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Disease progression in patients with COVID-19 in Jiangsu province, China: a retrospective cohort study

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Disease progression of COVID-19

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Summary

SETTING: Identification of the factors associated with disease progression could help physicians early and prospectively recognize patients at high risk of progression.

OBJECTIVE: This study aims to evaluate the clinical features in disease progression among patients with COVID-19 after admission.

DESIGN: This is a retrospective, multi-center cohort study. From January 10 and February 29, 2020, all cases diagnosed with COVID-19 at 24 hospitals in Jiangsu province, with complete medical records were involved. The primary outcome was the disease deterioration defined as the dramatic progression from asymptomatic or mild or moderate status on admission into severe or critically ill status during 14 day's follow-up.

RESULTS: Of the 625 patients in Jiangsu, none of patients died, and 597 patients were asymptomatic or mild or moderate on admission, of which 36 (6%) experienced disease deterioration to severe or critically ill status. Disease deterioration to severe or critically ill status was associated with age, pulmonary opacity score, lymphocyte count on admission, and pandemic center Wuhan exposure.

CONCLUSION: Disease deterioration to severe or critically ill status was observed in 6% patients during 14 days follow-up, and was associated with age, pulmonary opacity score, lymphocyte count, and pandemic center Wuhan exposure.

KEY WORDS: COVID-19; coronavirus; 2019-nCoV; disease deterioration; disease progression; severity

The World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) a pandemic affecting all continents on the 11th March 2020.[1] During the clinical course, some patients experienced deterioration in clinical symptoms, and some cases have progressed rapidly to acute respiratory distress syndrome (ARDS), septic shock, metabolic acidosis, coagulopathy, multi-organ system failure, death, or other poor outcomes.[2-4] A study on clinical course and mortality of adult inpatients with COVID-19 in Wuhan found that the mortality of severe and critically ill patients was 22% and 78%, respectively.[3] Another study has reported risk factors for progression from ARDS to death in patients with COVID-19.[2] However, either the pattern of the disease progression from moderate or less status to severe/critically-ill status or their associates has not been fully investigated in patients with COVID-19. Assessment of patterns of disease progression and identification of factors associated with disease progression could help physicians early and prospectively recognize patients at high risk of progression and help patients avoid entering a crisis phase linked to oxygen desaturation profiles. This multicenter retrospective cohort study set out to describe the occurrence of disease progression in patients with COVID-19 after admission and explore the factors associated with progression from moderate or less status to severe or critically illness.

Methods

Study design and participants

This retrospective cohort study included all the patients who met the patient inclusion and exclusion criteria. Inclusion criteria were as of February 29, 2020, all patients diagnosed with COVID-19 in Jiangsu according to diagnostic criteria of "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)" released by National Health Commission & National Administration of Traditional Chinese Medicine of China,[5] and admitted to designated hospitals for COVID-19 treatment in Jiangsu province. The diagnosis of COVID-19 was based on epidemiological history, clinical manifestations, imaging manifestations of pneumonia in computer tomography (CT) scans, and laboratory confirmation (positive real-time reverse transcription–polymerase chain reaction assays, RT-PCR).[5] Exclusion criteria was medical records unavailability. For patients presented to the hospital, those who had possible exposure to the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2, the etiological agent causing COVID-19), or had no identifiable exposure but clinical or imaging manifestations would be tested for SARS-CoV-2. The discharge standard was body temperature return to normal for more than 3 days,

symptoms become better if they have symptoms, and RT-PCR (throat swab samples, at least 1 day for sampling interval) showed negative for 2 consecutive times.

Data collection and definition of variables

The epidemiological, clinical, laboratory, and radiologic parameters were collected on admission. Data on disease severity were available at days 1, 2, 3, 4, 5, 6, 7 and 14 after admission, except for those who were discharged, and data on mortality and hospitalization status were available until February 29, 2020. The primary outcome was disease deterioration, i.e. dramatic progression from asymptomatic or mild or moderate status on admission, to severe or critically ill status during 2 weeks follow-up. Dramatic progression in our study does not include fragile progression such as progression from asymptomatic to mild status or from mild status to moderate status, or severe status to critically ill status. Two attending physicians adjudicated the disease severity (asymptomatic, mild, moderate, severe, or critically ill). Asymptomatic infection was defined as the absence of clinical symptoms but a positive nucleic acid test result. Mild disease was defined as having mild clinical symptoms and the absence of imaging manifestations of pneumonia in CT scans. Moderate disease was defined as the presence of fever, respiratory tract symptoms or other symptoms and imaging manifestations. Severe disease was defined as the presence of at least one of the following items: respiratory distress, respiratory rate $\geq$ 30 beats/min; oxygen saturation in resting state (SpO_2) $\leq$ 93%; or arterial blood oxygen partial pressure (PaO_2) / fraction of inspired oxygen (FiO_2) $\leq$ 300 mmHg (1 mmHg = 0.133kPa). Critically ill was defined as having respiratory failure requiring mechanical ventilation, shock or combined organ failure requiring intensive care unit (ICU) monitoring and treatment.

All of the patients in Jiangsu have taken a high-resolution CT of thorax examination which could truly reflect the lung lesions. CT images were assessed in a visual manner by two radiologists with more than 5 years of working experience in chest imaging. The radiologists were blinded to the patients' information. Quadrant scores were the sum of the number of quadrants containing pulmonary opacities extending from the proximal to the distal end of the chest and had a score between 0 and 4. For pulmonary opacity, bilateral lungs were scored manually and assigned an estimated percentage of pulmonary opacity relative to the whole lung, rounded to the nearest 5%.

Statistical analysis

A summary table was generated to present dynamic patterns of disease progression in severity at each follow-up day by three categorised disease severity groups (1=

asymptomatic/mild, 2=moderate, and 3=severe/critically ill) on admission. We also generated a table to present the disease progression to worst severity during 14-day hospitalization among COVID-19 patients. Continuous variables were reported as means ± standard deviation (SD) or median (interquartile range [IQR]) by group (patients with and without disease deterioration) and compared using Student's t-test or Mann–Whitney U test depending on their distributions. Categorical variables were summarized using frequency and percentage and compared by Chi-square/Fisher exact test.

Logistic regression models were used to identify the risk factors of developing a disease deterioration. Variables that were significant at the significance level of 5% in the univariate logistic regression analysis were included in the multivariate logistic regression. Missing covariates at admission were imputed in multivariate regression model analysis with multiple imputation using a Markov Chain Monte Carlo simulation method with 10 iterations. In the logistic regression analysis, odds ratios for having a disease progression for each variable were calculated along with 95% confidence intervals (CIs). The 2-tailed $P < 0.05$ was considered as statistically significant for all analyses. The analyses were performed using SAS 9.4 (SAS Institute).

Ethics approval

The study was approved by the Ethics Committee of Zhongda Hospital Affiliated to Southeast University (2020ZDSYLL013–P01 and 2020ZDSYLL019–P01). Patient informed consent was waived due to the retrospective study design.

Results

From January 10, 2020 to February 29, 2020, 721 suspected cases with possible COVID-19 were admitted in 24 hospitals in Jiangsu province, China, while 90 cases were excluded because of negative RT-PCR result. 631 cases were diagnosed with COVID-19 totally. This study included 625 cases who had complete medical records (Figure 1). The median age was 46 years (IQR, 32-57; range, 0.75-96 years), and 329 (52.6%) were men. No deaths were reported during this study.

Table S1 in the Supplement provides a table showing the dynamic patterns of disease progression by follow-up day among patients with COVID-19. On admission (day 1), overall, 109 (17.4%) patients were in asymptomatic or mild status, 488 (78.1%) in moderate status, and 28 (4.5%) severe or critically ill status. Overall, changes in disease severity from

admission show an increased proportion of moderate cases deteriorating into severe or critically ill cases with 8 (1.6%) at day 2 progressively increased up to 25 (5.2%) at day 7.

Table 1 presents the disease progression in severity from admission to the worst severity during 14-day hospital stay among COVID-19 patients. Of the 625 patients, 83.7% (523) patients had a stable condition or became better during 14 days' hospitalization whereas 16.3% (102) patients progressed to at least one degree in disease severity. Some patients had disease deterioration, i.e. dramatic progression from asymptomatic or mild or moderate status on admission, to severe or critically ill status, during 2 weeks of hospital stay. 36 out of 597 (6%) patients had dramatic progression from day 2 to 14 after admission.

Compared to patients without dramatic progression (n = 561) during 14-day hospitalization, patients with dramatic progression (n = 36) were significantly older (mean [SD], 60.97 [12.67] vs 42.71 [16.75]; $P < .0001$), were more likely to be imported cases who had a history of the pandemic center Wuhan contact (52.8% vs 34.6%; $P = 0.0272$), to have prior histories of hypertension (27.8% vs 13.5%; $P = 0.0184$), and diabetes (16.7% vs 5.3%; $P = 0.0057$), to have lower SpO_2 (mean [SD], 97.17 [1.81] vs 97.92 [1.15]; $P = 0.0003$), and higher CT quadrant score (median [IQR], 4.0 [0.0-4.0] vs 2.0 [0.0-4.0]; $P < .0001$) and pulmonary opacity volume percentage (median [IQR], 50.0 [0.0-80.0] vs 20.0 [0.0-80.0]; $P < .0001$) (Table 2). Patients with disease deterioration had also significantly lower lymphocyte count (10^9/L) (median [IQR], 0.8 [0.2-1.5] vs 1.4 [0.3-3.6]; $P < .0001$) and platelet count (10^9/L) (median [IQR], 155.5 [92.0-236.0] vs 188.5 [51.0-530.0]; $P = 0.0004$) than those without. In addition, patients with disease deterioration had significantly higher level of C-reactive protein (mg/L) (median [IQR], 26.2 [0.5-250.4] vs 10.0 [0.5-208.2]; $P = 0.0020$) and fibrinogen (g/L) (median [IQR], 4.2 [1.5-7.0] vs 3.4 [0.9-8.2]; $P = 0.0175$) than those without.

Eleven variables were selected into univariate and multivariate logistic regression analyses (Table 3). For multivariable logistic regression model, 4 variables measured at admission were identified to be independently related to the occurrence of disease: age (year) (odds ratio [OR], 1.08; 95% confidence interval [CI]: 1.04-1.12; P < 0.0001), pulmonary opacity score (per 5%) (OR, 1.30, 95% CI: 1.10-1.52; P = 0.0016), lymphocyte (10^9/L) (OR, 0.28, 95% CI: 0.09-0.91; P = 0.0357), and imported cases (exposed to the pandemic center Wuhan) (OR, 2.45, 95% CI: 1.03-5.80; P = 0.0421).

Table S2 demonstrates that oxygen was delivered to patients with disease deterioration via nasal cannulae (31 [86.1%]), simple face masks (7 [19.4%]), high-flow nasal cannulae (11 [30.6%]), or prone position (6 [16.7%]). Ventilatory support was used in approximately 50% of patients with clinical progression.

Discussion

This is one of the largest study to describe disease progression in patients hospitalized with COVID-19. As of February 29, 2020, in Jiangsu, China, 625 cases with available data were included in this study. On admission to hospital, 17.4% patients had asymptomatic or mild disease, 78.1% had moderate disease, and 4.5% were severely or critically ill. During the study period (to February 29, 2020) there were no deaths; 81.6% had been discharged, and less than 1% were requiring ongoing ICU care. Jiangsu province reported no death mainly due to early recognition of high-risk and critically ill patients, early intervention, hierarchical management strategies, and reasonable allocation of materials and human resources.[6]

We found that over four-fifths of patients with COVID-19 had a stable or improving clinical course with a minority deteriorating during 14-day follow-up period. This is consistent with a previous study which found that after 2 weeks from admission, 14.1% (11) of patients had worsened status and 85.9% (67) of patients had improved or stable status.[7] Several studies showed clinical deterioration may occur within two weeks after onset of illness.[3,8-10] In comparison, other fatal zoonotic coronavirus diseases, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) progress rapidly to respiratory failure and organ injury.[11] Within 7 days from admission, CT shows clinical signs of 31% (4) of patients progressed, while within 14 days, 85.7% (54) of patients progressed.[12-14]

Studies on SARS and MERS have raised a tri-phasic pattern for disease progression combined with time course of viral load. For SARS, week 1 with increasing viral load which may be related to mild symptoms; week 2 with falling viral load and severe clinical worsening and immunopathological damage as a result of overexuberant host response, rather than uncontrolled viral replication; phase 3 with either resolution of symptoms or further deterioration.[15] MERS showed a similar pattern.[16] For SARS-CoV-2, two correspondences reported viral loads peaked at around 5–6 days after symptom onset and a patient presented an extremely high viral load,[17] and virus loads in asymptomatic patients was similar to that in symptomatic patients.[18] Except for severe cases, most of the patients with COVID-19 were able to clear the virus and their disease progression fits the biphasic model well, i.e. first

phase characterized by fever and other systemic symptoms, followed by week 2 with symptoms relief.[19]

Our study reported that only 6% (36) patients experienced disease deterioration, i.e. progression from moderate or less status on admission, to severe or critically ill status within 2 weeks from admission. This study showed features including symptoms and abnormal radiologic and laboratory presentation on admission may be early signs of deterioration of respiratory, immune, and coagulation system. In particular, age, pulmonary opacity score in CT, lymphocyte count, and pandemic center Wuhan exposure were independent predictors for disease progression. This is in line with a study that identified several risk factors for disease progression of COVID-19, including age, respiratory failure, and C-reactive protein.[7] The severity of opacity evaluated from initial CT of patients with COVID-19 was closely related to the progression of opacity presented in the subsequent CT, which are of value for monitoring disease progress.[20] Older age and coagulation dysfunction were associated with progression from ARDS to death in patients with COVID-19.[2] Old age and severe lymphopenia seem to be statistically significant in predicting clinical deterioration in patients with SARS.[15,21] Patients who have been to Wuhan may have been exposed to a large amount of virus, so the disease may be more likely to deteriorate.

The progress and outcome of SARS may be associated with specific temporal patterns of development in combination with several non-specific signs and symptom complexes.[22] Further study suggests that clinical progression at week 2 may not be associated with uncontrolled viral replication, but with immunopathological damage.[15] These evidence indirectly supported our study results: symptoms and abnormal laboratory and radiologic manifestation on admission provided early signs for short-term immunopathological damage and disease progression of COVID-19 in the near future.

This cohort consisted of almost all COVID-19 patients in this province with a population over 80 million and its results should be generalizable to other similar places outside Hubei province. This study also has some limitations. First, severity data were only available during the first 14-day hospital stays, and we were unable to assess the disease progression and its risk factors beyond this period. Second, the data were collected retrospectively, hence we could not assess the impact of some key predictive variables including clinical management (e.g. oxygen supportive and medical drugs treatments), viral load (e.g. the quantity of viral RNA in blood), some other laboratory parameters (e.g. LDH), and host genetic factors

because of lack of available data. As a result, observed risk factors may still be subject to unobserved confounders.

Conclusions

In this multi-center cohort of 625 patients with COVID-19 in Jiangsu province, China, we found that 16.3% of patients experienced a deterioration in their clinical condition and that 6% of patients with moderate or less status deteriorated to being severe or critically ill but ultimately survived. Age, pulmonary opacity score, lymphocyte count on admission, and pandemic center Wuhan exposure were identified as the independent risk factors of disease deterioration. Careful attention to these risk factors for deterioration may help guide clinical care.

Author contributions

S. J., D. W. and Y. Y. conceived and designed the study. H. L., Y. W., S. J. and S. L. contributed to the literature search. S. L., Y. W., S. J., Y. Y., and D. W. contributed to data collection, quality checks and data management. D. W., S. J., S. L, H. L., K. M., Y. W. and Y. Y. contributed to data analysis and results presentation. D. W., S. J., S. L., H. L., K. M., and Y. Y. were responsible for results interpretation. H. L., Y. W., K. M., D. W., S. J., S. L. and Y. Y. contributed in the drafting and review of the manuscript.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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373 Table 1: Disease progression to worst severity during 2-week follow-up from admission among patients with COVID-19

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Severity at admission	Worst severity during 2-week follow-up					
	Asymptomatic	Mild	Moderate	Severe	Critically ill	Total
Asymptomatic	44% (24/55)	13% (7/55)	42% (23/55)	2% (1/55)	0% (0/55)	55
Mild	0% (0/54)	52% (28/54)	46% (25/54)	2% (1/54)	0% (0/54)	54
Moderate	0% (0/488)	0% (0/488)	93% (454/488)	4% (19/488)	3% (15/488)	488
Severe	0% (0/20)	0% (0/20)	%0 (0/20)	45% (9/20)	55% (11/20)	20
Critically ill	0% (0/8)	0% (0/8)	0% (0/8)	0% (0/8)	100% (8/8)	8
Total	4% (24/625)	6% (35/625)	80% (502/625)	5% (30/625)	5% (34/625)	100% (625/625)

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Table 2: Demographic and clinical characteristics of patients with COVID-19 at admission

			Disease progression*		
Category	Characteristics	All (N=597)	Yes (N=36)	No (N=561)	P-value**
Demographic	Male, n(%)	309(51.8%)	21(58.3%)	288(51.3%)	0.4924
	Age (year), mean(SD)	43.82(17.07)	60.97(12.67)	42.72(16.73)	<.0001
Exposure type, n(%)	Imported cases	384(64.3%)	19(52.8%)	194(34.6%)	0.0272
	Local cases	293(49.1%)	17(47.2%)	367(65.4%)	
Types of disease onset, n(%)	Single onset	309(51.8%)	23(63.9%)	270(48.1%)	0.0667
	Clustering onset	304(50.9%)	13(36.1%)	291(51.9%)	
Initial symptoms, n(%)	Fever	388(65.0%)	28(77.8%)	360(64.2%)	0.0971
	Cough	322(53.9%)	22(61.1%)	300(53.5%)	0.3730
	Sputum	153(25.6%)	12(33.3%)	141(25.1%)	0.2747
Medical history, n(%)	Hypertension	86(14.4%)	10(27.8%)	76(13.5%)	0.0184
	Diabetes	18.87(2.05)	6(16.7%)	30(5.3%)	0.0057
Vital signs, mean(SD)	Temperature	37.04(0.72)	37.26(0.89)	37.02(0.70)	0.0507
	HR (bpm)	86.88(13.39)	87.39(15.73)	86.84(13.25)	0.8135
	Respiratory rate (breath per min)	18.87(2.05)	19.00(2.32)	18.87(2.04)	0.7051
	SpO_2 (%)	97.88(1.21)	97.17(1.81)	97.92(1.15)	0.0003
CT image, N, median (IQR)	Quadrant score (1-4)	471,2.0(0.0-4.0)	33,4.0(0.0-4.0)	438,2.0(0.0-4.0)	<.0001
	Pulmonary opacity (%)	471,20.0(0.0-80.0)	33,50.0(0.0-80.0)	438,20.0(0.0-80.0)	<.0001
Lab test, N, median (IQR)	Lymphocyte (10^9/L)	481,1.3(0.2-3.6)	28,0.8(0.2-1.5)	453,1.4(0.3-3.6)	<.0001
	Platelet (10^9/L)	472,184.5(51.0-530.0)	26,155.5(92.0-236.0)	446,188.5(51.0-530.0)	0.0004
	C-reactive protein (mg/L)	455,10.0(0.5-250.4)	25,26.2(0.5-250.4)	430,10.0(0.5-208.2)	0.0020
	Fibrinogen (g/L)	473,3.4(0.9-8.2)	30,4.2(1.5-7.0)	443,3.4(0.9-8.2)	0.0175

* The primary outcome was disease deterioration, i.e. dramatic progression from asymptomatic or mild or moderate status on admission, to severe or critically ill status during 2 weeks follow-up.

** The p-values were from testing whether these characteristics are different between patients with and without disease deterioration.

Table 3: Factors associated with disease progression in patients with COVID-19: Results from logistic regression analysis (N=597)

	Univariate analysis*			Multivariate analysis**		
Variables	Odds ratio (95%CI)	P-value	Chi-square	Odds ratio (95%CI)	P-value	Chi-square***
Age (year)	1.08(1.05,1.11)	<.0001	33.0	1.08(1.04,1.12)	<.0001	17.1
Pulmonary opacity (per 5%)	1.36(1.24,1.49)	<.0001	41.7	1.32(1.12,1.57)	0.0015	10.4
Lymphocyte (10^9/L)	0.06(0.02,0.18)	<.0001	23.6	0.28(0.09,0.91)	0.0357	4.5
Imported	2.11(1.07,4.16)	0.0302	4.7	2.45(1.03,5.80)	0.0421	4.1
SpO_2 (per 5%)	0.14(0.04,0.41)	0.0004	12.4	0.31(0.07,1.33)	0.1147	2.5
Platelet (10^9/L)	0.99(0.98,0.99)	0.0012	10.6	1.00(0.99,1.00)	0.3187	1.0
Diabetes	3.54(1.37,9.16)	0.0091	6.8	1.84(0.49,6.93)	0.3685	0.8
Quadrant score (1-4)	2.45(1.64,3.67)	<.0001	19.0	0.83(0.47,1.47)	0.5275	0.4
Fibrinogen (g/L)	1.54(1.16,2.04)	0.0029	8.9	0.91(0.59,1.41)	0.6871	0.2
C-reactive protein (mg/L)	1.01(1.01,1.02)	0.0002	13.7	1.00(0.99,1.01)	0.7880	0.1
Hypertension	2.99(1.41,6.33)	0.0043	8.2	0.89(0.33,2.40)	0.8138	0.1

* Univariate analysis is based on the complete cases without missing value.

** Multivariate analysis is based on imputed values for missing data in Quadrant score, Pulmonary opacity score, WBC Count, Lymphocyte, Platelet, C-reactive protein, Fibrinogen, using multiple imputation method.

*** Factors are ranked according to Chi-square values to indicate their relative importance

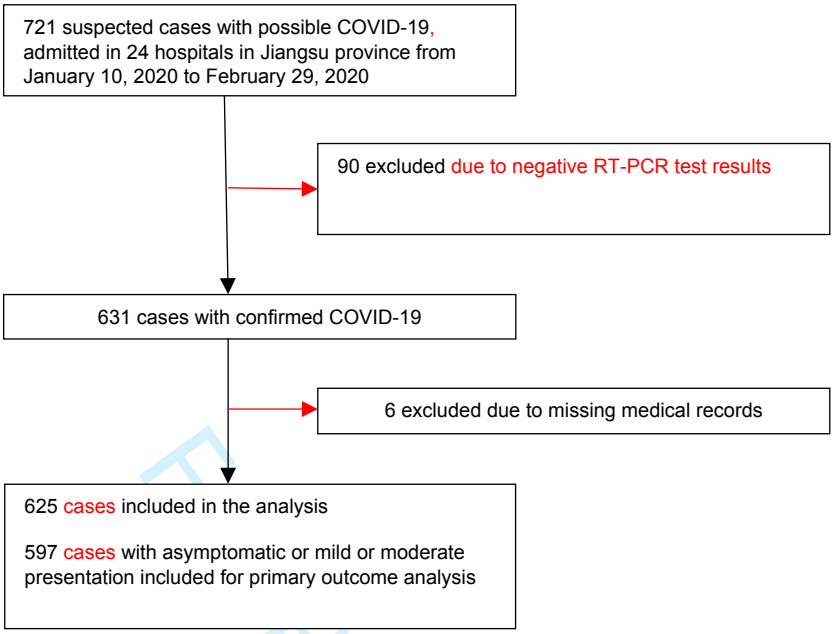

Figure 1: Study flow diagram

Table S1: Disease progression by day among patients with COVID-19

		Disease severity at Day 1			
Day	Statistics	Asymptomatic/Mild	Moderate	Severe/Critically ill	All
Day 2	n	109	488	28	625
	Asymptomatic or mild	101(92.7%)	0(0.0%)	0(0.0%)	101(16.2%)
	Moderate	7(6.4%)	480(98.4%)	0(0.0%)	487(77.9%)
	Severe or critically ill	1(0.9%)	8(1.6%)	28(100%)	37(5.9%)
Day 3	n	109	488	28	625
	Asymptomatic or mild	90(82.6%)	6(1.2%)	0(0.0%)	96(15.4%)
	Moderate	17(15.6%)	469(96.1%)	0(0.0%)	486(77.8%)
	Severe or critically ill	2(1.8%)	13(2.7%)	28(100%)	43(6.9%)
Day 4	n	109	488	28	625
	Asymptomatic or mild	83(76.1%)	3(0.6%)	0(0.0%)	86(13.8%)
	Moderate	24(22.0%)	465(95.3%)	0(0.0%)	489(78.2%)
	Severe or critically ill	2(1.8%)	20(4.1%)	28(100%)	50(8.0%)
Day 5	n	109	488	28	625
	Asymptomatic or mild	77(70.6%)	8(1.6%)	0(0.0%)	85(13.6%)
	Moderate	31(28.4%)	458(93.9%)	1(3.6%)	490(78.4%)
	Severe or critically ill	1(0.9%)	22(4.5%)	27(96.4%)	50(8.0%)
Day 6	n	105	481	28	614
	Asymptomatic or mild	57(54.3%)	15(3.1%)	0(0.0%)	72(11.7%)
	Moderate	48(45.7%)	443(92.1%)	4(14.3%)	495(80.6%)
	Severe or critically ill	0(0.0%)	23(4.8%)	24(85.7%)	47(7.7%)
Day 7	n	105	481	28	614
	Asymptomatic or mild	76(72.4%)	20(4.2%)	0(0.0%)	96(15.6%)
	Moderate	29(27.6%)	436(90.6%)	6(21.4%)	471(76.7%)
	Severe or critically ill	0(0.0%)	25(5.2%)	22(78.6%)	47(7.7%)
Day 14	n	65	328	24	417
	Asymptomatic or mild	35(53.8%)	50(15.2%)	1(4.2%)	86(20.6%)
	Moderate	30(46.2%)	260(79.3%)	10(41.7%)	300(71.9%)
	Severe or critically ill	0(0.0%)	18(5.5%)	13(54.2%)	31(7.4%)

Table S2: Clinical management and outcome of patients with COVID-19 during hospital stay

		Disease progression, n(%)			
Category	Clinical management/outcome	Yes (N=36)	No (N=561)	All (N=597)	P-value
Supportive treatments	Inotropic and vasoconstrictive agents	4(11.1%)	0(0.0%)	4(0.7%)	<.0001
	Nasal cannula	31(86.1%)	168(29.9%)	199(33.3%)	<.0001
	Mask	7(19.4%)	2(0.4%)	9(1.5%)	<.0001
	High-flow nasal cannula oxygen therapy	11(30.6%)	1(0.2%)	12(2.0%)	<.0001
	Non-invasive ventilation	16(44.4%)	0(0.0%)	16(2.7%)	<.0001
	Intermittent mandatory ventilation	3(8.3%)	0(0.0%)	3(0.5%)	0.0002
	Prone position	6(16.7%)	1(0.2%)	7(1.2%)	<.0001
Medical drugs	Chinese medicine	17(47.2%)	69(12.3%)	86(14.4%)	<.0001
	Immunoglobulin	27(75.0%)	106(18.9%)	133(22.3%)	<.0001
	Interferon	25(69.4%)	456(81.3%)	481(80.6%)	0.0857
	Antioxidants	15(41.7%)	117(20.9%)	132(22.1%)	0.0063
	Glucocorticoid	30(83.3%)	90(16.0%)	120(20.1%)	<.0001
	Thymosin	22(61.1%)	101(18.0%)	123(20.6%)	<.0001
	Neurotrophic drugs	13(36.1%)	81(14.4%)	94(15.7%)	0.0017
	Any antibiotics	33(91.7%)	277(49.4%)	310(51.9%)	<.0001
	Any antivirals	36(100%)	516(92.0%)	552(92.5%)	0.0995
Clinical outcome	Death	0(0.0%)	0(0.0%)	0(0.0%)	NC
	ICU	19(52.8%)	1(0.2%)	20(3.4%)	<.0001
	Shock	0(0.0%)	0(0.0%)	0(0.0%)	NC
	Respiratory failure	31(86.1%)	1(0.2%)	32(5.4%)	<.0001
	Renal failure	1(2.8%)	0(0.0%)	1(0.2%)	0.0603