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Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19)

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Running head: Factors associated with severity and prognosis

Summary

The proportion of severe cases remains high, so it is very urgent to seek the factors that affect the severity and prognosis. The elderly and patients with underlying diseases are more likely to experience a severe progression of COVID-19. It is recommended that timely antiviral treatment should be initiated to slow the disease progression and improve the prognosis.

Abstract

Background. At present, the severity of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been a focal point.

Methods. To assess the factors associated with severity and prognosis of patients infected with SARS-CoV-2, we retrospectively investigated the clinical, imaging, and laboratory characteristics of confirmed 280 cases of novel coronavirus disease (COVID-19) from January 20 to February 20, 2020.

Results. The median age of patients in the mild group was 37.55 years old, while that in the severe group was 63.04 years old. The proportion of patients over 65 years old in the severe group was significantly higher than that of the mild group (59.04% vs. 10.15%, $P < 0.05$). 85.54% of severe patients had diabetes or cardiovascular diseases, which was significantly higher than that of the mild group (51.81% vs 7.11%, $P = 0.025$; 33.73% vs 3.05%, $P = 0.042$). Patients in the mild group experienced earlier initiation of antiviral treatment (1.19 ± 0.45 vs 2.65 ± 1.06 days in the severe group, $P < 0.001$). Our study showed that comorbidity, time from illness onset to antiviral, and age >=65 were three major risk factors for COVID-19 progression, while comorbidity and time from illness onset to antiviral were two major risk factors for COVID-19 recovery.

Conclusions. The elderly and patients with underlying diseases are more likely to experience a severe progression of COVID-19. It is recommended that timely antiviral treatment should be initiated to slow the disease progression and improve the prognosis.

Keywords. severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); Coronavirus disease-19 (COVID-19); antiviral treatment; disease progression; prognosis

Background

Since December 2019, pneumonia patients of unknown aetiology have been reported in Wuhan, Hubei. These patients were subsequently discovered to be infected with a novel coronavirus, that is, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1,2] The virus had a single strand positive RNA, and was mainly transmitted via respiratory droplets and contacts.[3,4] All the population was generally susceptible to this new coronavirus.[5]

Up to February 22, 2020, 76,392 confirmed cases and 2348 death cases of novel coronavirus disease (COVID-19) have been reported in China. Hubei Province, especially Wuhan City, accounted for 74.3% and 43.2% of the nation's cumulative confirmed cases, and was of the top priority for epidemic prevention and control.[6] Meanwhile, 1408 confirmed cases and 12 deaths were reported in 25 countries and regions outside China.

So far, the proportion of severe cases remains high, calling for effective regimens for this highly contagious disease.[7,8] In this study, we analyzed the clinical characteristics, treatment and prognosis of 280 patients from four hospitals from January 20 to February 19, 2020, and proposed several risk factors for COVID-19 progression and recovery. We believe that our findings will facilitate clinical management of COVID-19 patients.

Patients and methods

Patients

All enrolled 280 patients were enrolled from First People's Hospital of Yancheng City, the Second People's Hospital of Fuyang City, the Second People's Hospital of Yancheng City, and the Fifth People's Hospital of Wuxi from Jan 20 to Feb 19, 2020. The present study was performed in

accordance with the Helsinki Declaration and was approved by the Ethics Committee of the First People's Hospital of Yancheng City. Written informed consents were obtained from participants when data were collected retrospectively.

Data collection

We collected all the data including clinical, demographic, laboratory parameters, chest CT, length of hospitalization, body mass index (BMI) and prognosis from patients' medical records and attending doctors. The data endpoint was Feb 19, 2020. The clinical data included demography, comorbidities, date of accident, symptom and sign, timing of antiviral therapy, clinical progress and so on. Comorbidities included cardiovascular and cerebrovascular diseases, endocrine system diseases, digestive system diseases, respiratory system diseases, malignant tumors and nervous system diseases. Treatments included antiviral therapy, antibiotic therapy, hormone therapy, immunoglobulin therapy, traditional Chinese Medicine and so on. At the time of admission, all patients were examined in the laboratory, including blood routine, blood biochemistry, coagulation function, infection-related biomarkers, co-infection and so on.

Definition and clinical classification of cases

All of the enrolled patients infected with SARS-CoV-2 met the criteria from WHO and National Health Commission of the People's Republic of China.[9] We defined the case with epidemiological history and consistent with any two clinical manifestations and the pathogenic evidence, as previously described.[10] Throat swab and/or nose swab of each patient were collected to detect the coronavirus RNA with real-time RT-PCR.[10] The detailed definition of clinical classifications was in the Table S1.

The patients were further categorized into four subgroups according to epidemiolocal history: Generation I [14 patients (5.00%) who had an exposure history to Huanan seafood market in South China], Generation II [164 patients (58.57%) who had a travel history to Wuhan], Generation III [86 patients (30.71%) who were infected by imported cases]; Generation IV [16 people (5.72%) who were infected by Generation Ⅲ patients].

Statistical analysis

Statistical analyses were performed with SPSS (ver. 18.0; SPSS Inc., Chicago, IL, USA). Continuous data were expressed as means ± standard deviations and were analyzed using Student's t test. A value of $P < 0.05$ was considered statistically significant. Categorical data were shown as numbers (percentages) and compared with the Chi-squared test. Ordered categorical data were analyzed with the Spearman rank correlation. Univariate and multivariate logistic regression analyses were performed to identify independent severity and prognosis indicators of patients with COVID-19. Orthogonal partial least squares discriminant analysis (OPLS-DA) was used to evaluate and rank the ability of the parameters with severity factors of patients with COVID-19 using SIMCA software.

Results

Baseline characteristics

A total of 280 eligible COVID-19 patients were recruited from four hospitals in Jiangsu and Anhui Province, China. The demographic and clinical characteristics of all recruited patients were summarized in Table 1. Among the enrolled cases, the overall mean age was 43.12 years (SD 19.02). 84 patients (30.00%) were aged 50-64 years, which accounted for the highest proportion. The proportion of patients aged under 18 years, 18-24 years and 25-49 years were 12.50%, 5.00% and 27.86%, respectively. Moreover, 49 patients (17.50%) were mild type, 148 patients (52.86%) were moderate type, 75 patients (26.79%) were severe type and 8 patients (2.85%) were critically ill (see detailed definition of clinical classifications in the Table S1).

We further divided these patients into two subgroups: (1) mild group (including mild type and moderate type) and (2) severe group (including severe type and critically ill type) The severe group had a significantly higher proportion of patients over 65 years old (59.04% vs. 10.15% in the mild group, $P < 0.05$) (Figure 1A) and BMI values (25.8 ± 1.8 vs. 23.6 ± 3.2, $P = 0.005$). Moreover, patients with underlying diseases were more likely to develop severe symptoms, as 82 out of the 83 severe patients had at least one underlying disease. The proportion of cardiovascular and cerebrovascular diseases and endocrine system diseases in the severe group were significantly higher than those of the mild group (51.81% vs 7.11%, $P = 0.025$; 33.73% vs 3.05%, $P = 0.042$)

(Figure 1B). Other diseases, such as digestive system diseases, respiratory system diseases, malignant cancers and nervous system diseases, exhibited no statistical difference between the two groups. In addition, over 10% of the patients didn't get a positive result until a third or fourth nucleic acid test both in mild group and severe group.

Laboratory results

The laboratory findings of all recruited patients were summarized in Table 2. Briefly, patients in the severe group exhibited a significant lower level of white blood cell, lymphocyte and platelet compared to that of the mild group [3.4 (2.9-8.4) vs 5.0 (4.2-6.6), $P = 0.043$; 0.5 (0.4-0.8) vs 1.3 (0.9-1.9) , $P = 0.006$; 86 ± 15 vs 196 ± 59, $P = 0.012$].No significance were detected with respect to the level of neutrophil, monocyte, and hemoglobin between the two groups (all $P > 0.05$).

As for blood biochemistry, 7 patients (2.50%) showed liver dysfunction; 5 patients (1.79%) had varying degrees of renal function damage; 29 patients (10.36%) developed hyperglycemia. There was no statistical difference in the liver function, renal function and blood glucose (GLU) level between the two groups of patients. Of note, the level of creatine kinase (CK) and creatine kinase–MB in the severe group were both significantly higher than that of the mild group [76 (41-268) vs 67 (52-104), $P = 0.049$; 13 (7-24) vs 9 (7-14), $P = 0.038$], while the level of PaO_2 and PaO_2/FiO_2 in severe group were significantly lower than that of the mild group [68 (53-88) and 91(82-106), $P = 0.019$; 165 (109-298) and 359 (293-495), $P = 0.009$].

Blood coagulation tests showed that the level of activated partial thromboplastin time (APTT) and prothrombin time (PT) of both groups was within the normal range. On the other hand, patients in the severe group showed a significantly increased D-dimer level [3.0 (0.6-5.0) vs. 0.2 (0.2-0.5), $P = 0.001$]. Of the 280 cases, only 3 patients (1.07%) and 8 patients (2.86%) had elevated procalcitonin (PCT) and erythrocyte sedimentation rate (ESR) levels, respectively. In addition, the level of C-reactive protein (CRP) in severe group was significantly elevated than that of the mild group [21.3(14.3-36.6) vs. 6.9(1.6-10.0), $P = 0.036$].

Cultures for nine kinds of respiratory pathogens including viruses, and bacteria and fungi were conducted. The results showed that the bacterial infection rate in severe group was significantly higher than that of mild group (6.02% vs. 0.51%, $P = 0.049$).

Imaging features

Chest radiograph was performed on day of admission for each patient. Among the 280 patients, 245 (87.50%) showed abnormal chest CT images, including 122 cases (43.57%) of bilateral pneumonia and 123 cases (43.93%) of unilateral pneumonia. 35 cases (12.50%) had no abnormal density shadow in the parenchyma of both lungs (Table 1). There was no significant difference in the imaging features between the mild and severe group on day of admission (P = 0.204).

Treatment and clinical outcomes

All patients received antiviral treatment, including ribavirin, lopinavir or ritonavir. 67.14% of the patients were treated empirically with a single antibiotic, mainly moxifloxacin. 63.21% of the patients were supported with non-invasive ventilator (ie, face mask). The admission rate of ICU was 29.64%; the median length from symptom onset to ICU was 6 days (IQR 4 -10), and the median length of ICU stay was 18 days (IQR 7.0 -37.9). So far, 221 patients have been discharged from the hospital and no death has occurred.

Patients in the mild group experienced earlier initiation of antiviral treatment (1.19 ± 0.45 vs 2.65 ± 1.06 days in the severe group, $P < 0.001$) and non-invasive ventilation (Figure 1C). 35.36% of the patients received methylprednisolone sodium succinate or methylprednisolone but there was no significant difference between the mild group and the severe group.

Risk factors for COVID-19 progression

OPLS-DA analysis was performed to evaluate and rank the influences of the baseline parameters on COVID-19 progression. Distinct dot clusters of the severe group and mild group were observed in Figure 2B. Loading plot revealed ten parameters as major influential factors for COVID-19 progression (i.e age >=65, comorbidity, days from illness onset to antiviral treatment, D-dimer level, lymphocyte count, epidemiological history, BMI, non-invasive ventilation (ie,face mask), creatine kinase and creatine kinase–MB level) (Figure 2C).

Next, univariate and multivariate analysis were conducted to evaluate the association between the above factors and clinical outcomes. Specifically, univariate analysis demonstrated that all the

factors were statistically significant between the severe group and mild group, while multivariate analysis further revealed that comorbidity, time from illness onset to antiviral treatment, and age >=65 were independent risk factors for COVID-19 progression (Table 3).

Risk factors for COVID-19 recovery

Finally, we investigated the risk factors for COVID-19 recovery within 221 currently discharged patients. The recovery time was defined as the duration from the first positive nucleic acid result to the first negative nucleic acid result.

Of the 221 discharged patients, the average time of COVID-19 recovery was 11 days (IQR 6-13). Patients in the severe group underwent a significantly longer recovery period than those in the mild group (18.70 ± 2.50 vs 10.63 ± 1.93 days, $P < 0.001$) (Figure 1D). Comorbidity and time from illness onset to antiviral treatment were both highly correlated with the average time of COVID-19 recovery ($r = 0.759$ and $r = 0.785$, both $P < 0.001$) (Figure 3).

Discussion

Up to now, the proportion of severe COVID-19 cases has dropped significantly. [11,12] Specifically, this number has decreased from 32.4% on January 28 to 21.6% in Wuhan[13] and to 7.2% in other provinces of China on February 15. Measures such as strengthened medical support and centralized isolation greatly contributed to the improved circumstances, and laid a solid foundation for further enhancing the cure rate and reducing the mortality rate.[14,15] However, there are still hundreds of severe patients dying every day. It is extremely important to make timely and efficient diagnosis and initiate treatment for severe patients.

In this study, we conducted a retrospective study of 280 patients from multiple centers in Jiangsu and Anhui Province and proposed several risk factors for COVID-19 progression and recovery. Intriguingly, we investigated and categorized the epidemiological history of patients and found that that all the patients in severe group were from Generation Ⅰ or Generation II. In terms of laboratory tests, the level of CK, CK-MB and D-dimer in severe group were significantly higher than that of the mild group, while the level of WBC, lymphocyte, PaO_2 and PaO_2/FiO_2 in severe group were significantly lower than that of mild group. As for CT imaging features, there

was no significant difference in the imaging features between the mild and severe group on day of admission.

In this study, the median age of patients in the mild group was 37.55 years old, while that in the severe group was 63.04 years old. In addition, the proportion of patients over 65 years old in the severe group was significantly higher than that of the mild group, which was consistent with the report of Du et al.[16] Notably, patients aged 50-64 years constituted the the highest proportion within the severe group. We speculate that this population conduct more daily activities (such as work, transportation) than the elderly and therefore have higher chance of infection. Our study further revealed that age was an important risk factor for the progression but not recovery of COVID-19, which may be attributed to the degeneration of physiological functions and immune responses among the elderly, who were more likely to develop severe pneumonia after SARS-CoV-2 infection. [17-19]

Several studies[20,21] have reported that 75% of COVID-19 death cases previously suffered 1-2 underlying diseases, a majority of which were diabetes and cardiovascular diseases. Other researches stated that novel coronavirus pneumonia was more common among people with diabetes, hypertension and obesity, who were also easy to have serious complications, even death.[22,23] In line with those evidence, our study also found that 60% of the severe patients had 1-2 basic diseases, such as cardiovascular diseases, cerebrovascular diseases and endocrine system diseases. Comorbidity was also confirmed as an important risk factor for the severity and prognosis of COVID-19. As pneumonia can aggravate the burden of lung and heart[24], it is plausible that patients were more likely to develop myocardial infarction and heart failure when pneumonia coincides with pre-existing cardiovascular problems. In addition, blood glucose level may also play a pivotal role in the pathogenesis of infectious diseases. The rationale is that the immune system of diabetic patients may be disturbed by the abnormal blood glucose level, leading to dysregulation and reduced responses of immune components.[25,26] As a result, these patients are susceptible not only to SARS-CoV-2, but also to varying types of bacteria. Similarly, the level of blood glucose for obese people is generally higher, making them susceptible to infection.[27] In addition, obesity contributed to various chronic diseases, decreased immunity and

cardiopulmonary problems and subsquently increased the risk of infections.[28] However, BMI was not an independent risk factor in our study.

The guideline for diagnosis and treatment of COVID-19 issued by WHO and National Health Commission of the People's Republic of China suggests that ribavirin, lopinavir / ritonavir antiviral therapy should be used in COVID-19 patients. Our study found that patients in the mild group experienced earlier initiation of antiviral treatment, indicating that early and timely antiviral treatment may significantly slow COVID-19 progression and improve the prognosis of patients. However, the therapeutic effect of the three individual drugs was not evaluated due to limited sample size in this manuscript. Further studies including well designed clinical trials were needed to optimize therapeutic regimen.

This study had several limitations. First of all, the results and conclusions should be further verified by larger samples from multiple centers. Secondly, therapeutic measures (such as nursing and medical equipment) employed by one hospital might differ from another, which may potentially skew the results. Third, this study is a retrospective study, so the possibility of recall bias can't be completely ruled out.

In conclusion, there is a high mortality rate in the patients infected with SARS-CoV-2 in severe group. It is necessary to analyze the epidemic history, clinical characteristics, routine laboratory test, CT examination and continuous respiratory nucleic acid test. We found that comorbidity, time from illness onset to antiviral, and age >=65 were the main risk factors associated with severity of patients, while comorbidity and time from illness onset to antiviral were the main risk factors associated with prognosis of patients. Hence, it is recommended that antiviral treatment should be carried out timely and pay attention to the treatment of comorbidities, especially for diabetes and cardiovascular diseases

Note

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Ethics approval. This study was performed in accordance with the Helsinki Declaration and was approved by the Ethics Committee of the First People's Hospital of Yancheng City. Informed

consents were obtained from all participants or their families.

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Figure legends

Figure 1 Comparison of age >=65 (y), comorbidity，time from illness onset to antiviral, and the average time of nucleic acid turning negative between the mild group and the severe group. (A) The proportion of age >=65 (y); (B) The proportion of comorbidity; (C) The time from illness onset to antiviral; (D) The average time of nucleic acid turning negative.

Figure 2 OPLS-DA was used to evaluate and rank the influences of the parameters with severity for patients infected with SARS-CoV-2. (A) ROC of OPLS-DA; (B) In the three-dimensional scatter plot of all samples in the OPLS-DA model, the predictive component was used to mild cases and severe cases; (C) Loading plot showing the relation of each parameter to the predictive component (x) and the first orthogonal component (y); parameters that deviated from zero on the x-axis were considered potentially predictive; (D) The higher predictive VIP (VIP pred) value.

Figure 3 Association between age >=65 (y), time from illness onset to antiviral, comorbidity and the average time of nucleic acid turning negative.

Table S1. Clinical classifications

Table 1. Demographics, baseline and clinical characteristics of patients with SARS-CoV-2

Variables	Total Patients (n = 280)	Mild and Moderate type Patients (n= 197)	Severe and Critically ill type Patients (n=83)	*P*
Age(y)				0.000
Mean(SD)	43.12 ± 19.02	37.55 ± 17.10	63.04 ± 10.20	
Range				
<18	35(12.50%）	33(16.75%）	2(2.41%）	
18-24	14(5.00%）	12(6.09%）	2(2.41%）	
25-49	78(27.86%)	73(37.06%)	5(6.02%)	
50-64	84(30.00%)	59(25.81%)	25(30.12%)	
>=65	69(24.64%)	20(10.15%)	49(59.04%)	
BMI	24.1 ± 3.0	23.6 ± 3.2	25.8 ± 1.8	0.005
Sex				0.950
Female	129(46.07%)	91(46.19%)	38(45.78%)	
Male	151(53.93%)	106(53.81%)	45(54.22%)	
Agglomerative epidemic				0.000
Generation Ⅰ	14(5.00%)	1(0.51%)	13(15.66%)	
Generation Ⅱ	164(58.57%)	109(55.33%)	55(66.27%)	
Generation Ⅲ	86(30.71%)	72(36.55%)	14(16.87%)	
Generation Ⅳ	16(5.72%)	15(7.61%)	1(1.20%)	
Number of nucleic acid tests				0.324
The first time	148(52.86%)	101(51.27%)	47(56.63%)	
The second time	97(34.64%)	71(36.04%)	26(31.33%)	
The third time	30(10.71%)	23(11.68%)	7(8.43%)	
The fourth time	5(1.79%）	2(1.01%）	3(3.61%）	

Table 1 continued

Variables	Total Patients (n = 280)	Mild and Moderate type Patients (n= 197)	Severe and Critically ill type Patients (n=83)	*P*
Comorbidities				0.021
Cardiovascular and cerebrovascular	57(20.36%)	14(7.11%)	43(51.81%)	
Endocrine system diseases	34(12.14%)	6(3.05%)	28(33.73%)	
Digestive system disease	9(3.21%)	4(2.03%)	5(6.02%)	
Respiratory system diseases	6(2.14%)	3(1.52%)	3(3.61%)	
Malignant tumour	5(1.79%)	3(1.52%)	2(2.41%)	
Nervous system diseases	3(1.07%)	1(0.51%)	2(2.41%)	
Chronic kidney disease	3(1.07%)	1(0.51%)	2(2.41%)	
Chronic liver disease	7(2.50%)	3(1.52%)	4(4.82%)	
COPD	1(0.36%)	0(0.00%)	1(1.20%)	
HIV infection	1(0.36%)	0(0.00%)	1(1.20%)	
Septic shock	1(0.36%)	0(0.00%)	1(1.20%)	
Signs and symptoms at admission				0.058
Fever	237(84.64%)	154(78.17%)	83(100.00%)	
Cough	197(70.36%)	114(57.87%)	83(100.00%)	
Shortness of breath	150(53.57%)	67(34.01%)	83(100.00%)	
Muscle ache	71(25.36%)	28 (14.21%)	43(51.81%)	
Headache and mental disorder	43(15.36%)	11 (5.58%)	32(38.55%)	
Sore throat	31(11.07%)	6(3.05%)	25(30.12%)	
Rhinorrhoea	27(9.64%)	16(8.12%)	11(13.25%)	
Chest pain	11(3.93%)	2(1.02%)	9(10.84%)	
Diarrhoea	7(2.50%)	1(0.51%)	6(7.23%)	
Nausea and vomiting	3(1.07%)	1(0.51%)	3(3.61%)	

Table 1 continued

Variables	Total Patients (n = 280)	Mild and Moderate type Patients (n= 197)	Severe and Critically ill type Patients (n=83)	*P*
Chest x-ray and CT findings				0.204
Bilateral pneumonia	122(43.57%）	92(46.70%）	30(36.14%）	
Unilateral pneumonia	123(43.93%）	80(40.61%）	43(51.81%）	
No abnormal density shadow	35(12.50%)	25(12.69%)	10(12.05%)	
Treatment				0.285
Antibiotic treatment	188(67.14%)	105(53.30%)	83(100.00%)	
Antiviral treatment	280(100.00%)	197(100.00%)	83(100.00%)	
hormone therapy	99(35.36%)	27(13.71%)	72(86.75%)	
Intravenous immunoglobulin	90(32.14%)	22(11.17%)	68(81.93%)	
Non-invasive(ie,face mask)	177 (63.21%)	94(47.71%)	83(100.00%)	
Mechanical ventilation	84(0.30%)	1(0.51%)	83(100.00%)	
ECMO	12(4.29%)	0(0.00%)	12(14.46%)	
Traditional Chinese medicine	34(12.14%)	23(11.68%)	11(13.25%)	
Clinical outcome				0.000
Remained in hospital	59(21.07%）	8(4.06%）	51(61.45%）	
Discharged	221(78.93%）	189(95.94%)	32(38.55%)	
Died	0(0.00%)	0(0.00%)	0(0.00%)	

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; BMI, body mass index; ECMO, extracorporeal membrane oxygenation.

Table 2. Laboratory findings of patients with SARS-CoV-2

Variables	Total Patients (n = 280)	Mild and Moderate type Patients (n= 197)	Severe and Critically ill type Patients (n=83)	*P*
Blood routine				
White blood cell count (× 10^9/L)	4.9(3.9-6.8)	5.0(4.2-6.6）	3.4（2.9-8.4）	0.043
Neutrophil count (× 10^9/L)	3.0(2.3-3.6)	3.1(2.5-3.9）	2.2（1.9-2.6）	0.015
Lymphocyte count (×10^9/L)	1.1(0.6-1.6)	1.3(0.9-1.9)	0.5(0.4-0.8)	0.006
Monocyte count (× 10^9/L)	0.5(0.3-0.7)	0.4(0.3-0.7)	0.5 (0.3-0.8)	0.286
Platelet count (× 10^9/L)	182 ± 66	196 ± 59	86 ± 15	0.012
Haemoglobin (g/L)	124.1±13.0	123.9±12.9	125.1±13.5	0.415
Blood biochemistry				
Alanine aminotransferase(U/L)	21(16-38）	20(16-38）	24(18-38）	0.664
Aspartate aminotransferase(U/L)	26(22-34）	26(21-34）	26(23-39）	0.487
Albumin(g/L)	40.3(37.3-44.1）	42.0(39.0-45.0）	37.8(33.0-39.2）	0.039
Total bilirubin(μmol/L)	6.6(5.4-12.4)	6.6(5.2-12.1)	6.7(5.5-12.6)	0.098
Blood urea nitrogen(mmol/L)	4.1(3.4-5.3）	4.0(3.4-5.2）	4.4(3.5-7.6）	0.181
Serum creatinine(μmol/L)	58.8(48.8-73.8）	57.6(47.8-73.0）	62.8(51.5-79.5）	0.140
Lactate dehydrogenase(U/L)	195(159-270）	184(155-262）	235(170-355）	0.030
Glucose(mmol/L)	5.7(4.8-6.8）	5.5(4.7-6.7）	6.3(5.4-7.1）	0.028
Creatine kinase (U/L)	70(47-123）	67(52-104）	76(41-268）	0.049
Creatine kinase–MB(U/L)	11(8-18）	9(7-14）	13(7-24)	0.038
PaO2	84 (64-98)	91(82-106)	68 (53-88)	0.019
PaO2/FiO2	316 (263-476)	359 (293-495)	165 (109-298)	0.009

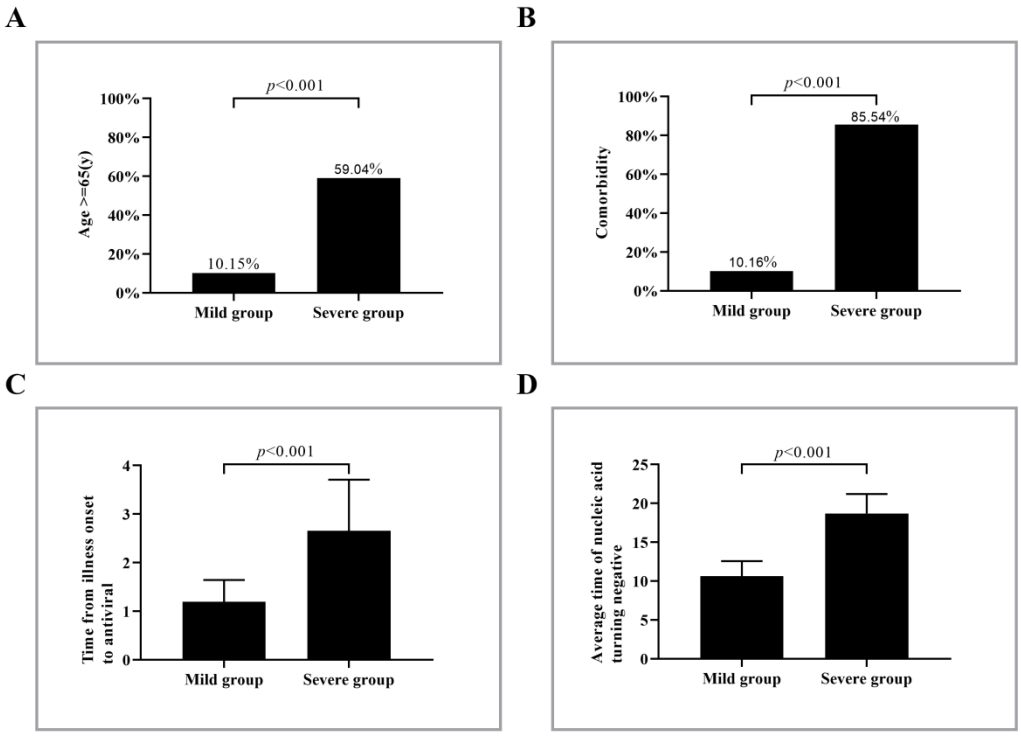
Table 2 continued

Variables	Total Patients (n = 280)	Mild and Moderate type Patients (n= 197)	Severe and Critically ill type Patients (n=83)	*P*
Coagulation function				
Activated partial thromboplastin time (s)	38.7 ± 6.4	39.0 ± 6.1	36.9 ± 8.0	0.346
Prothrombin time (s)	13.2(12.5-13.5)	13.2(12.5-13.5)	13.2(12.8-13.2)	0.905
D-dimer(μg/L)	0.3(0.2-0.8)	0.2(0.2-0.5)	3.0(0.6-5.0)	0.001
Infection-related biomarkers				
C-reactive protein	7.6(2.2-11.9)	6.9(1.6-10.0)	21.3(14.3-36.6)	0.036
Procalcitonin	1.4 (0.4-2.8）	1.3 (0.3-2.7）	1.5 (0.5-2.9）	0.877
Erythrocyte sedimentation rate	12.5(9.3-17.7)	11.9(8.9-17.0)	13.9(9.8-18.5)	0.162
Co-infection				
Other viruses	1(0.36%)	1(0.51%)	0(0.00%)	0.486
Bacteria	6(2.14%)	1(0.51%)	5(6.02%)	0.049
Fungi	0(0.00%)	0(0.00%)	0(0.00%)	1.000

Table 3. Logistic regression analysis of risk factors with severity for patients with SARS-CoV-2

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age >=65(y)	16.32(4.59-58.01)	0.001	81.20(1.10-5988.12)	0.045
BMI	1.30(1.09-1.54)	0.003		
Agglomerative epidemic	0.39(0.24-0.65)	0.012		
Comorbidity	47.77(13.68-166.77)	0.002	54.74(1.14-2634.81)	0.043
Time from illness onset to antiviral	11.63(4.51-30.03)	0.001	26.98(1.81-402.93)	0.017
Lymphocyte count	0.09(0.02-0.29)	0.014		
Non-invasive(ie,face mask)	3.97(1.58-9.93)	0.025		
D-dimer	3.20(1.75-5.88)	0.031		
Creatine kinase	1.00(1.00-1.01)	0.083		
Creatine kinase–MB	1.07(1.01-1.14)	0.026		

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; BMI, body mass index



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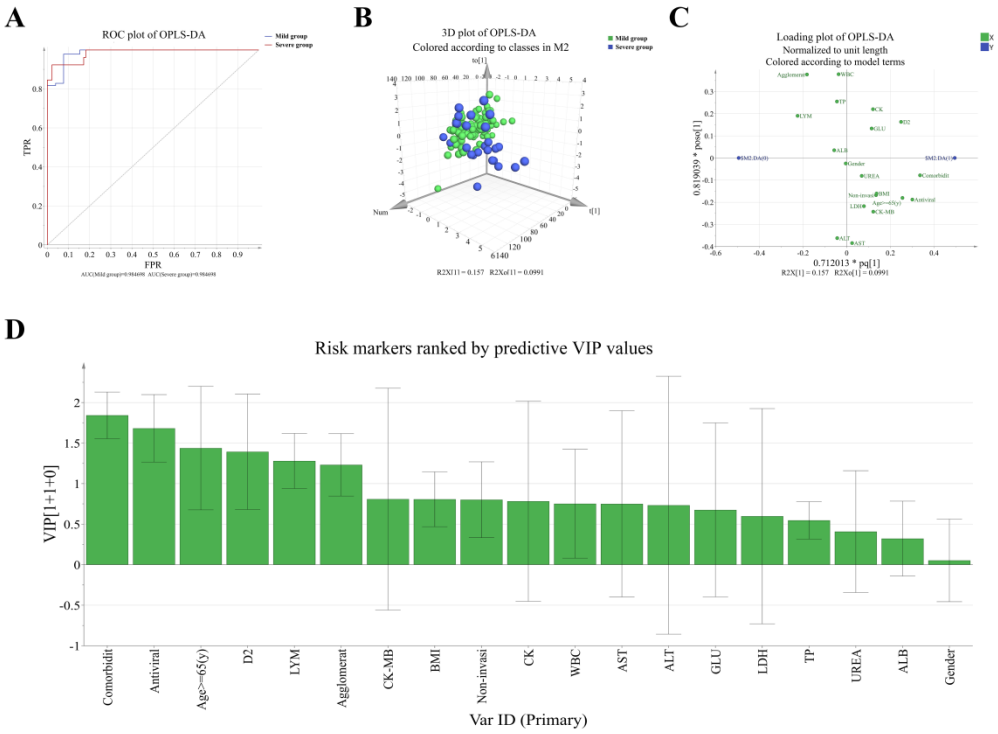

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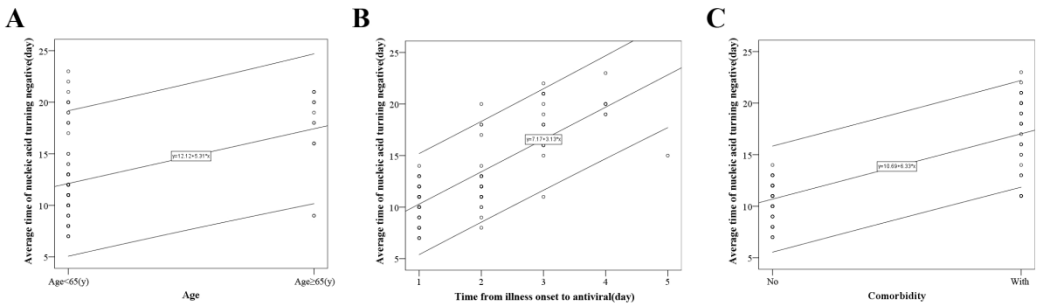

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