



## Early View

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# Association Between Ages and Clinical Characteristics and Outcomes of Coronavirus Disease 2019

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## Summary

Global outbreak of novel coronavirus 2019 (COVID-19) has been a matter of international concern as the disease is spreading fast. Older COVID-19 patients are at an increased risk of death, while few studies have compared the differences of clinical features and outcomes of COVID-19 patients at

different age. This study showed that clinical features and prognosis of the disease vary among patients of different ages and a thorough assessment of age may help clinicians worldwide to establish risk stratification for all COVID-19 patients. Patients over 60 years showed heavier clinical manifestations, greater severity and longer disease courses compared with those under 60 years. Closer monitoring and more medical interventions may be needed for the elder.

The rapid outbreak of novel coronavirus 2019 (COVID-19) has been a matter of international concern as the disease is spreading fast<sup>[1, 2]</sup>. Considering that the contagious disease has led to an enormous impact globally, there is an urgent need to identify the risk populations with poor prognosis. Aging is associated with certain changes in pulmonary physiology, pathology and function, during the period of lung infection. Therefore, the age-related differences in responsiveness and tolerance become obvious and lead to the worse clinical outcome in elderly individuals<sup>[3]</sup>. Previous studies mentioned that older COVID-19 patients are at an increased risk of death<sup>[4-7]</sup>. However, the ages related clinical characteristics, diseases courses and outcomes other than death in COVID-19 patients remain unclear.

Totally, 221 COVID-19 patients who were diagnosed by the fever clinics of designated hospitals were included in this study. They were administratively admitted to Shanghai Public Health Clinical Center to receive medical care. The diagnosis was based on the positive response to the viral nucleic acid detection according to the updated versions of the guideline for the diagnosis and treatment of 2019 novel coronavirus-infected pneumonia issued by the National Health Commission of China<sup>[8]</sup>. Data on demographics, symptoms, disease severity and course, radiologic and laboratory examination were analyzed in our study. A unified observation endpoint date was set (March 7, 2020) in our study, primary outcome of the disease course and second outcome of respiratory failure rate for all COVID-19 patients in both groups were compared.

All 221 COVID-19 patients were divided into two groups when taking 60 years old as the threshold. The age distribution for all patients was shown in Figure 1a. 136 cases (61.5%) were under 60 years old (<60), and other cases were over 60 years old ( $\geq 60$ ). In total, 176 patients (79.6%) had fever, other common symptoms included cough (48.0%), sputum (25.8%), sore throat (8.6%), and diarrhea (5.4%), among which only sore throat showed a significant difference between two groups (11.8% vs 3.5%,  $p=0.034$ ). The significant negative correlations between ages of patients and lymphocyte counts ( $r=-0.432$ ,  $p<0.001$ ) as well as albumin levels ( $r=-0.569$ ,  $p<0.001$ ) were observed in our study (Figure 1b, 1c). Compared with the young, patients over 60 presented with higher levels of blood urea nitrogen (5.83 vs 4.42,  $p<0.001$ ), LDH (272.8 vs 249.0,  $p=0.004$ ) and inflammatory indicators (Figure 1d, all  $p<0.01$ ), more lobes involved (4.15 vs 3.34;  $p<0.001$ ) in bilateral lesions (89.4% vs 74.3%,  $p=0.006$ ) (Figure 1e) and higher proportion of bacteria co-infection (12.9% vs 4.4%,  $p=0.021$ ). The severity of COVID-19 was milder in those under 60, showing lower proportion of severe and critical patients (Figure 1f). In turn, the utilization of antibiotic therapy, intravenous corticosteroids, and assisted ventilation were more common in those over 60 (Figure 1g). Longer disease courses and higher proportion of cases with respiratory failure in patients over 60 were observed (Figure 1h). The median time of disease courses was significantly longer in patients over 60 years (24.0 vs 21.5 days,  $p=0.026$ ) (Figure 1i). Interestingly, this difference was markedly significant in male patients (25.0 vs 21.0 days,  $p=0.036$ ) but not in female patients (Figure 1i). Big difference of courses was

observed in cases with respiratory failure in two ages groups, although it showed no statistical significance (38.0 vs 30.0 days,  $p=0.100$ ) (Figure 1i).

This is the first study to systematically evaluate the impact of age on the clinical characteristics and important outcomes for COVID-19 patients, thus helping clinicians to establish risk stratification of COVID-19 patients as early as possible. Sporadic studies mentioned that the elderly people may tend to die after infection<sup>[5, 7, 9]</sup>, calling on the public to pay more attention to protecting the elder from the virus. In this study, we demonstrated that the clinical characteristics and outcomes of 221 COVID-19 patients were closely related to the different ages. This study provided clear evidence of relationship between disease severity and the age, which other studies did not refer to. Comprehensive analysis of these indicators provided physicians worldwide with important information for the disease perception, the condition assessment and the effective treatments for COVID-19.

The proportions of patients with the usage of antibiotics were higher in patients  $\geq 60$  years than those in patients  $< 60$  years, possibly due to the higher proportion of patients with bacteria co-infection in this group. Besides, older patients showed more serious illness, leading to higher frequency of adjuvant therapies including corticosteroids and assisted ventilation in this group of patients. Contrastive analysis with recent reports<sup>[10, 11]</sup>, older patients presented significantly lower level of lymphocyte than young patients. Lymphocytes are generally elevated in response to common viral infections, while abnormally decreased in SARS and COVID-19<sup>[12-14]</sup>. Although the underlying mechanism is still unclear, the low level of lymphocyte could be a key indicator of disease severity in COVID-19. Furthermore, other serological indexes, such as albumin level, blood urea nitrogen, lactate dehydrogenase and inflammatory indicators also showed a progressive trend with age. The phenomenon is obvious, however, we cannot identify whether these indicators changed result in or result from the differences of the diseases severity with age.

Although most patients had favorable prognosis in this study, some patients required longer periods of treatment, which might turn worse under the high risk of hospital-acquired or iatrogenic infections. Age was one of the risk factors in disease severity and mortality of viral infections studies<sup>[5, 9]</sup>, while the data about age in those studies are rough. Our study found that COVID-19 patients over 60 years had a higher rate of respiratory failure and needed prolonged treatment than those at age below 60 years, demonstrating that elderly COVID-19 patients were much more severe and showed poorer response to treatments than the younger. The cure rate of patients over 60 years old (89.4%) was relatively lower than that of patients under 60 years old (95.6%), especially in male and those with respiratory failure. Previous study had indicated that there might be a sex predisposition to COVID-19, with men more prone to be affected, but no evidence of an association between the severity of COVID-19 and the male sex<sup>[15]</sup>. More attention needs to be paid on these old patients with respiratory failure, and aggressive early intervention should be made to improve their prognosis. With more cases being examined from different ethnic and genetic backgrounds, the findings related to the age in this study may be approved by physicians worldwide.

In conclusion, the clinical features and prognosis of the disease vary among patients of different ages and a thorough assessment of age may help clinicians worldwide to establish risk stratification for all COVID-19 patients. Patients over 60 years showed heavier clinical manifestations, greater severity and longer disease courses compared with those under 60 years. Closer monitoring and more medical interventions may be needed for the elder.

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**Figure 1. Comparison of clinical features and outcomes of COVID-19 patients between two age groups.**

Age distribution for all 221 COVID-19 patients in Shanghai is shown in panel a); Correlations between the age of patients and indicators including Lymphocyte ( $r=-0.432$ ,  $p<0.001$ ) and Albumin ( $r=-0.569$ ,  $p<0.001$ ) are shown in panel b) and c); Significant laboratorial and radiologic features including CRP, ESR and affected lobes of patients among different age groups are shown in panel d) and e); The difference of disease severity, treatment, disease course and rate of respiratory failure in two groups are shown in panel f), g) and h). The cure rate of COVID-19 patients in different subgroups are shown in panel i). \*:  $p<0.05$ ; \*\*:  $p<0.01$ ; \*\*\*:  $p<0.001$ .

