Predictors of coronavirus disease 2019 severity: A retrospective study of 64 cases

Running head: Factors predicting the severity of COVID-19

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Summary

To analyze clinical characteristics and potential predictors of disease severity in patients with COVID-19.Clinical data from 64 patients with COVID-19 were retrospectively analyzed. Of the 64 patients, 37 were male and 27 were female. Their mean age was 47.8 years, 43 (67.2%) cases were non-severe, 21 (32.8%) were severe, and 2 patients (3.1%) died. Age and serum ferritin were significantly associated with COVID-19 severity. Repeated monitoring of ferritin, interleukin-6, C-reactive protein, lactic acid dehydrogenase, and erythrocyte sedimentation rate during COVID-19 treatment may assist the prediction of disease severity and evaluation of treatment effects. There were no significant differences in the duration of severe illness or the number of days on high-level respiratory support between a low-dose methylprednisolone group and a high-dose methylprednisolone group. The mean number of days in hospital in the high-dose group was higher than that in the low-dose group. Repeated monitoring of ferritin, interleukin-6, C-reactive protein, lactic acid dehydrogenase, and erythrocyte sedimentation rate during COVID-19 treatment may assist the prediction of disease severity and evaluation of treatment effects.

Introduction

In December 2019 patients with pneumonia of unknown etiology began to present in Wuhan City, Hubei Province, China. Epidemiological investigation indicated that these patients or a contact of theirs may have been exposed at the Huanan wholesale seafood market in Wuhan (1-3). Sequencing of virus from the lower respiratory tracts of patients implicated a novel coronavirus (4). The World Health Organization (WHO) subsequently named the virus "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2), and the disease caused by the virus "coronavirus disease 2019" (COVID-19) (5). COVID-19 spread rapidly to the whole of China and other countries (3, 6-11). By 25 March 2020 there had been 375,498 confirmed cases, and 16,362 deaths had occurred in 195 countries. According to recently published reports SARS-CoV-2 is mainly transmitted through respiratory droplets, aerosols, or direct contact, and people are generally susceptible to the virus. It mainly invades the respiratory system, and patients with mild disease seldom have serious damage of organ function, and tend to make a full recovery. However, patients with severe disease can develop respiratory failure, multiple organ failure, septic shock, and they may die.

To date, the pathogenesis of COVID-19 has not been clearly elucidated. Despite the concerted efforts of scientists, no specific antiviral drug or treatment for COVID-19 has been developed. Cumulative reports have described the clinical characteristics of COVID-19 (3, 11-17), and the data indicate that its severity varies in different individuals. Given the unprecedented nature of the current epidemic, more studies are urgently needed to achieve a better understanding of factors that predict COVID-19

severity. In the current study the cases of 64 COVID-19 patients treated at Fifth Medical Center of Chinese PLA General Hospital from 13 January 2020 to 10 March 2020 were retrospectively reviewed. The aims were to describe clinical characteristics, identify factors that may predict disease severity and mortality, and provide further insight into the treatment of COVID-19.

Materials and Methods

Patients

All COVID-19 patients diagnosed at Fifth Medical Center of Chinese PLA General Hospital from 13 January 2020 to 10 March 2020 were included in the study. Diagnostic criteria, degree of disease severity, and clinical cure standards were determined in accordance with the guidelines for the diagnosis and treatment of new coronavirus pneumonia (version 7) (18) released by the National Health Commission of China. SARS-CoV-2 infection was confirmed in all patients included in the study via genetic sequencing or real-time reverse transcriptase polymerase chain reaction (RT-PCR). All patients were assessed for disease severity at the time of hospital admission. The specific criteria for assessing disease severity were: Non-severe type—mild clinical symptoms, with or without fever, imaging with or without pneumonia; severe type—shortness of breath or dyspnea after activity, or a respiratory rate $\geqslant$30 breaths/min, or oxygen saturation $\leqslant$ 93% without supplementary oxygen inhalation, or an PaO2/FiO2 of < 300 mmHg. Patients whose body temperature returned to normal for > 3 days and who tested negative in two SARS-CoV-2 nucleic acid tests conducted > 1

day apart were defined as clinically recovered. Base on the mean methylprednisolone dose the patients were divided into two groups, a high-dose group (>1.5 mg/kg/day) and a low-dose group (< 1.5 mg/kg/day).

This study was approved by the institutional review boards of Fifth Medical Center of Chinese PLA General Hospital and the study subjects were given informed consent in line with the Declaration of Helsinki.

Data collection

All patient data were obtained via the hospital's medical information system. Whether or not the patient had a history of living in Wuhan or Hubei Province was recorded, as were histories of any chronic diseases of the heart, lung, brain, kidney, or other organs. Clinical symptoms such as fever, cough, fatigue, chest distress, dyspnea, headache, nausea, vomiting, and diarrhea were recorded. Other data analyzed included the results of routine blood tests and erythrocyte sedimentation rate (ESR), blood biochemistry, serum levels of ferritin, procalcitonin, C-reactive protein (CRP), and interleukin-6 (IL-6), glucocorticoid dose and duration of administration, respiratory support mode, and prognosis.

SARS-CoV-2 nucleic acid detection

SARS-CoV-2 nucleic acid detection was conducted in accordance with the guidelines for laboratory testing of novel coronavirus infection released by the National Health Commission of China, which has been approved by the WHO (19). Briefly, sputum, secretions from the nasopharynx, or secretions from the lower respiratory tract

were collected and real-time RT-PCR was used to detect the virus. Target 1 (orf1ab) was amplified using the forward primer (f) ccctgtggtttacacttaa, the reverse primer (R) acgatttgcatcactga, and the probe (P) 5'-fam-ccgtctgcgtatgtggaaggtttagtg-bhq1-3'. Target 2 (n) was amplified using (f) gggggaacttcctgctagat, (R) cagacatttgctcacgtg, and (P) 5'-fam-ttgctgctgcttgagatt-tamra-3'. Laboratory confirmation of SARS-COV-2 was required to satisfy one of the following: (1) the two targets (ORF1ab and n) in the same sample were both positive. If a single target was positive, another sample was collected and the test was repeated. If that sample was single-target positive, the testing was deemed to be positive. (2) A single target was positive in two types of samples in simultaneous testing, or two different tests on the same type of sample were single-target positive.

Statistical analysis

Statistical analyses were performed using SPSS 25.0 software (Chicago, IL, USA). Quantitative data were expressed as mean ± the standard deviation or median and quartile. Qualitative data were expressed as number or rate. The *t*-test, rank sum test, or analysis of variance were used to compare quantitative data between groups, and the chi square test was used to compare qualitative data between groups. Logistic regression was used for multivariate analysis. Receiver operating characteristic (ROC) curve analysis was used to evaluate the capacity of factors to predict disease severity, only those factors whose area under curve more than 0.7 were chosen into the ROC analysis. $p < 0.05$ was deemed to indicate statistical significance.

Results

Comparation of clinical characteristics, laboratory examination and treatment between severe type and non-severe type COVID-19 patients

Forty-three patients (67.2%) were non-severe type, 21 (32.8%) were severe type and 2 patients (3.1%) died. The comparation of clinical characteristics, laboratory examination and treatment between severe type and non-severe type COVID-19 patients are shown in Table 1. In all patients, thirty-seven (57.8%) were male, and 27 (42.2%) were female. The mean age of all patients was 47.8 ± 18.5 years, the mean age of severe patients was significantly higher than that of non-sever patients (61.4 ± 16.4 vs. 41.2 ± 15.7 , $p = 0.001$). Half of the patients (32/64; 50%) had been to Wuhan area or Hubei province, and 27 (42.2%) were members of a cluster of infections. With regard to coexisting conditions, hypertension was significantly more prevalent in severe patients (42.9% vs. 11.6%, $p = 0.009$). The most common symptom was fever (87.5%), however, there was no significant difference in the duration of fever between non-severe (5.2 ± 3.4 days) and severe patients (6.9 ± 4.9 days) ($p = 0.18$). The other symptoms include cough (53.1%), fatigue (34.4%), chest distress (17.2%), dyspnea (9.4%), headache (20.3%), muscle soreness (15.6%), nausea (3.1%), and diarrhea (6.3%).

There were no significant differences in white cell counts or platelet counts between severe and non-severe patients. The mean number of granulocytes was significantly higher in severe patients ($4.0 \pm 2.3 \times 10^9$/L vs. $2.6 \pm 0.9 \times 10^9$/L, $p = 0.001$), the median number of lymphocytes was lower (0.83×10^9/L vs. 1.53×10^9/L, $p = 0.001$), and the

mean hemoglobin level was lower (128.2 ± 16.3 g/L vs. 138.1 ± 13.8 g/L, p = 0.02). Serum albumin was lower in severe patients (34.4 ± 5.2 g/L vs. 40.7 ± 4.0 g/L, p = 0.001), serum lactic acid dehydrogenase (LDH) was higher (356.9 ± 204.6 U/L vs. 209.2 ± 52.2 U/L, p = 0.005), and blood glucose was higher (7.4 ± 2.4 mmol/L vs. 5.3 ± 2.5 mmol/L, p = 0.003). With regard to coagulative function there was no difference in prothrombin time between the severe patients (12.7 ± 1.7 sec) and non-severe patients (12.2 ± 1 sec) (p = 0.15). Serum IL-6 was significantly higher in severe patients (median 18.7 pg/mL vs. and 10.6 pg/mL, p=0.002), as was serum CRP (median 19.5 mg/L vs. 6.7 mg/L, p = 0.001). ESR was significantly higher in severe patients (42.6 ± 24.5 mm/60min vs. 21.4 ± 18.3 mm/60min, p = 0.002), as was serum ferritin (766.1 ± 564.4 ng/mL vs. 304.3 ± 251.9 ng/mL, p = 0.005).

Forty-seven patients were treated with oral litonavir/lopinavir combined with atomized inhalation interferon alpha, 1 was treated with oral litonavir/lopinavir combined with arbidol, 3 were treated with oral arbidol combined with atomized inhalation interferon alpha, 6 were treated with atomized inhalation interferon alpha, and 7 were not administered any antiviral drugs because of drug interactions or intolerance to side effects. There was no significant difference of antiviral therapy between sever patients and non-sever patients (p = 1.0). Nineteen patients (29.7%) underwent respiratory support therapy. Twenty-eight patients were treated with methylprednisolone. The proportion and the dose of methylprednisolone usage in severe patients were significantly higher than that of non-severe patients. The mean days from illness to hospital was 7.1 ± 4.7 days, and the median hospital stay was 18

(10-26) days. The time from illness to hospital and the hospital days were significantly longer in severe patients (9.0 ± 4.5 days vs. 6.1 ± 4.3 days, p = 0.02; 26(17, 29) vs 15 (9, 19), p = 0.00, respectively).

Predicting factors analysis for the severity of COVID-19 patients

We used the data with significant difference in Table 1 for logistic regression analysis, the result showed that age and serum ferritin level were significantly associated with COVID-19 severity (Table 2). ROC curve analysis suggested that various parameters could be used to assist the prediction of disease severity in patients with COVID-19, with areas under the curve of 0.80 for age, 0.79 for IL-6, 0.78 for LDH, 0.82 for CRP, 0.75 for ESR, and 0.95 for ferritin (Figure 1). The specificity of predicting the severity of COVID-19 based on being aged > 48 years was 71.4%, and the sensitivity was 80.0%. For LDH > 258 U/L the specificity was 99.1% and the sensitivity was 60.0%. For IL-6 > 3.8 pg/mL the specificity was 69.6% and the sensitivity was 80.0%. For CRP > 11.6 mg/L the specificity was 82.9% and the sensitivity was 70.0%. For ESR > 32 mm/60 min the specificity was 77.1% and the sensitivity was 70%. For serum ferritin > 493 ng/mL the specificity was 85.7% and the sensitivity was 90%. Over the course of treatment, and in conjunction with improvement in patient condition, serum ferritin, LDH, CRP, ESR, and IL-6 decreased gradually in the severe group, and albumin gradually increased (Figure 2).

Effects of glucocorticoid therapy on the prognosis of severe COVID-19

Studies investigating the virus responsible for many cases of severe acute respiratory syndrome (SARS) in 2003 (the virus formally named SARS-CoV) (20-22) and the virus responsible for Middle East respiratory syndrome (MERS; the virus formally named MERS-CoV) (23) implied that glucocorticoid administration may help to reduce lung inflammation and improve prognoses. Notably however, it has also been reported that high-dose corticosteroid therapy may have some disadvantages (24). In the current study all patients with severe disease were treated with methylprednisolone. The mean days of methylprednisolone use were 6.8 ± 2.1 in the low-dose group and 11.6 ± 6.3 in the high-dose group. The mean methylprednisolone doses were 0.9 ± 0.3 mg/kg/day in the low-dose group and 3.3 ± 0.6 mg/kg/day in high-dose group. There were no significant differences in death rate, days of high-level respiratory support, or duration of severe illness in the low-dose and high-dose groups (Table 3). Patients in the high-dose group stayed significantly more days in hospital than those in the low-dose group (32.3 vs. 23.3, $p = 0.01$).

Discussion

SARS-CoV-2 reportedly has high affinity for angiotensin-converting enzyme 2 receptors in the human airway, rendering humans highly susceptible to infection. COVID-19 has rapidly become a worldwide epidemic and had enormous effects globally. Recent WHO estimates suggest that the death rates associated with COVID-19 vary from 2% to 12% in different countries. Despite unprecedented efforts by governments and scientists, to date no reliably effective treatment for COVID-19 has

been identified. Currently the main treatments are respiratory function support, organ function maintenance, and experimental antiviral therapy. Diligent and accurate recording and timely reporting of the clinical aspects of as many COVID-19 patients as possible during this early stage of the pandemic—particularly those of severe patients—will provide valuable insights into the development of effective treatment strategies.

In the current study, fever and cough were the most common symptoms in COVID-19 patients, and there was no significant association between fever duration and the severity of COVID-19. SARS-COV-2 clearly invaded the lungs, potentially leading to pneumonia and hypoxemia of varying severity. Notably, however, whether the virus caused damage to other organs was uncertain. Blood indexes of the heart, kidney, and pancreas were all within normal ranges in most patients on admission, and there were no significant differences between severe and non-severe patients in these respects. Those results are consistent with some previous reports (3,25), but in other reports functional abnormalities of the liver, kidney, brain, and other systems have been detected to different degrees (26-29), which may be related to organ injury due to prolonged hypoxemia.

In the present study serum ferritin, CRP, IL-6, LDH, and ESR were significantly higher in severe patients than in non-severe patients, and these parameters gradually decreased as patient condition improved. These results are consistent with those reported by Cao et al (30). In logistic regression analysis age and serum ferritin were associated with COVID-19 severity. ROC curve analysis implied that these parameters could be helpful with respect to predicting the severity of COVID-19. Serum ferritin >

493 ng/mL predicted severe COVID-19 with specificity of 85.7% and sensitivity of 90%. These data suggest that CRP, IL-6, ESR, LDH, and serum ferritin should be closely monitored to facilitate timely evaluation of severity and recovery in patients with COVID-19, especially patients aged > 48 years.

Zhe et al. (31) reported that some COVID-19 patients exhibited systemic inflammatory responses, particularly pulmonary inflammatory responses. In the present study IL-6 was significantly higher in severe patients, and multiple previous studies (32-34) have also found that other inflammatory factors were increased in severe COVID-19 patients. Those reports imply that inflammatory response levels were closely related to the progression of COVID-19 severity. Inflammatory responses can aid viral clearance, but excessive inflammatory responses can cause severe lung injury even lung failure and this may cause COVID-19 to become severe. Timely control of excessive inflammatory responses in COVID-19 patients may contribute to negating progression to severe disease.

Previous studies investigating MERS and SARS suggest that glucocorticoids may contribute to patient recovery (20-23, 35), Russell (24) reported that glucocorticoids can delay disease progression, but that excessive use of glucocorticoids may prolong viral clearance. Different conclusions may be related to different doses and timing of glucocorticoid administration in different studies. In the current study there were no significant differences in the duration of severe illness or the duration of high-level oxygen therapy in the high-dose methylprednisolone treatment group and the low-dose methylprednisolone treatment group. Notably however, the duration of hospitalization

was longer in the high-dose group, whether this was due to the longer virus clearance time caused by the immunosuppression induced by high dose methylprednisolone administration need further research. Currently the treatment of severe COVID-19 with glucocorticoids remains controversial. Large scale randomized controlled clinical studies are needed to further clarity the clinical effect of glucocorticoid in treating COVID-19, the time starting/stopping glucocorticoid and the individualized dose for each patient.

Evidence to date suggests that the overall mortality rate of infection with SARS-CoV-2—at least in those who develop clinical disease—is higher than that of infection with SARS-CoV and lower than that of infection with MERS-CoV. With appropriate care the vast majority of COVID-19 patients evidently recover. COVID-19 can become severe relatively rapidly in elderly patients however, and such rapid progression is associated with a poor prognosis. Accordingly, elderly patients should be monitored very closely in clinical practice. The small number of cases is a limitation of the present study.

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Conflict of interest

None to declare.

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Figure legends

Figure 1: Indicators that can be used to judge coronavirus disease 2019 (COVID-19) severity.

Receiver operating characteristic curve analysis suggested that age, interleukin 6, lactic acid dehydrogenase, C-reactive protein, erythrocyte sedimentation rate, and serum ferritin could be used to assist the prediction of COVID-19 severity.

Figure 2: Comparison of indicators in patients with severe coronavirus disease 2019 (COVID-19) and patients with non-severe COVID-19.

Serum ferritin (ng/mL) (a), lactic acid dehydrogenase (U/L) (b), interleukin 6 (pg/mL) (c), C-reactive protein (mg/L) (d), and erythrocyte sedimentation rate(mm/60min) (e) were all higher in severe patients than in non-severe patients, and they all gradually decreased as disease improved. Albumin (g/L) kept higher in non-severe patients compared with severe patients (f). The time from symptom onset to hospitalization was significantly longer in severe patients than in non-severe patients (g).

Table 1: Comparison of clinical characteristics and laboratory tests between severe type and non -sever type patients with COVID-19.

Charactersitc	Normal Range	All patients n=64	Nonsevere n=43	Severe n=21	*P* Value
Sex(M/F), n	NA	37/27	25/18	12/9	1.0
Age, yeas	NA	47.8±18.5	41.2±15.7	61.4±16.4	0.001
BMI, Kg/m^2	NA	24.6±3.37	24.2±3.5	25.7±2.8	0.07
Recently visited Wuhan, n(%)	NA	32(50%)	24(55.8%)	8(38.1%)	0.18
Clustering infection, n(%)	NA	27(42.2%)	18(41.9%)	9(42.9%)	0.94
Smoking history, n(%)	NA	7(10.9%)	3(7.0%)	4(19.0%)	0.2
Alcohol intake history, n(%)	NA	14(21.9%)	7(16.3%)	7(33.3%)	0.19
Comorbidity, n/%	NA				
Hypertension	NA	14(21.9%)	5(11.6%)	9(42.9%)	0.009
Diabetes	NA	6(9.4%)	3(7.0%)	3(14.3%)	0.38
Chronic kidney disease	NA	1(1.6%)	0	1(4.8%)	0.33
Cerebral infarction	NA	1(1.6%)	0	1(4.8%)	0.33
Asthma	NA	1(1.6%)	1(2.3%)	0	1.0
HIV	NA	1(1.6%)	0	1(4.8%)	0.33
Tumor	NA	1(1.6%)	0	1(4.8%)	0.33
Duration of fever, days	NA	5.8±4.0	5.2±3.4	6.9±4.9	0.18

Blood routine					
White Blood Cell, ×10^9/L	4-10	4.9±1.7	4.7±1.3	5.3±2.3	0.2
Granulocyte, ×10^9/L	2-7	3.1±1.7	2.6±0.9	4±2.3	0.001
Lymphocyte, ×10^9/L	0.8-4.0	1.42(0.85, 1.68)	1.53(1.25, 2.02)	0.83(0.45, 1.47)	0.001
Platelet, ×10^9/L	100-300	185.2±61.8	180.5±62.7	194.1±61.9	0.41
Hemoglobin, g/L	110-160	134.9±15.6	138.1±13.8	128.2±16.3	0.02
Biochemical test results					
Albumin, g/L	35-50	39.2±5.1	40.7±4.0	34.4±5.2	0.001
Alanine aminotransferase, U/L	5-40	24(14, 38)	22(14, 36)	31(14, 45)	0.47
Aspartate aminotransferase, U/L	5-40	25(22, 38)	24(21, 30)	29(22, 60)	0.14
Total bilirubin, umol/L	3.4-17.1	11.2(8.2 14.9)	10(7.7, 15)	11.3(8.5, 13.9)	0.98
Blood urea nitrogen, mmol/L	2.0-7.1	3.8(3.3, 5.1)	3.7(3.2, 4.3)	4.56(3.4, 5.78)	0.01
Creatinine, umol/L	44-106	77.8±14.7	77.2±14.1	78.8±16.2	0.68
Amylase, U/L	25-125	58.8±22.3	60.9±24.8	55.1±14.9	0.34
Troponin, ng/mL	0-0.15	0.005(0.004, 0.008)	0.004(0.003, 0.005)	0.007(0.004, 0.016)	0.003
Glucose, mmol/L	3.9-6.1	6.3±2.3	5.3±2.5	7.4±2.4	0.003
Triglyceride, mmol/L	<2.3	1.15(0.85, 1.5)	1.09(0.76, 1.5)	1.16(1.0, 1.5)	0.19

Lactic dehydrogenase, U/L	109-245	246.6±100.1	209.2±52.2	356.9±204.6	0.005
Natrium, mmol/L	136-145	137.7±2.9	138.8±2.6	136.8±3.3	0.056
Potassium, mmol/L	3.5-5.5	4.3(3.9, 4.5)	4.3(4.0, 4.5)	4.1(3.8, 4.5)	0.42
Chlorine, mmol/L	96-106	102.2±5.3	102.0±6.1	102.7±3.5	0.612
Prothrombin time, seconds	11-15	12.4±1.2	12.2±1.1	12.7±1.7	0.15
Procalcitonin, ug/L	<0.5	0.051 (0.037,0.079)	0.043 (0.033,0.058)	0.085 (0.049,0.22)	0.001
Interleukin-6, pg/mL	0-7	12.5(5.6,25.7)	10.6(5.8, 21.4)	18.7(14.7, 43.7)	0.002
C-reactive protein, mg/L	0.068-8.2	8.5(3.0, 21.3)	6.7(1. 8, 10.7)	19.5(9.4, 41.1)	0.001
Erythrocyte sedimentation rate, mm/60min	0-20	28.8±24.3	21.4±18.3	42.6±24.5	0.002
Serum ferritin, ng/mL	13-150	461.3±436	304.3±251.9	766.1±564.4	0.005
Antiviral therapy, n(%)	NA	57(89.1%)	38(88.4%)	19(90.5%)	1.0
Litonavir/lopinavir + Interferon-a	NA	47(73.4%)	34(79.1%)	13(61.9%)	
Litonavir/lopinavir + Arbidol	NA	1(1.6%)	0	1(4.8%)	
Arbidol + Interferon-a	NA	3(4.7%)	1(2.3%)	2(9.5%)	
Interferon-a	NA	6(9.3%)	3(7.0%)	3(14.3%)	
without antiviral drug	NA	7(10.9%)	5(11.6%)	2(9.5%)	
Respiratory support therapy, n(%)	NA				

High flow humidification treatment	NA	19(29.7%)	0	19(90.5%)	
Noninvasive mechanical ventilation	NA	9(14.1%)	0	9(42.9%)	
Invasive mechanical ventilation	NA	2(3.1%)	0	2(9.5%)	
Glucocorticoid Therapy, n(%)	NA	28(43.8%)	7(16.3%)	21(100%)	0.00
>1.5mg/kg.d	NA	11(17.2%)	1	10	
≤1.5mg/kg.d	NA	17(26.6%)	6	11	
Death, n(%)	NA	2(3.1%)	0	2(9.5%)	0.1
From illness to hospital, days	NA	7.1±4.7	6.1±4.3	9.0±4.5	0.02
Hospital stay, days	NA	18 (10, 26)	15 (9, 19)	26(17, 29)	0.00

Note: NA, not applicable; the data of normal distribution is represented by mean and standard deviation, the data of non normal distribution is represented by median and quartile. P value is the comparison between non-severe and sever patients; the tumor of 1 patient is prostate cancer.

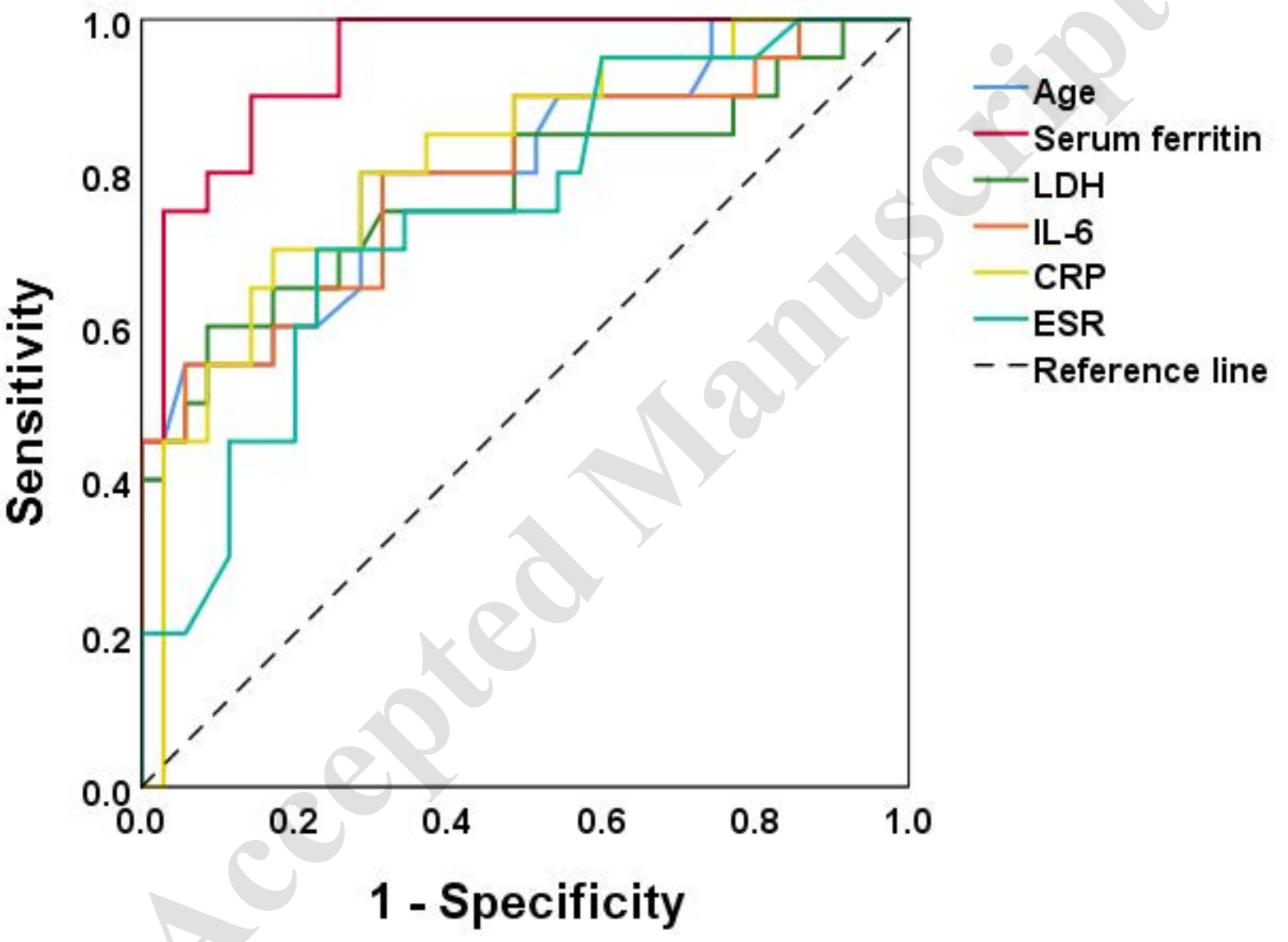
Table 2: Logistic regression analyses for factors predicting the severity of COVID-19

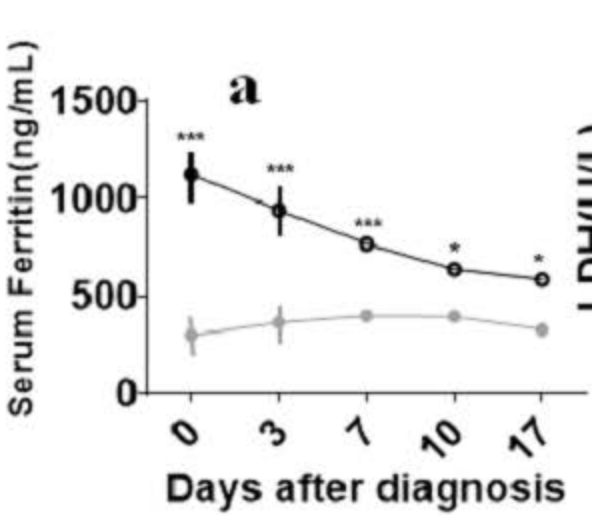
Covariate	OR ((95% CI)	P
Age, years	**1.196 (1.005-1.422)**	**0.04**
Serum ferritin, ng/mL	**1.006 (1.001-1.012)**	**0.02**
ALB	0.666(0.362-1.228)	0.19
HGB	0.967(0.819-1.141)	0.69
Lymphocytes	0.988(0.961-1.016)	0.39
Glu	0.964(0.409-2.268)	0.93
LDH, U/L	1.008 (0.978-1.039)	0.61
IL-6, pg/mL	0.979 (0.917-1.045)	0.52
CRP, mg/L	1.057 (0.955-1.169)	0.28
ESR, mm/60min	0.979 (0.884-1.084)	0.68

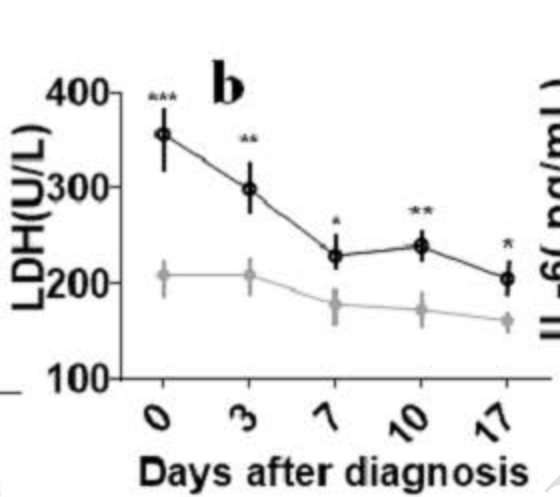
Table 3: Prognosis comparison of sever patients with different doses of methylprednisolone

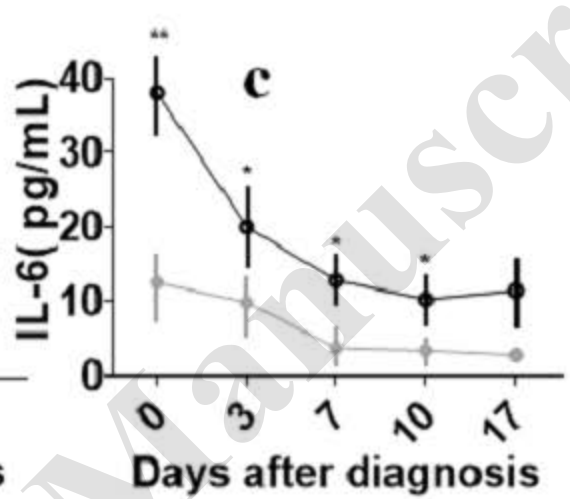
	Average dose of prednisolone (mg/kg.d)		P
	≤1.5	>1.5	
Numbers, n	11	10	
Days of methylprednisolone usage, days	6.8±2.1	11.6±6.3	0.04
Dose of methylprednisolone, mg/kg.d	0.9±0.3	3.3±0.6	0.000
Duration of severe illness, days	12.7±5.6	13.3±7.4	0.82
Days of high levels respiratory support, days	13.3±6.1	11.6±7.3	0.59
Hospital stay, days	23.3±7.3	32.3±7.8	0.01
Death, n	0	2	0.21

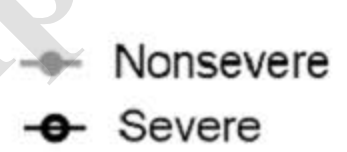
Note: Severe illness refer to patients with shortness of breath or dyspnea after activity, or a respiratory rate ≥30 breaths/min, or oxygen saturation ≤ 93% without supplementary oxygen inhalation, or an oxygenation index of < 300 mmHg. Days of high levels respiratory support mean the days that patients treated with high flow humidification treatment, noninvasive mechanical ventilation and invasive mechanical ventilation.











Days after diagnosis	0	3	7	10	17
Number of nonsevere patients	43	43	34	31	19
Number of sereve patients	21	21	21	21	18