The corticosteroid treatment and response of patients with COVID-19 in Hubei, China: a retrospective, cohort study

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Research

Keywords: COVID-19, Corticosteroid Treatment, Lymphocyte, Outcome

Posted Date: May 8th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-26761/v1

Abstract

Background Since December 2019, COVID-19 has emerged in Wuhan, China and spread globally. As of now, there is still no explicit therapeutic regimen and the use of corticosteroid is also controversial. We aimed to explore the effectiveness of corticosteroid and provide evidence for the rational use of corticosteroid in different patients with COVID-19.

Methods In this multi-centered, retrospective study, we extracted the clinical data of 649 cases with COVID-19 with definite outcome (discharged or dead) from 14 hospitals in Hubei province, and evaluated the clinical characteristics, treatment regimens, and their association with outcomes.

Results Ninety-five of 649 patients had died. Older male patients with comorbidities had an increased risk of death and more obvious abnormalities in clinical indicators. Corticosteroid, γ-globulin treatment and invasive ventilation were more frequently used in non-survivors. Survivors with corticosteroid treatment had a prolonged hospitalization. The median time duration for temperature restore for non-survivors after corticosteroid treatment was longer than that of both survivors. The lymphocyte count on admission was lower in the patients treated with corticosteroids compared to those without corticosteroid treatment. Lymphocyte count recovered significantly after corticosteroid treatment in survivors, but not in non-survivors.

Conclusions The responses to corticosteroid treatment were different in COVID-19 patients with different outcomes. The surviving patients with relatively lower lymphocyte count were more likely to be given corticosteroids. For non-survivors, the lymphocyte count was too low and the effect of corticosteroids was poor. Survivors under corticosteroid treatment had a prolonged hospitalization, but had a recovery of lymphocytes. The recovery of lymphocyte count and temperature after corticosteroid treatment may be used as predictors of prognosis of patients with COVID-19.

Background

In December 2019, the first pneumonia case caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), now known as coronavirus disease 2019 (COVID-19), was identified in Wuhan, Hubei Province, China[1]. SARS-Cov-2 infection is now quickly spreading globally[2, 3]. Evidence shows that the person-to-person transmission is the main cause of the large-scale outbreak of COVID-19[4]. As of Apr 29, 2020, the number of confirmed cases had reached 3,061,615 around the world.

With the increased understanding of the disease and the accumulation of treatment experience, the diagnosis and treatment schemes for COVID-19 are being better consummate. For COVID-19 patients with different severity, the treatment schemes are slightly different, mainly including the application of symptomatic support, antiviral, antibacterial drugs, respiratory support and corticosteroid application, etc. However, there is no evidence-based basis to support the assessment of therapeutic effect. Recent studies had documented the clinical manifestations of 41, 99 and 138 patients infected with COVID-19, respectively[1, 5, 6]. In the wake of uninterrupted expansion of the sample capacity, we had a deeper comprehension of the epidemiology and clinical characteristics of COVID-19. Unfortunately, definite outcomes were not tracked for these subjects, and we were unable to assess the therapeutic effect. Recently, a retrospective cohort study of 191 COVID-19 patients with definite outcomes showed that the potential risk factors of older age, high SOFA score, and d-dimer greater than 1 μg/L could help clinicians to identify patients with poor prognosis at an early stage[7]. It was an improvement in understanding of COVID-19, but we had to admit the interpretation of findings might be limited by the sample size. Thus, there still exists a big margin in our

understanding of COVID-19 treatment. The data on the clinical characteristics and clinical remedy of COVID-19 patients with definite outcomes (discharged or dead) are scarce, but are of paramount importance to improve the treatment efficacy and reduce mortality.

In this multi-centered, cohort study, we extracted the clinical data of 649 confirmed cases of COVID-19 with definite outcomes from 14 hospitals in Hubei province, and depicted their clinical characteristics and treatment regimens. We particularly explored the use of corticosteroid, treatment response, and their associations with outcome in those patients, committing to provide new testimony for the clinical remedy of COVID-19.

Method

Patients inclusion

This retrospective, multi-centered, cohort study included 649 adult (≥18 years old) patients confirmed with COVID-19 who died or were discharged between Dec 29, 2019 and Feb 17, 2020 from 14 hospitals in Hubei Province of China. The 14 hospitals involved in the study are government-designated hospitals to receive and treat the patients with COVID-19, and seven of them were from Wuhan, the outbreak center of COVID-19. According to WHO interim guidance(https://www.who.int/) and Chinese New Coronavirus Infected Pneumonia Diagnosis and Treatment Plan(http://www.nhc.gov.cn/; Trial Version 7), all patients enrolled in this study were classified into general survivor, severe/critical survivor, and non-survivor. The diagnostic criteria of severe/critical are as follows: 1) respiratory distress, respiratory rate ≥ 30 times/min; 2) means oxygen saturation ≤ 93% during the resting state; 3) arterial blood oxygen partial pressure / oxygen concentration ≤ 300mmHg (1mmHg = 0.133kPa); 4) lesions progress > 50% on pulmonary images within 24-48 hours; 5) occurrence of respiratory failure and requirement of mechanical ventilation; 6) shock; 7) requirement of ICU monitoring and treatment for combined organ failure. Patients were discharged from hospitals when they met the following criteria: 1) the body temperature returns to normal for more than three days; 2) respiratory symptoms improve significantly; 3) pulmonary imaging shows a marked improvement in acute exudative lesions; 4) nucleic acid tests of two consecutive (at least one day interval) respiratory specimens are negative.

Data collection

All data including epidemiological, demographic, clinical and laboratory data, and treatment information, were collected and reviewed by the experienced doctors of every hospital from their hospital's electronic medical record system. These data were then collated, analyzed and interpreted by researchers from the Department of Respiratory and Critical Care Medicine, Tongji Hospital, Huazhong University of Science and Technology. The recorded information is mainly related to the following five aspects: demographic data, medical history, symptoms and signs, laboratory findings and treatment measures, the details as follows:

Signs and symptoms: The main symptoms included cough, fever, and pant. The signs included body temperature, respiratory rate, and heart rate. Additionally, we divided the body temperature into three levels: normal (<37.3℃), low fever (37.3~38℃), and fever (>38℃), to evaluate the body temperature distribution among patients in each group.

Laboratory parameters: Laboratory data were collected throughout the whole hospitalization period, and the main tests included blood routine, and C-reactive protein and biochemical examination.

Therapeutic regimen: The main treatment measures in this study were constituted of medications (corticosteroid, antiviral, and antibacterial), γ-globulin, and respiratory support (mask breathing, non-invasive, invasive, and Extracorporeal membrane oxygenation [ECMO]). We also recorded the use of corticosteroids, including the average

daily dosage, duration, and the occasion of use. The injections and oral tablets of methylprednisolone, prednisone acetate, and dexamethasone were mainly used. The corticosteroid values recorded in the study were all calculated and analyzed after conversion to methylprednisolone. Antivirals included lopinavir/ritonavir, oseltamivir, interferon, etc., two or three of which were routinely used. Antibacterials included amoxicillin, ceftazidime, moxifloxacin, linezolid, meropenem, etc., one or two of which were commonly administrated.

Chest radiology: Chest x-rays and/or chest CT were performed for all patients enrolled. This examination revealed that all patients had varying degrees of imaging manifestations related to COVID-19 infection (not shown in this article).

Statistical analysis

Continuous variables are expressed as mean (SD) if they are normally distributed or median (IQR) if they are not, and categorical variables are expressed as number (%). The Student t test or one-way ANOVA was employed for comparison of continuous data that are normally distributed between these three groups involved; Otherwise, the Mann-Whitney U test or Kruskal-Wallis test was used. To compare the categorical data, we used chi-square test or the Fisher exact test as appropriate. Some variables possibly affecting clinical outcomes (discharged or dead) were included in univariate analysis to screen for potential confounding factors, including ages, gender, any comorbidities, leukocyte count, neutrophil count, lymphocyte count, AST, total bilirubin, urea, creatinine and lactate dehydrogenase, and further Cox regression were processed. Statistical analyses were performed using SPSS (Version 26.0). A two-sided α of less than 0.05 was considered statistically significant.

Result

Basic characteristics of patients

A total of 649 patients with COVID-19 were included in this study. Therein, 554 patients with COVID-19 were discharged (consisting of 272[42%] general type and 282[43%] severe/critical type), and 95(15%) patients had died. In the non-survivors, the median age was 68(IQR 62-77), older than that in the general-type survivors (45[32-56]) and severe/critical-type survivors (54[42-64]), and patients were predominantly males (61%[58/95]). There were 71(26%) cases in the general-type survivor group, 129(46%) cases in the severe/critical-type survivor group, and 69(73%) cases in the non-survivor group had concomitant diseases. There were significant differences in the median time from symptom onset to admission among the three groups (general-type survivors: 6[4-9]); severe/critical-type survivors: 8[6-11]; non-survivors:7[4-10]) (Table 1).

The main clinical manifestations of the patients recorded on admission were fever, cough, and pant etc. There were significant differences in symptoms among different groups, and the specific values of which are shown in table 1. On admission, for blood routine results, the median of leukocyte count, neutrophil count and neutrophil percentage showed a gradual trend of increase among these three groups (from the general-type survivor group to the severe/critical-type survivor group to the non-survivor group, P<0.0001). In contrast, the lymphocyte count and lymphocyte percentage in the non-survivor group were significantly lower than those in the two survivor groups (the general-type group and the severe/critical-type group, P<0.0001). The median value of C-reactive protein was 14.9 in the general-type survivors, 28.8 in the severe/critical-type survivors, and 54.5 in the non-survivors. The Biochemical test results on admission showed that the myoglobin and lactate dehydrogenase etc. levels in the non-survivors were significantly higher than those in the two survivor groups, the specific values of which are shown in table 1.

The main treatments and outcomes in our study

In terms of treatment approaches, almost all patients were given antiviral therapy, and the utilization rate was around 90% in each group. In the non-survivor group, the use of antibacterial (93[98%]) and γ-globulin (68[72%]) were significantly more frequent than that in the general-type survivors (178[65%]; 53[19%]), and the severe/critical-type survivors (249[88%]; 99[35%]). Corticosteroid therapy was given, in an increasing tendency, to the general-type survivors (73[27%]), the severe/critical-type survivors (171[61%]), and the non-survivor group (75[79%]). Respiratory support was given to all the patients with severe/critical illness. In the survivors, oxygen was mainly inhaled by mask (237[84%]), and the proportions of noninvasive and invasive ventilation in non-survivors (49[56%]; 25[29%]) were significantly higher than those in the severe/critical-type survivor group (41[15%]; 2[1%]) (Table 2).

Corticosteroid treatment in patients

Further comparison of corticosteroid treatment among different groups showed that the median daily corticosteroid dosage in the non-survivors was 60.0 mg (IQR[40.0-80.0]), which was higher than that in general-type survivors (40.0 mg[33.3-40.0]) and severe/critical-type survivors (40.0 mg[31.4-50.0]). The median treatment duration for the severe/critical-type survivors was 8.0 days (IQR[5.0-10.0]), longer than that of general-type survivors (6.0 days[4.0-9.0]). However, the median time duration for temperature restore after corticosteroid treatment in the non-survivors was 5.0 days (IQR[1.0-10.0]), longer than that in general-type survivors (1.0 days[1.0-3.0]) and severe/critical-type survivors (1.0 days[1.0-2.0]). General-type and severe/critical-type survivors who received corticosteroid treatment had longer hospitalization days compared to the corresponding subjects in each group without corticosteroid treatment (general-type: 13.0 days[9.0-16.5] vs 10.0 days[7.0-14.0]; severe/critical-type: 13.0 days[9.0-18.0] vs 11.0 days[8.0-14.0]) (Table 3). Corticosteroid treatment prolonged the hospitalization for general-type (Fig. 1A), and severe/critical-type survivors (Fig. 1B).

The recovery of lymphocyte count after corticosteroid treatment can be found in survivors

Regarding the blood counts on admission, there was an upward trend after corticosteroid treatment among three groups for leukocyte and neutrophil count. In the two survivor groups (general-type survivors and severe/critical-type survivors), the count remained within the normal range, but was significantly abnormal in the non-survivor group after corticosteroid treatment (Fig. 2A and 2B). Compared to those without corticosteroid treatment, patients in two survivor groups who received corticosteroid treatment had lower lymphocyte count (general-type survivors: 0.9×10^9/L[0.7-1.4] vs 1.3×10^9/L[0.9-1.7], P=0.0002; severe/critical-type survivors: 0.9×10^9/L[0.6-1.2] vs 1.0×10^9/L[0.8-1.4], P=0.0005). In contrast, there was no significant difference in lymphocyte count between patients with and without corticosteroid treatment in non-survivors (P=0.22), and lymphocyte count was at a low level for all non-survivors. The lymphocyte count in non-survivors (0.6×10^9/L[0.4-0.9]) was significantly lower than those in the two survivor groups (general-type survivors: 0.9×10^9/L[0.7-1.4]; severe/critical-type survivors: 0.9×10^9/L[0.6-1.2], P<0.0001). Comparing blood routine test results before and after corticosteroid treatment, we found that the lymphocyte count were elevated in general-type survivors (0.9×10^9/L[0.7-1.4] vs 1.5×10^9/L[0.9-2.1], P=0.002) and severe/critical-type survivors (0.9×10^9/L [0.6-1.2] vs 1.4×10^9/L [0.9-2.0], P<0.0001), however, the opposite was true for non-survivors (0.6×10^9/L [0.4-0.9] vs 0.4×10^9/L [0.3-0.7)], P=0.003) (Fig. 2C).

Discussion

Our study is a multi-centered, cohort study involving 649 patients with COVID-19. Therein, 554 patients with COVID-19 who were discharged from the hospital, consisting of 272 general-type survivors and 282 severe/critical-type

survivors, and 95 died patients were included in our study. Older male patients with comorbidities had an increased risk of death and more obvious abnormalities in clinical indicators. Antiviral and antibacterial treatments were widely used in every group of patients. The use of different kinds of respiratory supports for the severe/critical-type survivors and non-survivors were different, although both types of patients were given to respiratory support more frequently than general-type survivors. In the severe/critical-type survivors, oxygen was mainly inhaled by mask (237[84%]), and the proportions of noninvasive and invasive ventilation in non-survivors (49[56%]; 25[29%]) were significantly higher than those in the severe/critical-type survivor group (41[15%]; 2[1%]). Corticosteroid treatment and γ-globulin usage were more common in non-survivors. Physicians tended to give corticosteroid treatment to patients with lower levels of peripheral lymphocytes. Under corticosteroid treatment, survivors had a longer duration of hospitalization. Interestingly, for the first time, we discovered that survivors, but not non-survivors, had a significant recovery of lymphocyte count after corticosteroid treatment.

In our study, the death was more commonly occurred in older males with higher incidences of various chronic comorbidities. The median age of non-survivors was 68 years, which was significantly greater than that of the common-type severe/critical-type survivors. It is consistent with a recent report with smaller sample size that old age and comorbidity might be the high-risk factors for mortality in patients with COVID-19[7]. The low immune function of elderly patients and dysfunction of organs impaired by underlying diseases make those patients more prone to have disease progression and unresponsive to current treatments[8]. Regarding laboratory tests, it was clearly observed in non-survivors increased neutrophil count and decreased lymphocyte count. Lymphocytopenia have also been detected in patients with SARS and MERS, whose lymphocytes were destroyed by SARS-CoV and MERS-CoV[9, 10]. The increased neutrophil count may indicate secondary bacterial infections[11]. It is noting that, recently, the neutrophil-to-lymphocyte ratio (NLR) has been identified as an independent risk factor for COVID-19 patients with severe illness. In addition, LDH has been found increased in non-survivors, which reflected organ destruction and multiple organ failure.

Antiviral and antibacterial treatments were used frequently in all three kinds of patients, and γ-globulin use was more common in critically ill patients. All patients in severe/critical-type survivor group and the non-survivor group had received respiratory supports of differing types. Referring to corticosteroid treatment, we found that it was more commonly used in non-survivors (75[79%]) and severe/critical-type survivors (171[61%]) than in the general-type survivor group (73 [27%]). Corticosteroid treatment for viral pneumonias, such as SARS, pandemic influenza A (H1N1pdm09) and MERS, remain controversial[12–14]. Some studies demonstrated that corticosteroid treatment was associated with delayed MERS and SARS coronavirus RNA clearance[15, 16]. A recent study reported a similar pathological feature of COVID-19 as SARS and MERS[17]. At present, the effect of corticosteroid treatment on patients with COVID-19 is unclear, however, corticosteroids are still commonly used in clinical practice in order to control the secondary severe inflammation in response to viral infection. Therefore, it is important to study the effect of corticosteroid treatment on patients with COVID-19.

For general and severe/critical-type survivors, we found a longer duration of hospitalization for patients with corticosteroid treatment by multivariate regression analysis with baseline confounders adjusted. Nevertheless, we found that the survivors with corticosteroid treatment had lower lymphocyte count than those without corticosteroids. It is consistent with the feeling that physicians tend to give corticosteroid treatment to patients with more severe disease in clinical practice. Lower lymphocyte count on admission may reflect a severe damage of the immune system upon SARS-CoV-2 infection and indicate severe disease condition. Thus, it is possible that prolonged hospitalization of survivors with corticosteroid treatment may be due to the more severe condition of patients. Notably, the lymphocyte count was increased significantly and a recovery of temperature was achieved one day after

corticosteroid treatment in survivors with general-type and severe/critical-type COVID-19, suggesting an unneglectable benefit to use corticosteroids in certain patients with COVID-19. In the non-survivors, the increase of lymphocyte count and the timely recovery of temperature did not be achieved after corticosteroid treatment. Thus it can be seen, corticosteroid treatment was not effective for all patients, which may be due to many complicated factors affecting the treatment of patients with severe/critical illness. Despite this, the corticosteroid treatment should not be denied absolutely. For patients with lower lymphocyte count on admission, corticosteroids should be tried appropriately. The recovery of lymphocyte count and temperature can be used as predictors of disease prognosis.

Previously, it has been shown that a variety of inflammatory mediators, such as IL1β, IL-8, and MCP, were elevated in the serum of COVID-19 patients, indicating an undergoing systemic inflammatory response in patients with COVID-19[1]. The lymphopenia has also been observed commonly in patients with systemic inflammation reaction syndrome (SIRS), suggesting that inflammatory reaction may be a potential menace of lymphopenia or dysfunction of lymphocyte[18, 19]. Based on the available evidences, we speculate that, for survivors with corticosteroid treatment, the use of corticosteroids may inhibit the inflammatory response, and therefore lead to the recovery of lymphocytes. As for why the non-survivors did not have recovery of lymphocyte count, even worse, and why the leukocyte count and neutrophil count increased significantly, we ascribed them to aging, more common comorbidities, low immunity, and poor response to treatment. It prompted the discussion for the clinicians whether the increase of corticosteroids (dosage and duration) should be considered for the patients with relatively severe conditions, or perhaps, the combined application of other anti-inflammatory drugs, such as humanized blocking antibodies for inflammatory cytokines, to minimize complications and improve the prognosis of critical patients.

Our study has several limitations. The retrospective study design makes us impossible to control every influencing factor on our results, particularly for the corticosteroid treatment, although we tried to adjust baseline confounders by multivariate regression analysis. More importantly, although we found the clear benefit of corticosteroid treatment in patients with COVID-19. Questions are still open regarding the patient selection and timing for corticosteroid treatment.

Conclusions

Our results confirm that older male patients with comorbidities had an increased risk of death and more obvious abnormalities in clinical indicators. Corticosteroid treatment can restore peripheral lymphocyte and temperature in certain patients with COVID-19. The recovery of lymphocyte count and temperature after corticosteroid treatment may be used as predictors of prognosis of patients with COVID-19. Our findings may be helpful for guiding the rational use of corticosteroid in different patients according to the results of admission test and evaluate the therapeutic effect timely.

Abbreviations

COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; IQR: Interquartile range; ECMO: Extracorporeal membrane oxygenation; SIRS: Systemic inflammation reaction syndrome; NLR: Neutrophil-to-lymphocyte ratio

Declarations

Acknowledgments

Thank you all cooperation unit for your support. We acknowledge all health-care workers involved in the prevention and control of the epidemic situation. I would like to thank them for their contributions to the diagnosis and treatment of patients and the staff who record and collect the clinical data carefully. Thank you to every patient involved in the study.

Author's contributions

JX and ZL participated in study design. JS, RD, QL, JW, SX, ZK, ZC, JY, YL, YH, HZ, HH, ZX, XL, WH, JG, WK, ZS collected the epidemiological and clinical data. JX, YG, QH, and YZ performed the statistical analysis and drafted the manuscript. JX and ZL revised the final manuscript. All authors reviewed and approved the final version of the manuscript.

Funding

Supported by the National Natural Science Foundation of China (No. 81973986 and 81570033) and a COVID-19 Emergency Project from Wuhan Science and Technology Bureau (2020020401010096).

Availability of data and materials

The dataset used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The ethics committee reviewed and approved this study (Ethics committee, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China, IRB ID:TJ-C20200144). Written informed consent was waived for the emerging infectious disease.

Consent for publication

Not applicable

Conflicts of interest: The authors declare that they have no conflicts of interest.

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Tables

Table 1 Demographic, clinical and laboratory findings of patients on admission

	Survivor（Discharged）		Non-survivor (n=95)	p value
	General (n=272)	Severe/Critical (n=282)		
Demographic information				
Age, years	45(32~56) *^	54(42~64) *	68(62~77)	<0.0001
Gender				0.001
Male	108(40%)*	136(48%)	58(61%)	
Female	164(60%)*	146(52%)	37(39%)	
Comorbidity	71(26%)*^	129(46%)*	69(73%)	<0.0001
Days from the onset to admission	6(4~9) ^	8(6~11)	7(4~10)	<0.0001
Signs and symptoms				
Fever	218(80%) ^	255(90%)	84(88%)	<0.0001
Admission temperature, °C				
<37.3	139(51%)	172(61%)	49(51%)	
37.3~38.0	51(19%)	37(13%)	13(14%)	
>38.0	82(30%)	73(26%)	33(35%)	
Cough	184(68%) *	186(66%) *	50(53%)	0.03
Pant	43(16%) *^	116(41%) *	66(69%)	<0.0001
Respiratory rate, bpm	20(20~21) *	20(20~21) *	21(20~25)	<0.0001
Heart rate, bpm	86(78~98)	87(80~98)	89(78~106)	0.24
Blood routine				
White blood cell count, × 10^9/L	4.5(3.5~5.7) *	4.7(3.7~6.0) *	7.1(4.1~11.3)	<0.0001
Neutrophil count, × 10^9/L	2.8(1.8~3.8) *^	3.3(2.3~4.7) *	6.0(2.9~10.4)	<0.0001
Neutrophil, %	58.4(44.5~68.7) *^	71.3(59.8~79.6) *	82.1 (69.1~90.7)	<0.0001
Lymphocyte count, × 10^9/L	1.2(0.9~1.6) *^	1.0(0.7~1.3) *	0.7(0.5~1.0)	<0.0001
Lymphocyte, %	26.8(15.7~34.6) *^	20.2(13.1~28.8) *	10.8(4.8~17.0)	<0.0001
CRP	14.9 (6.0~32.8) *^	28.8(12.7~56.4) *	54.5(20.0~106.1)	<0.0001
Biochemical tests				
Alanine aminotransferase, U/L	19.0(14.0~29.0) *^	22.0(14.1~35.8)	24.0(17.0~36.5)	0.004
Aspartate aminotransferase, U/L	22.0(17.0~31.0) *^	26.0(19.0~39.8) *	33.4(22.3~53.8)	<0.0001
Total bilirubin, umol/L	9.0(7.1~12.0)	8.4(6.0~11.2) *	9.9(7.4~15.6)	0.002
Direct bilirubin, umol/L	3.6(2.4~5.2) *^	2.7(1.8~4.0) *	4.9(3.3~6.8)	<0.0001
Alkaline phosphatase, U/L	57(49~71)	58(47~70)	62(48~79)	0.38
r-glutamyl transpeptidase, U/L	21.0(14.5~33.6) *^	26.0(16.0~48.8)	30.0(20.0~47.0)	<0.0001
Urea, mmol/L	3.9(3.1~5.1) *^	4.4(3.4~6.0) *	6.5(4.6~11.5)	<0.0001
Creatinine, umol/L	63.7(51.5~78.6) *	66.0(55.0~80.0) *	83.0(65.5~101.1)	<0.0001
Myoglobin, ug/L	21.5(11.2~44.2) *	25.4(15.6~41.9) *	112.2(37.2~193.0)	<0.0001
Lactate dehydrogenase, U/L	208.0(173.0~253.5) *^	264.0(210.5~324.5) *	353.0(250.0~569.0)	<0.0001

Data are expressed as n (%), median (IQR). *P < 0.05 vs Non-survivor and ^ P <0 .05 vs Severe/Critical Survivor.

Table 2 Treatments and outcomes

	Survivor（Discharged）		Non-survivor (n=95)	p value
	General(n=272)	Severe/Critical(n=282)		
Corticosteroids treatment	73(27%) *^	171(61%) *	75(79%)	<0.0001
Antiviral	249(92%)	264(94%)	87(92%)	0.61
antibacterial	178(65%) *^	249(88%) *	93(98%)	<0.0001
γ-globulin	53(19%) *^	99(35%) *	68(72%)	<0.0001
Respiratory support	1(1%) *^	280(99%)	87(92%)	<0.0001
Masked	1(100%)	237(84%)	12(14%)	
Noninvasive	0	41(15%)	49(56%)	
Invasive	0	2(1%)	25(29%)	
ECMO	0	0	1(1%)	

Data are expressed as n (%). * P <0.05 vs Non-survivor and ^ P <0 .05 vs Severe/Critical Survivor. ECMO=Extracorporeal Membrane Oxygenation.

Table 3 Patients with or without corticosteroid treatment in survivor and non-survivor

	Survivor（Discharged）				Non-survivor (n=95)	
	General(n=272)		Severe/Critical(n=282)			
Corticosteroid treatment	Yes	No	Yes	No	Yes	No
Number	73(27%)	199(73%)	171(61%)	111 (39%)	75(79%)	20(21%)
The usage of corticosteroid						
Dosage, mg/d	40.0(33.3~40.0) *	_	40.0(31.4~50.0) *	_	60.0(40.0~80.0)	_
Treatment period, days	6(4~9) ^	_	8(5~10)	_	7(5~10)	_
Hospitalization, days	13.0(9.0~16.5) #	10.0(7.0~14.0)	13.0(9.0~18.0) #	11.0(8.0~14.0)	11.0(8.0~16.0)	9.5(6.3~14.5)
Days from corticosteroid treatment to temperature restore	1(1~3) *	_	1(1~2) *	_	5(1~10)	_

Data are expressed as n (%), median (IQR). * $P < 0.05$ vs Non-survivor with corticosteroid treatment. ^ $P < 0.05$ vs Severe/Critical Survivor. # $P < 0.05$ vs the same group without corticosteroid treatment.

Figures

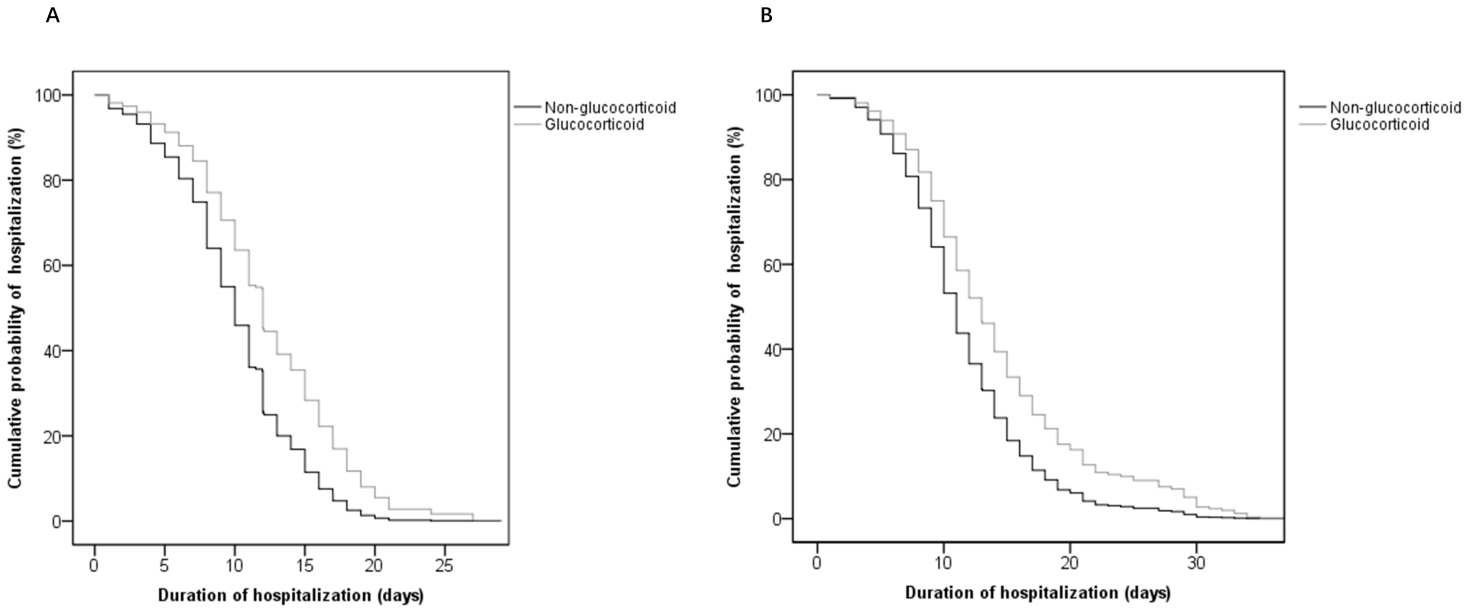

Figure 1

Time from admission to discharge of survivors. A. for the general group B. for the severe/critical group

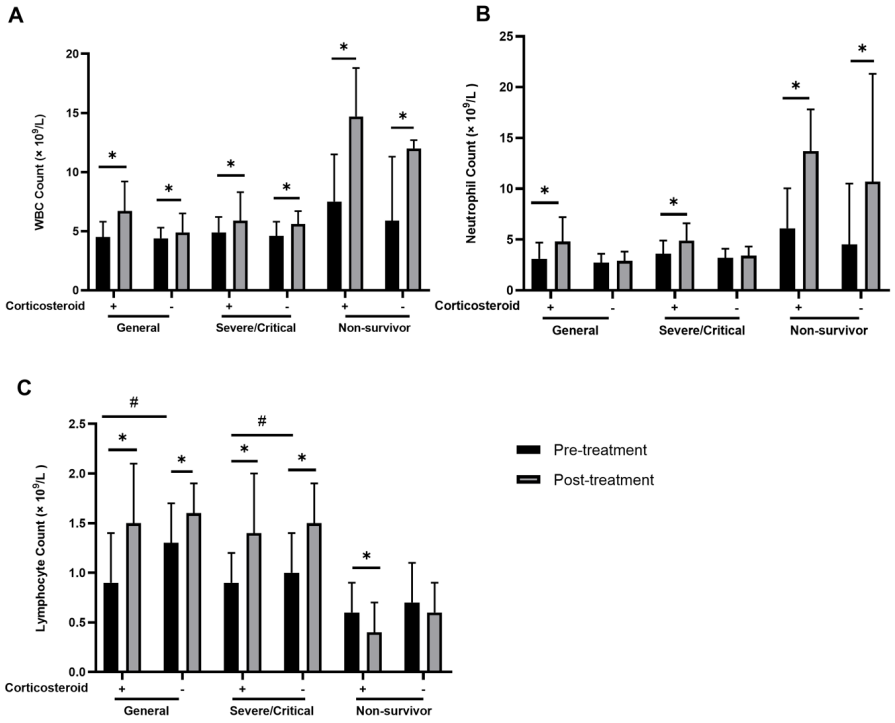

Figure 2

Changes of leukocytes, neutrophils and lymphocytes, in patients before and after corticosteroid treatment. A. for leukocyte count B. for neutrophil count C. for lymphocyte count (+): Corticosteroid treatment; (-): No corticosteroid treatment. Data are expressed as median (IQR). * P <0.05 Pre-treatment vs Post-treatment in the same group; # P < 0.05 Corticosteroid treatment vs No corticosteroid treatment in the same group on admission.