



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

Journal:	<i>The International Journal of Tuberculosis and Lung Disease</i>
Manuscript ID	IJTLD-05-20-0386.R1
Manuscript Type:	Original Article
Date Submitted by the Author:	n/a
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Key Words:	epidemiology < General:, infection < Lung disease:, lung function < Lung disease:

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

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35 **Running head**

36 Disease progression of COVID-19

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38 Word count of the summary: 195, word count of the text: 2468, no. of references: 22, no. of  
39 tables and figures: 4.

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For Review Only

## 58 **Summary**

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

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

63 **DESIGN:** This is a retrospective, multi-center cohort study. From January 10 and February  
64 29, 2020, all cases diagnosed with COVID-19 at 24 hospitals in Jiangsu province, with  
65 complete medical records were involved. The primary outcome was the disease deterioration  
66 defined as the dramatic progression from asymptomatic or mild or moderate status on  
67 admission into severe or critically ill status during 14 day's follow-up.

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

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

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

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

## 102 **Methods**

### 103 *Study design and participants*

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

118 symptoms become better if they have symptoms, and RT-PCR (throat swab samples, at least  
119 1 day for sampling interval) showed negative for 2 consecutive times.

### 120 *Data collection and definition of variables*

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

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

### 148 *Statistical analysis*

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

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

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

#### 167 *Ethics approval*

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

#### 171 **Results**

172 From January 10, 2020 to February 29, 2020, 721 suspected cases with possible COVID-19  
173 were admitted in 24 hospitals in Jiangsu province, China, while 90 cases were excluded  
174 because of negative **RT-PCR result**. 631 cases were diagnosed with COVID-19 totally. This  
175 study included 625 cases who had complete medical records (Figure 1). The median age was  
176 46 years (IQR, 32-57; range, 0.75-96 years), and 329 (52.6%) were men. No deaths were  
177 reported during this study.

178 Table S1 in the Supplement provides **a table** showing the dynamic patterns of disease  
179 progression by follow-up day among patients with COVID-19. On admission (day 1), overall,  
180 109 (17.4%) patients were in asymptomatic or mild status, 488 (78.1%) in moderate status,  
181 and 28 (4.5%) severe or critically ill status. Overall, **changes** in disease severity from

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

184 Table 1 presents the disease progression in severity from admission to the worst severity  
185 during 14-day hospital stay among COVID-19 patients. Of the 625 patients, 83.7% (523)  
186 patients had a stable condition or became better during 14 days' hospitalization whereas  
187 16.3% (102) patients progressed to at least one degree in disease severity. Some patients had  
188 disease deterioration, i.e. dramatic progression from asymptomatic or mild or moderate status  
189 on admission, to severe or critically ill status, during 2 weeks of hospital stay. 36 out of 597  
190 (6%) patients had dramatic progression from day 2 to 14 after admission.

191 Compared to patients without dramatic progression (n = 561) during 14-day hospitalization,  
192 patients with dramatic progression (n = 36) were significantly older (mean [SD], 60.97  
193 [12.67] vs 42.71 [16.75];  $P < .0001$ ), were more likely to be imported cases who had a  
194 history of the pandemic center Wuhan contact (52.8% vs 34.6%;  $P = 0.0272$ ), to have prior  
195 histories of hypertension (27.8% vs 13.5%;  $P = 0.0184$ ), and diabetes (16.7% vs 5.3%;  $P =$   
196  $0.0057$ ), to have lower SpO<sub>2</sub> (mean [SD], 97.17 [1.81] vs 97.92 [1.15];  $P = 0.0003$ ), and  
197 higher CT quadrant score (median [IQR], 4.0 [0.0-4.0] vs 2.0 [0.0-4.0];  $P < .0001$ ) and  
198 pulmonary opacity volume percentage (median [IQR], 50.0 [0.0-80.0] vs 20.0 [0.0-80.0];  $P$   
199  $< .0001$ ) (Table 2). Patients with disease deterioration had also significantly lower  
200 lymphocyte count (10<sup>9</sup>/L) (median [IQR], 0.8 [0.2-1.5] vs 1.4 [0.3-3.6];  $P < .0001$ ) and  
201 platelet count (10<sup>9</sup>/L) (median [IQR], 155.5 [92.0-236.0] vs 188.5 [51.0-530.0];  $P = 0.0004$ )  
202 than those without. In addition, patients with disease deterioration had significantly higher  
203 level of C-reactive protein (mg/L) (median [IQR], 26.2 [0.5-250.4] vs 10.0 [0.5-208.2];  $P =$   
204  $0.0020$ ) and fibrinogen (g/L) (median [IQR], 4.2 [1.5-7.0] vs 3.4 [0.9-8.2];  $P = 0.0175$ ) than  
205 those without.

206 Eleven variables were selected into univariate and multivariate logistic regression analyses  
207 (Table 3). For multivariable logistic regression model, 4 variables measured at admission  
208 were identified to be independently related to the occurrence of disease: age (year) (odds ratio  
209 [OR], 1.08; 95% confidence interval [CI]: 1.04-1.12;  $P < 0.0001$ ), pulmonary opacity score  
210 (per 5%) (OR, 1.30, 95% CI: 1.10-1.52;  $P = 0.0016$ ), lymphocyte (10<sup>9</sup>/L) (OR, 0.28, 95% CI:  
211 0.09-0.91;  $P = 0.0357$ ), and imported cases (exposed to the pandemic center Wuhan) (OR,  
212 2.45, 95% CI: 1.03-5.80;  $P = 0.0421$ ).



213 Table S2 demonstrates that oxygen was delivered to patients with disease deterioration via  
214 nasal cannulae (31 [86.1%]), simple face masks (7 [19.4%]), high-flow nasal cannulae (11  
215 [30.6%]), or prone position (6 [16.7%]). Ventilatory support was used in approximately 50%  
216 of patients with clinical progression.

## 217 Discussion

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

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

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

245 phase characterized by fever and other systemic symptoms, followed by week 2 with  
246 symptoms relief.<sup>19</sup>

247 Our study reported that only 6% (36) patients experienced disease deterioration, i.e.  
248 progression from moderate or less status on admission, to severe or critically ill status within  
249 2 weeks from admission. This study showed features including symptoms and abnormal  
250 radiologic and laboratory presentation on admission may be early signs of deterioration of  
251 respiratory, immune, and coagulation system. In particular, age, pulmonary opacity score in  
252 CT, lymphocyte count, and pandemic center Wuhan exposure were independent predictors  
253 for disease progression. This is in line with a study that identified several risk factors for  
254 disease progression of COVID-19, including age, respiratory failure, and C-reactive protein.<sup>7</sup>  
255 The severity of opacity evaluated from initial CT of patients with COVID-19 was closely  
256 related to the progression of opacity presented in the subsequent CT, which are of value for  
257 monitoring disease progress.<sup>20</sup> Older age and coagulation dysfunction were associated with  
258 progression from ARDS to death in patients with COVID-19.<sup>2</sup> Old age and severe  
259 lymphopenia seem to be statistically significant in predicting clinical deterioration in patients  
260 with SARS.<sup>15,21</sup> Patients who have been to Wuhan may have been exposed to a large amount  
261 of virus, so the disease may be more likely to deteriorate.

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

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

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

## 279 **Conclusions**

280 In this multi-center cohort of 625 patients with COVID-19 in Jiangsu province, China, we  
281 found that 16.3% of patients experienced a deterioration in their clinical condition and that  
282 6% of patients with moderate or less status deteriorated to being severe or critically ill but  
283 ultimately survived. Age, pulmonary opacity score, lymphocyte count on admission, and  
284 pandemic center Wuhan exposure were identified as the independent risk factors of disease  
285 deterioration. Careful attention to these risk factors for deterioration may help guide clinical  
286 care.

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## 290 *Author contributions*

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

## 297 *Conflict of Interest*

298 The Authors declare that they have no conflict of interests.

## 299 *Funding*

300 This work was supported, in part, by the Ministry of Science and Technology of the People's  
301 Republic of China (2020YFC084370067).

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

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

Category	Characteristics	All (N=597)	Disease progression*		P- value**
			Yes (N=36)	No (N=561)	
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 <sub>2</sub> (%)	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 <sup>9</sup> /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 <sup>9</sup> /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

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

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

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

Variables	Univariate analysis*			Multivariate analysis**		
	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 <sup>9</sup> /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 <sub>2</sub> (per 5%)	0.14(0.04,0.41)	0.0004	12.4	0.31(0.07,1.33)	0.1147	2.5
Platelet (10 <sup>9</sup> /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

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

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\*\* 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.

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

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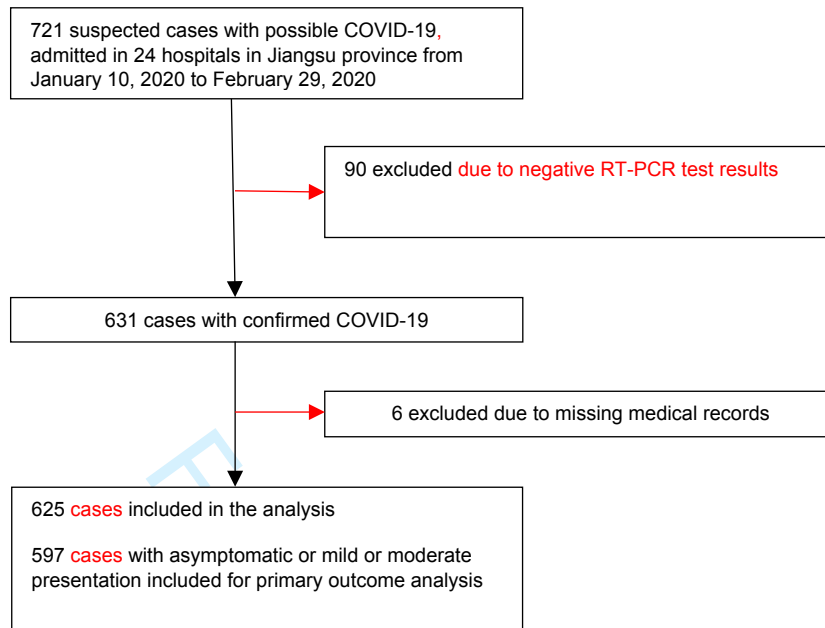


Figure 1: Study flow diagram

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

Category	Clinical management/outcome	Disease progression, n(%)			P-value
		Yes (N=36)	No (N=561)	All (N=597)	
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%)
	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