



Commentary

COVID-19: Risk factors for critical illness

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Critical illness only happens in 5% [1] overall and in 22% [2] hospitalized COVID-19 patients, but represents the major medical resource consumer for this disease. It includes patients with respiratory failure that requires mechanical ventilation, or the ones with shock and other organ failure that require ICU admission [3], and also those patients died or were discharged to hospice [4]. It is more frequently associated with complications such as acute respiratory distress syndrome, coagulopathy, acute myocardial injury and acute kidney injury [5]. The death rate of critical ill COVID-19 patients ranged from 26% [6], 39% [2], 60.4% [4] to 85.45% [3] in previous reports, and is much higher than that of moderate and severe patients. The reported risk factors associated with death rate of critical ill COVID-19 patients include male, older age (>65 years), higher Sequential Organ Failure Assessment score (SOFA), high blood d-dimer (>1000 ng/mL), cardiovascular comorbidities, higher concentrations of Interleukin-6 (IL-6) [2] and more affected pulmonary lobe numbers [7]. Therefore, preventing the progression to critical illness COVID-19 is critical to decreasing the death rate of the disease. However, the risk factors for the critical illness of COVID-19 are still not well delineated yet.

The study by Liu et al. provided data to explore the risk factors for developing into critical ill COVID-19 in 2044 hospitalized patients in Wuhan, China [3]. Among them, 268 were critical ill patients, with a death rate of 85.45%, which is the highest reported death rate so far. However, this is rational considering that all the critical cases in this study had definite final outcomes. Age > 60 years and with tumors were risk factors of developing into critical illness in both male and female COVID-19 patients. Hypertension and coronary heart disease (CHD) were risk factors only in male, and chronic obstructive pulmonary disease (COPD) and chronic kidney disease were risk factors in female. This is the first study showing the gender differences of risk factors for developing critical ill COVID-19. Although COPD was identified as a risk factor for the critical illness of COVID-19 in female, it

may not be of great importance due to the low prevalence of COPD in female in China.

Except age, other risk factors identified in Liu's report are different from a recent study in critical ill COVID-19 patients in New York city [4]. In the latter study, among 647 ICU admitted patients, the risk factors for critical illness include male, age (>65 years), heart failure, BMI > 40, diabetes, admission oxygen saturation < 88%, troponin level > 1 ng/ml, C-reactive protein (CRP) > 200 mg/L and d-dimer > 2500 ng/ml. The distinct risk factors identified in the two cohort studies may due to the varied criteria of critical illness, the selection of included laboratory parameters and also the ethnicity difference. All of the above-mentioned risk factors were referred in a meta-analysis which aims to identify risk factors associated with critical illness/death rate [8].

It is noticeable that in Liu's study, the median interval from symptom onset to hospital visit and to hospital admission in critical ill patients were 5.0 (IQR: 2.0–9.0) days and 11 (IQR: 7.0–16.0) days, respectively. Further studies are needed to investigate whether shorten the time interval from illness onset to hospital visit and admission will reduce the risk of critical ill COVID-19 development when sufficient medical resources are available. Additionally, Liu's report also showed significant difference in the treatment strategies between critical and non-critical patients. However, no treatment was identified as a protecting factor against the development of critical illness. The impacts of different treatments on the development and maybe the prognosis of critical illness need to be investigated more deeply.

A calculation tool has been established to predict the development of critical ill COVID-19 based on clinical, radiological and laboratory parameters on admission [9]. Since the risk factors such as gender, age, BMI and comorbidities are determined on admission, follow-up data of the dynamic changes of these laboratory parameters will be of great importance to detect the progression to critical illness in relative early phase. Liu et al. also reported the dynamic changes of laboratory parameters of critical ill patients. The patterns of longitudinal changes of IL-6, high sensitivity CRP, leucocyte count, lymphocyte count, d-dimer and high sensitivity cardiac troponin in critical ill patients are distinct from those of moderate and severe patients. Therefore, a predicting model including baseline demographic and clinical parameters as well as dynamic changes of laboratory findings is necessary to the early detection of risk factors of progression to critical ill COVID-19.

It is also very important to understand the impacts of COVID-19 on underlying comorbidities such as chronic cardiopulmonary

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diseases, renal disease, tumors and liver disease in critical ill COVID-19 patients. The high incidence of coagulopathy in critical ill patients [10] also raises the question- whether ultrasonography is useful for early detection and whether anticoagulants is effective in prevention and treatment of thrombosis and emboli. Finally, how to prioritize and optimize the treatments of these critical ill cases in order to reduce the mortality of COVID-19 patients needs to be further investigated.

Declaration of Competing Interest

The author declares no conflicts of interest.

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