liver function, renal function, routine blood tests, coagulation function, myocardial enzyme spectrum, and immunology indexes of different groups were analyzed to determine whether there were differences between the two groups. $P < 0.05$ indicates statistical significance. Spearman rank-order correlation was used to evaluate the relationship among the parameters (items of clinical features) that were not normally distributed, and Spearman's correlation coefficient (ρ) was reported. The chi-square test was used to assess associations among categorical variables including gender and potential confounding factors. Additionally, $p < 0.05$ was considered statistically significant.

Results

Demographics and visual measurements

Figure 1 shows the characteristics of patients infected with SARS-COV-2. Whether in common patients or critical patients infected with SARS-COV-2, there was a higher proportion of confirmed cases in patients with type A blood. Figure 2 shows computed tomography (CT) images of the lungs of COVID-19 patients at different stages. According to the results of the nucleic acid diagnosis test, there were no obvious differences in sex, age, BMI, incubation period, temperature, pulse frequency, systolic blood pressure, diastolic blood pressure, or number of lung lobes involved in the lesion (all $p > 0.05$) between the patients with or without positive nucleic acid tests. Therefore, the number of lung lobes involved in the lesion may

not be a valid criterion for COVID-19 diagnosis. There were obvious differences in contact history ($p < 0.001$), duration of symptoms ($p = 0.004$), and respiratory rate ($p = 0.029$) between the patients with or without positive nucleic acid tests (Table 1, Figure 2).

For confirmed patients, there were no obvious differences in sex, BMI, contact history, incubation period, duration of symptoms, temperature, pulse frequency, respiratory rate, systolic blood pressure, or number of lung lobes involved in the lesion when comparing common and severe patients (all $p > 0.05$). There were obvious differences in age ($p = 0.006$), duration of symptoms ($p = 0.001$), and diastolic blood pressure ($p = 0.046$) between common and severe patients. (Table 1)

Table 1

Figure 2

Laboratory findings

Between the patients with or without a positive nucleic acid test, there were no obvious differences in all items from routine blood tests and liver and kidney function tests. Details are presented in Table 2.

Between the common patients and severe patients, there were obvious differences in lymphocyte count ($p < 0.0001$), neutrophil count ($p = 0.019$), albumin ($p = 0.002$), lactate dehydrogenase ($p = 0.007$), and calcium ($p < 0.0001$). Additionally, there were no obvious differences in other items from routine blood tests and liver and kidney function tests. Details are presented in Table 2.

Table 2

Between the patients with or without a positive nucleic acid test, there were no obvious differences in all items of inflammatory indicators (Figure 3-A), coagulation function (Figure 3-C), and lymphocytes (Figure 3-E).

Between the common patients and severe patients, there were obvious differences in C-reactive protein (CRP) ($p = 0.004$), erythrocyte sedimentation rate ($p = 0.021$) (Figure 3-B), and international standard ratio ($p = 0.020$) (Figure 3-D). Compared with common patients, CD3 ($P = 0.001$), CD3 + CD4 ($P = 0.006$), and CD3 + CD8 ($P = 0.001$) levels in severe patients significantly decreased (Figure 3-F). This indicates that lymphocytes may be an important index to gauge the severity of the disease. There were no obvious differences in other items of inflammatory indicators or coagulation function (Figure 3).

Figure 3

Correlations

In patients infected with SARS-COV-2, the number of lung lobes involved in the lesion were positively correlated with lymphocytes ($R = 0.261$, $P = 0.044$); the BMI values were positively correlated with the number of lung lobes involved in the lesion ($R = 0.320$, $P = 0.034$); the age ($R = 0.391$, $P < 0.001$) and

respiratory rate ($R=0.352$, $P=0.001$) were positively correlated with neutrophil count; and the age ($R=0.349$, $P=0.001$) and the number of lung lobes involved in the lesion ($R=0.422$, $P=0.001$) were positively correlated with CRP (Figure 4).

Figure 4

Discussion

Beginning in December 2019, 41 cases of unexplained pneumonia occurred in Wuhan, Hubei Province, China. As a major transportation hub, Wuhan is about 300 kilometers away from Jiangxi.

Respiratory viruses can cause symptomatic infection at any age and at any location in the world. However, respiratory viruses are prone to antigen drift due to point mutations in the virus genome, resulting in the formation of new strains with pandemic potential. All these factors can increase the difficulty of rapid and accurate diagnosis of respiratory diseases. Therefore, it is necessary to identify mutations in the virus genome and understand the gene sequence of the new virus.

SARS is a zoonotic disease caused by SARS-CoV. Hospital transmission of SARS-CoV is very common. The main host is bats, and the intermediary is mosquitoes from the Guangdong wet goods market (Azhar et al., 2019). Middle East Respiratory Syndrome (MERS) is a new zoonotic deadly disease caused by the Middle East MERS Coronavirus (MERS-CoV), which appeared in 2012. It is believed that humans became infected with MERS-CoV through exposure to camels or camel products, and a lethal rate of approximately 35% was observed.

After detecting this new coronavirus, a Chinese science team announced at a national press conference that this was the pathogen that caused the epidemic, and the WHO designated the virus as the new coronavirus in 2019 (2019-nCoV) (Xinhuanet News Report, 2020). On February 12, pneumonia infection with the new coronavirus was collectively referred to as severe acute respiratory syndrome coronavirus 2 (SARS-COV-2).

The nucleic acid sequence of SARS-COV-2 differs from known human coronavirus species (SARS and MERS). After comparison, the new coronavirus was found to be similar to some β -coronaviruses found in bats (Yin et al., 2018; National Health Office Medical Letter, 2020b). At present, the homology with BAT-sl-covzc45 exceeds 85%. (de Wit E et al., 2016). It was detected in patients' lung fluid, blood, and throat swab samples, and viruses isolated under an electron microscope were found to exhibit typical coronavirus characteristics. In order to better understand this new coronavirus, further research will be carried out as soon as possible with the goal of developing antiviral drugs and vaccines (Zumla et al., 2016).

Table 3

As of January 26, 2020, 2,036 patients have been diagnosed with COVID-19. Symptoms include fever (90%), discomfort, dry cough (80%), shortness of breath (20%), and respiratory distress (15%).

Host range and tissue tropism vary greatly among different coronaviruses. In general, theta coronavirus and β -coronavirus can infect mammals, and gamma coronavirus and triangular coronavirus can infect birds, but some of these viruses can also infect mammals (Cui et al., 2019; Woo et al., 2012). Before 2019, there were only six coronaviruses with the capability of infecting humans and causing respiratory diseases: (i) HCoV-229E, HCoV-OC43, HCoV-NL63, and HKU1, which can cause only mild upper respiratory diseases, and in very few cases can cause severe infections; and (ii) SARS-CoV and MERS-CoV in infants and the elderly can infect the lower respiratory tract and cause severe respiratory syndrome. (Fehr et al., 2015; Su et al., 2016) The new coronavirus SARS-COV-2 belongs to the β -coronavirus group, according to genomic analysis. It can also infect the lower respiratory tract and cause pneumonia, but the overall symptoms are milder than those of SARS and MERS (Table 4).

Table 4

In the study by Ji et al. (Ji et al., 2020), relative synonymous codon usage (RSCU) values were used for comprehensive sequence analysis and comparison of relative synonymous codons between different animal species. The results showed that 2019-nCoV appeared to be a recombinant virus between bat coronavirus and unknown coronaviruses.

At present, because there is no effective antiviral treatment for coronavirus, the main treatment method is supportive therapy. Ribavirin-containing recombinant interferon (IFN) has a limited effect on coronavirus infections (Cinatl et al., 2003). After the prevalence of SARS and MERS, many anti-CoV drugs for CoV protease, polymerase, methyltransferase, and entry proteins have been developed, but have not been confirmed in clinical trials. (Chan et al., 2013; Cheng et al., 2015; Wang et al., 2015)

Patients may have mental anxiety, and memory or cognitive impairment, which can be assessed by the Hospital Anxiety and Depression Scale (HADS), Mini-Mental State Examination (MMSE), and the Dream Anxiety Scale to explore the relationship between mental cognitive function and COVID-19 patients. SARS-COV-2 can be spread by viral contact with the lung tissue and conjunctiva, causing damage to the human body as well as anxiety, cardiovascular disease, and endocrine disease (Figure 5).

Figure 5

There are many vaccine strategies for CoV. Inactivated, attenuated, and live viruses, viral vector-based vaccines, subunit vaccines, recombinant proteins, and DNA vaccines have been developed, but thus far, only animals have been tested. (Graham et al., 2013) Currently, there is no effective treatment or vaccine, and therefore, the most efficient methods to manage SARS-COV-2 infection are to control the source of infection, early diagnosis, reporting, isolation, supportive treatment, and timely release of epidemic information to avoid unnecessary panic. For individuals, good personal hygiene, appropriate masks, ventilation, and avoiding crowded places will help to prevent SARS-COV-2 infection.

To more closely study this new virus, in 2019, we examined the data from 42 patients diagnosed in our hospital, analyzed their symptoms, signs, complications, and cytokines, and then reported the results.

Through serological examination of COVID-19 patients, we found that patients exhibited a significant decrease in CD3, CD4, and CD8 compared with ordinary people, and the levels of CD3, CD4, and CD8 in severe patients were lower than those in common patients. We speculate that SARS-COV-2 and cellular immune response, and especially T cells, are closely related. 2019-nCoV may inhibit T cell function in the body, cause T cell dysfunction, and reduce the levels of CD3, CD4, and CD8. As the patient's immunity decreases and the greater the degree of decline, the more serious the patient's condition.

We also found that in the imaging examination of patients, there was no difference in the number of lesions in common patients compared with severe patients, and the average cumulative number of lung lobes was the same as that in severe patients. Therefore, it is unlikely that the number of lesions detected by imaging can be regarded as ordinary in common patients and severe patients.

Ultimately, we found that patients with blood type A accounted for 44.9% of all patients, which is significantly higher than patients with other blood types. We could not locate any previous studies that mentioned that patients with blood type A are more susceptible to SARS-COV-2. Therefore, we require a larger sample size to explore this inherent relationship.

Our study has some limitations. The limited number of cases when collecting samples led to a small number of samples, and some unknown variables may affect the experimental results. Most SARS-COV-2 patients are related to Wuhan. In addition to known variables (such as eating wild animals), there are also unpredictable variables, such as regional differences and customs differences, which may affect the experimental results.

Table 5

Declarations

Ethics approval and consent to participate

Not applicable

Availability of data and materials

All data and materials used in this work were publicly available.

Consent for publication

Not applicable

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Conflict of Interests

This was not an industry supported study. The authors report no conflicts of interest in this work.

Author contributions

Y.J.J., X.T.X., Q.K.J. and Z.W. conceived of the study. X.X.P., Z.W., Z.C.Y., L.Y., L.Y. and P.D.C. collected samples and data. Z.N., L.F., C.N., X.F., Y.S. and Y.J.B. processed samples. X.S.G., Y.J.J. and X.T.X. analyzed the data. Y.J.J., X.T.X., Q.K.J. and Z.W. wrote the manuscript with input from all the authors.

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No applicable

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Tables

Due to technical limitations, Tables 1 - 5 are only available for download from the Supplementary Files section.

Figures

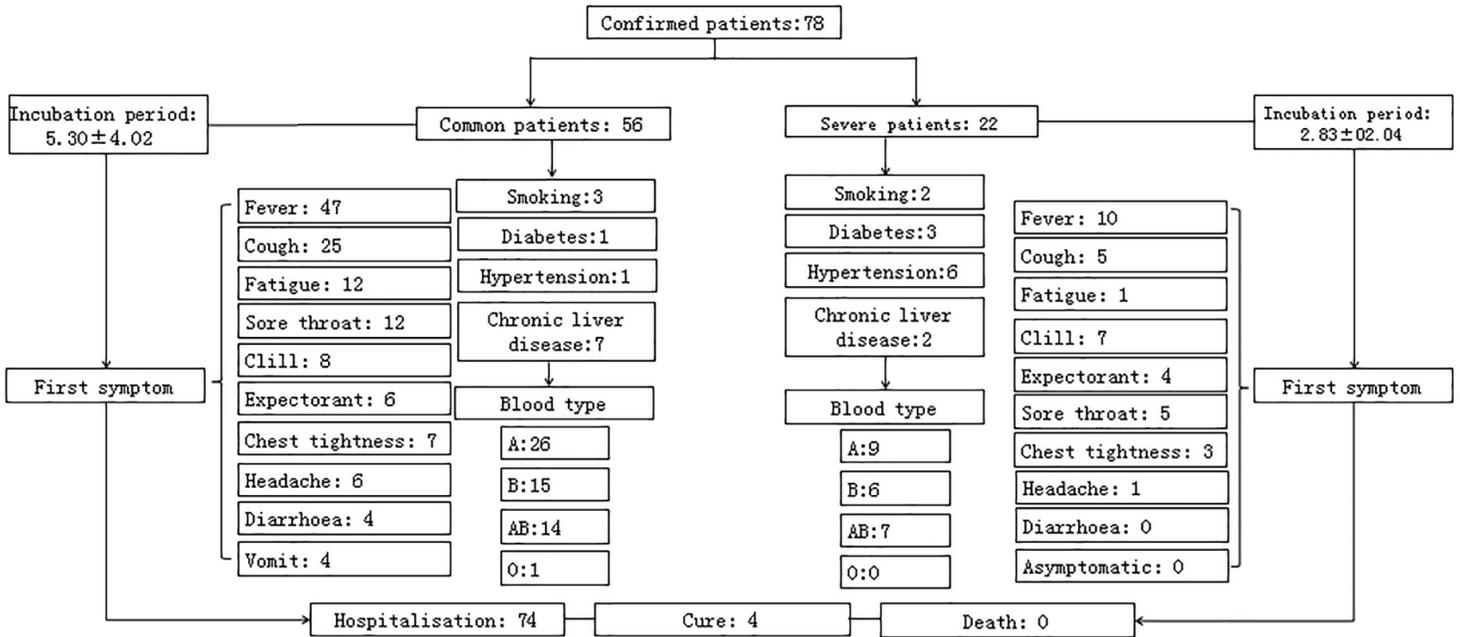


Figure 1

Characteristics, blood types and Prognosis of patients infected with SARS-COV-2.

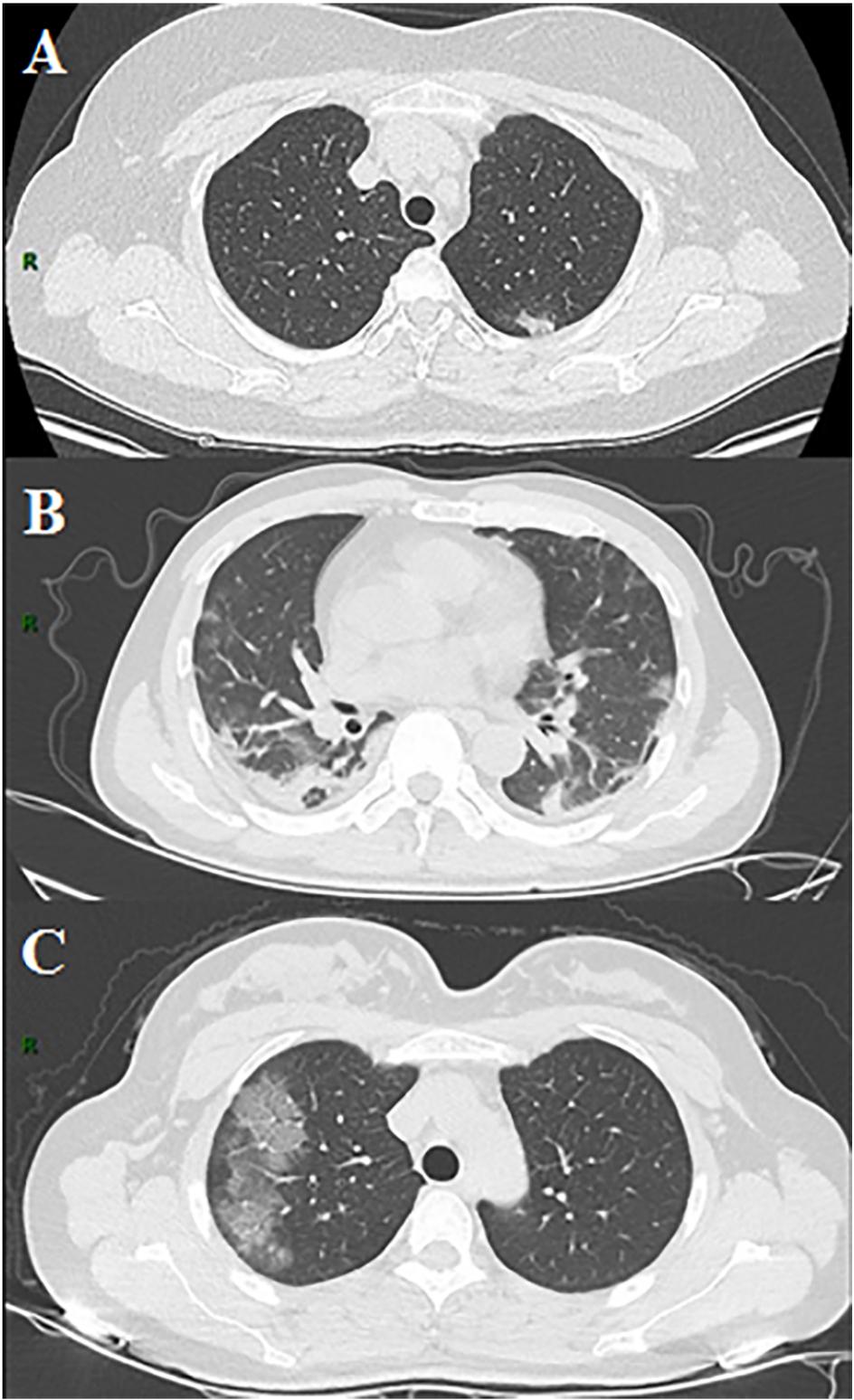


Figure 2

CT images of SARS-COV-2 patients. A. As for common patients, the early CT findings were not typical. Only small ground glass shadow was seen in the upper left lobe, with unclear boundary. B. In the progressive stage, multiple patchy, large ground glass shadows and consolidation shadows can be seen, and even pleural effusion can be seen. C. As for severe patients, diffuse lesions of both lungs may increase by 50% or even appear pulmonary fibrosis.

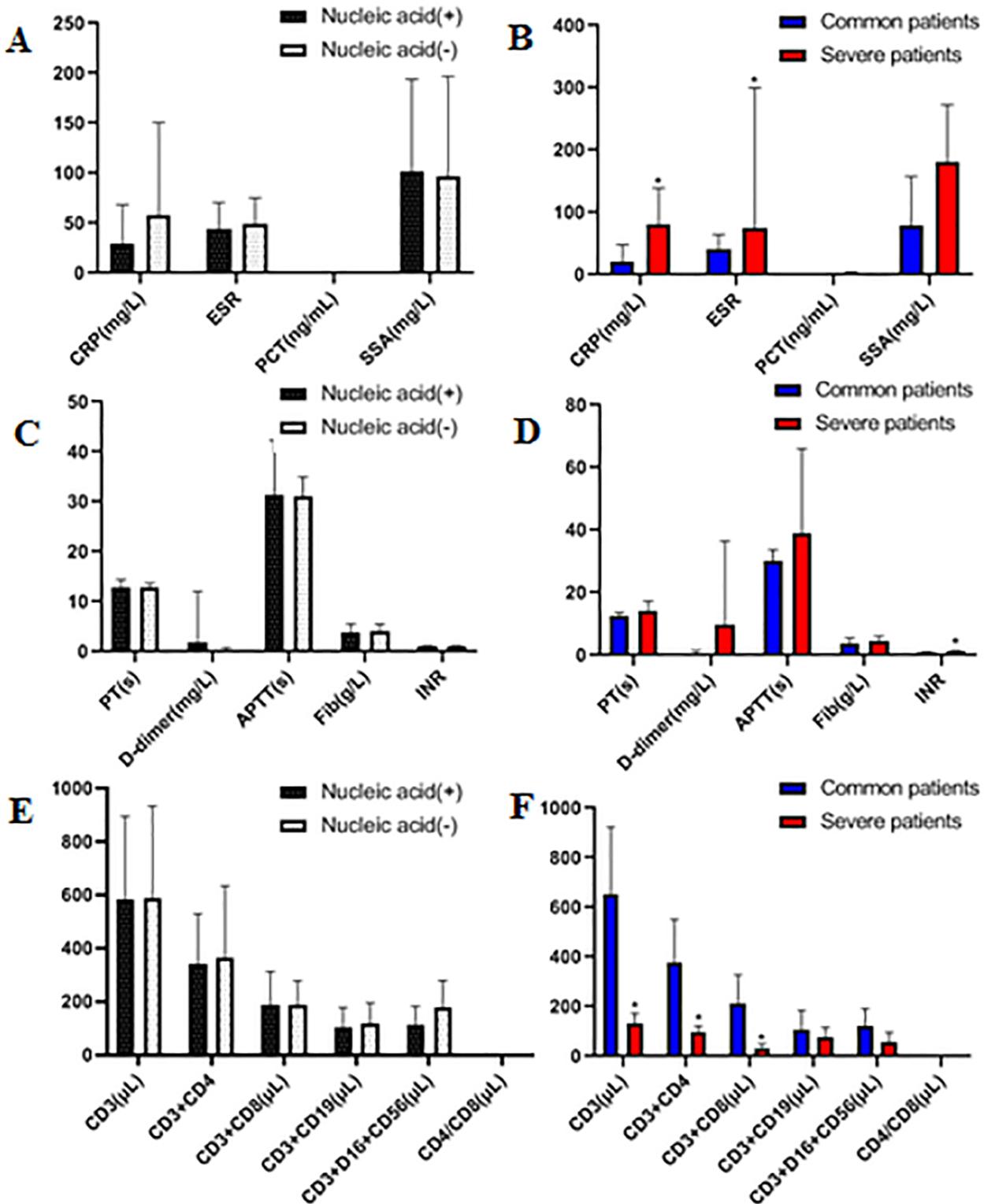


Figure 3

The inflammatory indicators and coagulation function change in both patients. A. Inflammatory indicators between the patients with or without positive nucleic acid test. B. Inflammatory indicators between the common patients and severe patients. C. Coagulation function between the patients with or without positive nucleic acid test. D. Coagulation function between the common patients and severe patients. E. Lymphocyte between the patients with or without positive nucleic acid test. F. Lymphocyte

between the common patients and severe patients. Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SAA, serum amyloid A; PT, prothrombin time; APTT, activated partial thromboplastin time; PCT, procalcitonin; Fib, fibrinogen; INR, international standard ratio.

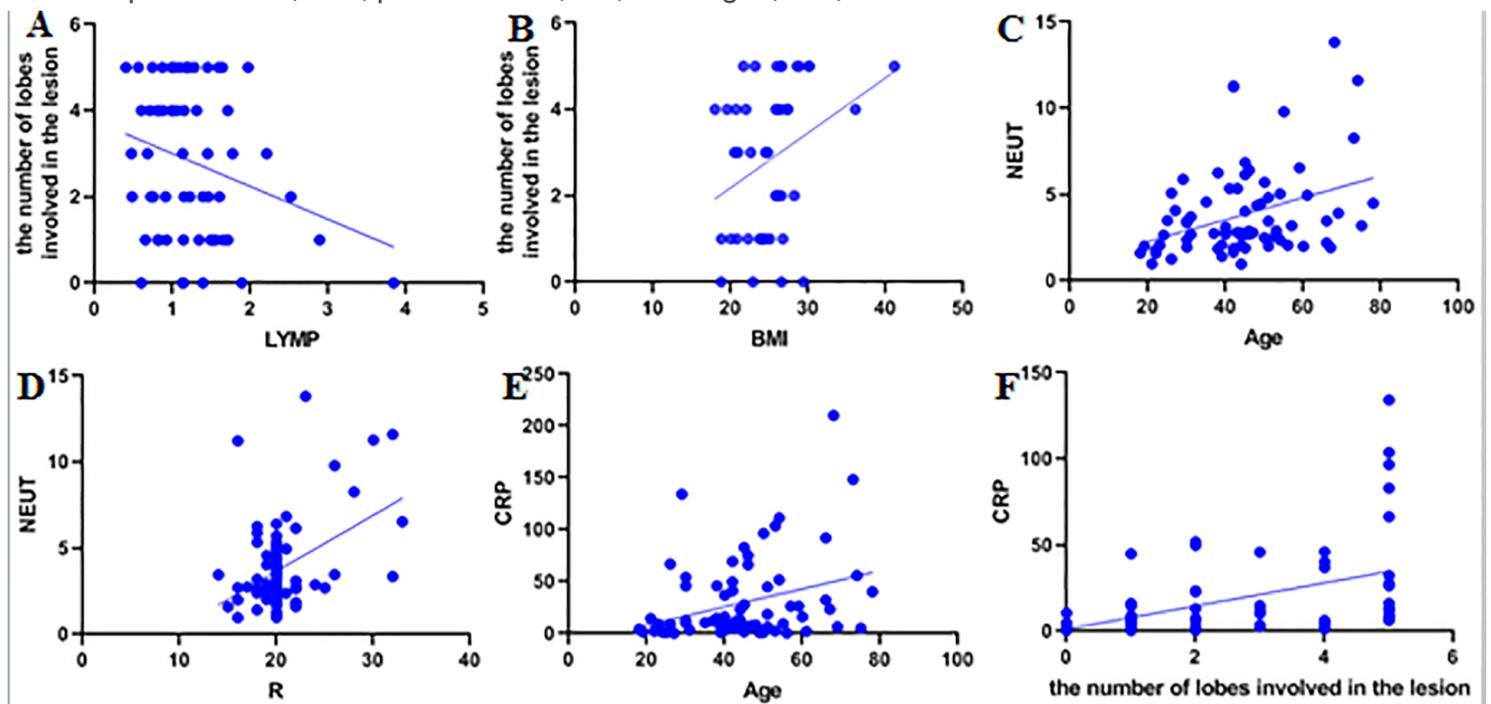


Figure 4

The correlation between the different items of clinical features. A. The correlation between the number of lobes involved in the lesion and the number of lymphocyte. B. The correlation between BMI and the number of lobes involved in the lesion. C. The correlation between the age and neutrophil count. D. The correlation between respiratory rate and neutrophil count. E. The correlation between age and CRP. F. The correlation between the number of lobes involved in the lesion and CRP. Abbreviations: LYMP, lymphocyte count; BMI, body mass index; NEUT, neutrophil count; R, respiratory rate; CRP, C-reactive protein.

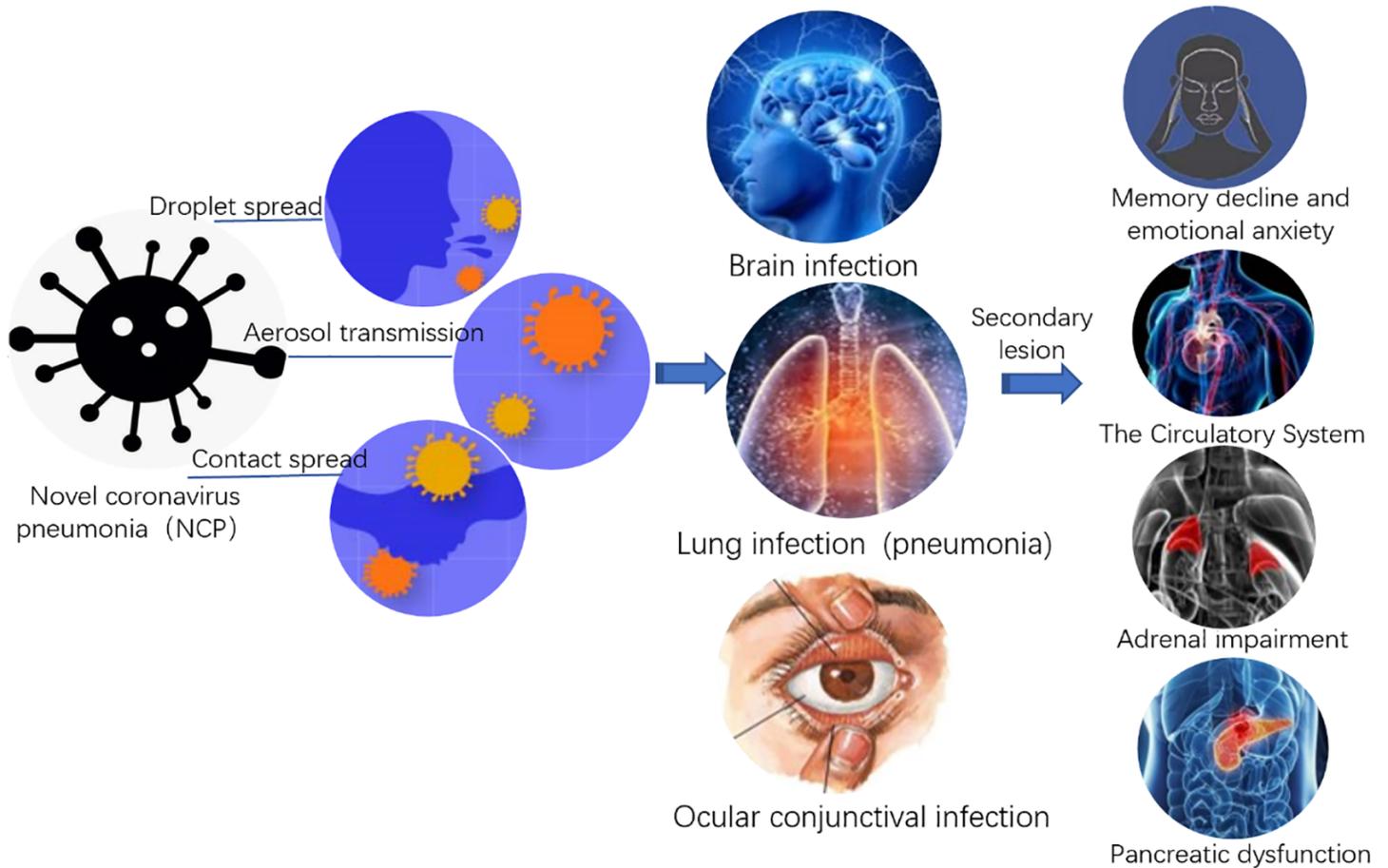


Figure 5

Ways and symptoms of a viral infection. Figure 5: 2019-nCoV can be transmitted into the lungs through the air, aerosol transmission or through contact with the conjunctiva, causing multiple system dysfunctions such as the endocrine system, the respiratory system, etc.

Supplementary Files

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