



## Early View

Research letter

### **Short-term Outcomes of Coronavirus Disease 2019 and Risk Factors for Progression**

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## **Short-term Outcomes of Coronavirus Disease 2019 and Risk Factors for Progression**

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### **Take home message**

With a median follow-up time of 24.0 (17.5-30.0) days, progression occurred in 19.6% moderate, 27.8% severe, 66.7% critical COVID-19. A neutrophil-to-lymphocyte ratio  $\geq 2.973$ , age  $\geq 50$  years, male gender, and comorbidity were associated with progression.

### **Summary conflict of interest statements for each author**

All authors declared no conflict of interest.

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*To the Editor:*

Coronavirus Disease 2019 (COVID-19) has now become a worldwide health concern. The severity of COVID-19 was classified as mild, moderate, severe and critical [1]. To date, there were a few studies focused on the clinical course and outcome of critical cases [2-4]. However, information regarding outcomes of mild to moderate cases are lacking, despite the fact that mild to moderate cases accounted for approximately 80% of laboratory-confirmed patients [1, 5]. This study aimed to investigate short-term outcomes of patients rated as different severities on admission, and to identify risk factors for progression, thereby, help the management of COVID-19 in clinical practice.

All consecutive patients with laboratory-confirmed COVID-19 admitted to the First People's Hospital of Jingzhou and Xiangyang Central Hospital, which were tertiary hospitals located in Jingzhou city and Xiangyang city, Hubei province, between January 16<sup>th</sup> and February 24<sup>th</sup>, 2020 were unselectively enrolled. Diagnosis of COVID-19 was made according to the Diagnosis and Treatment Scheme of COVID-19 (Interim Version 5) released by China's National Health Commission [6], and comply with World Health Organization interim guidance [7]. Mild cases were defined when patients only presented with mild symptoms and did not have a radiographic appearance of pneumonia. Moderate cases were defined when patients presented with fever and/or respiratory symptoms and have a radiographic appearance of pneumonia. Severe cases were defined when patients presented with one of the followings, 1) respiratory distress, respiratory rate  $\geq 30$  breaths/minute; 2) finger oxygen saturation  $\leq 93\%$  at resting state; 3) partial pressure of arterial oxygen ( $\text{PaO}_2$ )/fraction of inspired oxygen ( $\text{FiO}_2$ )  $\leq 300\text{mmHg}$ . Critical cases were defined when patients presented with one of the following, 1) respiratory failure occurs and requires mechanical ventilation; 2) shock occurs; 3) other organ failure occurs and should be admitted to the intensive care unit [6]. Progression would be determined once the severity got worse, the date was recorded to calculate the interval between admission date and progression date. Severe/critical disease condition on admission and unchanged severity at the endpoint assessment was not classified as progression. Clinical features, laboratory findings, treatments, as well as clinical outcomes (ie. Discharge, the severity of the disease, mortality, length of stay) of patients were recorded and monitored up to March 1<sup>st</sup>, 2020. This study was approved by the ethics commissions of both hospitals (The First People's Hospital of Jingzhou 42016803-T, Xiangyang Central Hospital 2020-001). Written informed consent was waived due to the emergency of the COVID-19 pandemic.

A total of 301 confirmed cases were enrolled, 150 (49.8%) were male, the median age was 51.0 (IQR 36.0-63.0) years. On admission, the median disease duration was 6.0 (4.0-9.0) days, and the proportion of mild, moderate, severe, critical cases was 8 (2.6%), 245 (81.4%), 36 (12.0%), 12 (4.0%), respectively. A standard treatment protocol was applied. As for mild/moderate patients, 214 (84.6%) were treated only with medical treatment as initial therapy (antiviral therapy combined with as needed antibiotics, expectorant, Chinese patent medicines, etc.), while 39 (15.4%) received both medical treatment and low-flow oxygen inhalation. All of the 48 severe/critical patients received both medical treatment and oxygen therapy, including 22 (45.8%) low-flow oxygen inhalation, 15 (31.3%) high-flow inhalation, 8 (16.7%) non-invasive ventilation, 3 (6.2%) invasive ventilation.

By the final day of follow-up, the median observation time was 24.0 (17.5-30.0) days, and the median disease duration of the included patients was 30.0 (23.0-36.0) days. Of the 301 included patients, 156 (51.8%) patients were treated only with medical treatment, and low-flow oxygen inhalation, high-flow oxygen inhalation, non-invasive ventilation, invasive ventilation, ECMO were given to 104 (34.6%), 42 (14.0%), 17 (5.6%), 4 (1.3%), 1 (0.3%) patients, respectively (some patients received more than one type of oxygen therapy). None of the mild cases had experienced progression. 48 (19.6%) out of the 245 moderate patients experienced progression during hospitalization, among them, 14 (5.7%) turned moderate, 6 (2.5%) were discharged, while 21 (8.6%) were severe, 2 (0.8%) were critical, 5 (2.0%) died at the endpoint. 10 (27.8%) out of the 36 severe cases had experienced progression, among them, 1 (2.8%) turned moderate, 1 (2.8%) were discharged while 2 (5.6%) were severe, 2 (5.6%) were critical, 4 (11.1%) died. As for the 12 critical cases, 1 (8.3%) turned moderate and 8 (66.7%) died. By the final day of follow-up, overall, 66 (21.9%) of patients had experienced progression. The proportion of discharged, mild, moderate, severe, critical and dead patients was 156 (51.8%), 5 (1.7%), 84 (27.9%), 34 (11.3%), 5 (1.7%) and 17 (5.6%), respectively. The median time from admission to disease progression was 6.0 (5.0-9.0) days, to discharge was 22.0 (16.0-25.0) days.

Assessing by ROC curve, the optimal cut-off value of age for differentiating progression and no progression patients was 50 years (area under the curve: 0.7366, sensitivity: 81.8%, specificity: 58.3%), the optimal value of the neutrophil-to-lymphocyte ratio was 2.973 (area under the curve: 0.7338, sensitivity: 75.8%, specificity: 66.8%). Variables including baseline characteristics, laboratory findings, and chest CT scan findings were analysed by univariate Cox regression analyses, and sex, age, comorbidities, the neutrophil-to-lymphocyte ratio, eosinophil count, C-reactive protein level were identified as significant variables, which were then included into multivariate Cox regression analyses. A neutrophil-to-lymphocyte ratio  $\geq 2.973$  (hazard ratio [95% CI]: 2.641 [1.421-4.908],  $p = 0.002$ ), age  $\geq 50$  years (2.504 [1.202-5.215],  $p = 0.014$ ), male gender (2.004 [1.101-3.647],  $p = 0.023$ ), and with comorbidity (1.969 [1.085-3.571],  $p = 0.026$ ) were identified as risk factors for progression by multivariate Cox regression analyses. Kaplan-Meier curve was used to estimate time-dependent hazards categorized by the above risk factors (Fig 1).

All patients who experienced progression during hospitalization had at least one of the risk factors. 54 (81.8%) of them were aged  $\geq 50$  years, 50 (75.8%) had a neutrophil-to-lymphocyte ratio  $\geq 2.973$ , 46 (69.7%) had comorbidity, 44 (66.7%) were male.

As far as we know, this is the first study that focuses on clinical outcomes of COVID-19 patients rated as different severities on admission. Considering a few of mild to moderate cases developed critically

ill condition, we chose the progression of COVID-19 as the primary outcome rather than a composite endpoint (one or more of death, admission to the ICU, the use of mechanical ventilation). We believe findings in this study would be more helpful to prevent progression in an earlier stage for the general COVID-19 patients, and could be a supplement to a recent study that reported patients with any comorbidity were more likely to achieve the composite endpoint than those without [8].

Our study has some limitations. First, hospitals would give a priority to more severe patients, which might lead to a lower proportion of mild cases in this study. Second, although we had a median follow-up time of 24.0 (17.5-30.0) days, at the endpoint, nearly half of the patients were still hospitalized. Progression could occur in a part of patients who did not get worse during our observation period, thus, the actual progression rate might be higher than the results shown in the present study.

In conclusion, with a median follow-up time of 24.0 (17.5-30.0) days, we found progression occurred in 19.6% of moderate cases, 27.8% of severe cases and 66.7% of critical cases during hospitalization. A neutrophil-to-lymphocyte ratio  $\geq 2.973$ , age  $\geq 50$  years, male gender, and comorbidity were associated with progression.

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## FIGURE LEGENDS

Fig 1. Time from admission to progression categorized by risk factors. a) age < 50 years vs age  $\geq$  50 years. b) neutrophil-to-lymphocyte ratio < 2.973 vs neutrophil-to-lymphocyte ratio  $\geq$  2.973. c) with comorbidity vs without comorbidity. d) female vs male.

