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## Letter to the Editor

### Critical patients with coronavirus disease 2019: Risk factors and outcome nomogram



Dear Editor,

We read Yang's paper with great interest. It illustrated clinical characteristics and imaging manifestations of 149 hospitalized patients with coronavirus disease 2019 (COVID-19) in Wenzhou. It showed most patients presented with a mild infection and some patients even presented with a normal chest finding despite testing positive for COVID-19.<sup>1</sup>

However, the cases in Wuhan were more severe compared to Wenzhou. Fatalities associated with COVID-19 were of great public health concern. Most of all, the relationship between possible risk factors during the early period and outcome in critical cases with COVID-19 are not fully interpreted.

In our study, 82 patients with critical type were selected randomly from 204 confirmed COVID-19 cases (50 death cases, 32 recovery cases and rest cases were not match or still hospitalized) occurring in Renmin hospital of Wuhan University, during Feb 1, 2020 and Feb 24, 2020.

In univariate analysis, the following factors had significant differences between death group and recovery group: increased white blood cell count ( $p=0.001$ ), increased initial neutrophil count ( $p < 0.001$ ), initial lymphocyte count less than  $0.6 \times 10^9/L$  ( $P=0.007$ ), C-

reactive protein more than 100 mg/L ( $p < 0.001$ ), D-dimer more than 20 mg/L ( $p=0.037$ ), increased hypersensitive troponin I ( $p=0.003$ ), increased blood urea nitrogen ( $p=0.003$ ), and increased lactate dehydrogenase ( $p < 0.001$ ).

However, multivariate analysis confirmed in early stage of disease, only four independent predictors: age  $> 70$  years (HR 1.71, 95% CI 0.94–3.12), initial neutrophil count (HR 2.04, 95% CI 1.08–3.85), blood urea nitrogen (HR 1.87, 95% CI 1.03–3.41) and LDH (HR 4.16, 95% CI 1.85–9.33) were related to outcome of COVID-19. The survival rate of critical COVID-19 at early stage of disease could be calculated by nomogram which derived based on the multivariate Cox regression coefficients (Fig 1).

Comorbidities are associated with old age generally. Chen suggest that 2019-nCoV is more likely to infect older adult males with chronic comorbidities as a result of the weaker immune functions of these patients.<sup>2</sup> Although chronic diseases such as hypertension, diabetes mellitus, renal diseases, heart diseases, COPD, mental diseases and malignant tumors were not different between died and recovered groups with critical COVID-19. However, as one of independent risk factors, old age ( $> 70$  years) related chronic comorbidities still plays an important role in outcome of critical cases.

One of the independent risk factors related to morbidity of COVID-19 was neutrophil count. The increased neutrophil count may indicate progression of disease initially.<sup>3</sup> While it may relate to secondary infection especially at the end stage of disease.

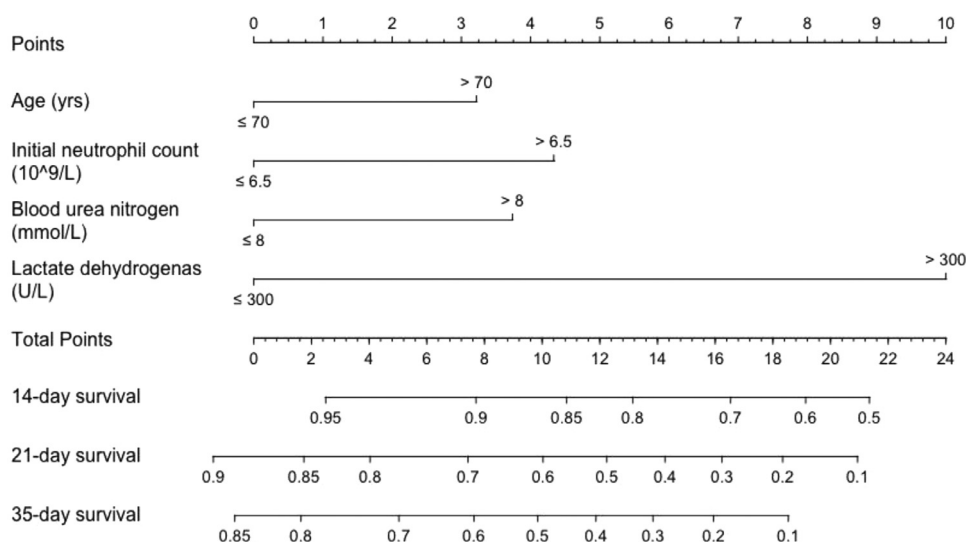


Fig. 1. Nomogram for predicting survival of critical patients with COVID-19.

The nomogram derived based on the multivariate Cox regression coefficients are shown in Figure 1. To use the nomogram, locate the first variable. Draw a line straight upwards to the Points axis to determine the number of points received for the variable. Repeat this process for the other three variables and sum up the points achieved for each variable. Sum of these numbers is located on the Total Points axis, and a line is drawn downwards to the survival axes to determine the likelihood of 14-, 21-, 35-day survival. Calculation of survival can be automated through computerized programming.

Fungal infection was rare than bacterial infection in this study, but it still needs to be concerned.

The other two independent high-risk factors, increased blood urine nitrogen and lactate dehydrogenase were related to renal failure, heart failure or multi organ failure (MOF) which may lead to fatality of COVID-19. It was reported that cardiovascular complications were common in patients with SARS.<sup>4</sup> Recent study demonstrated ACE-2 receptor of SARS-CoV was highly expressed in renal tubules.<sup>5</sup> The kidney injury may be caused by coronavirus which entering kidney cells through an ACE2-dependent pathway.<sup>6</sup> Moreover, MOF is regarded as a predictive factor related to most end stage of diseases.

As a gauge of inflammation, C-reactive protein showed a significant difference between death and recovery groups, so as D-Dimer. Nonetheless, those were excluded from final multivariate risk model. It needs more clinical data to interpret.

The severity of our patients is more than that of Wenzhou may due to lack of medical resources during the outbreak. But another concern maybe virulence evolution.<sup>7</sup>

In conclusion, during early period of COVID-19, old age (>70 years), increased neutrophil count and multi organ failure were high-risk factors related to outcome of critical patients. Early identification of critical type is more crucial.

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