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Letter to the Editor: Discussion of the Article "Prognostic Accuracy of the SIRS, qSOFA, and NEWS for Early Detection of Clinical Deterioration in SARS-CoV-2 Infected Patients"

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We read with interest the article by Dr. Jang and colleagues[1] on the ability of disease severity scores to predict more rapid clinical deterioration in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infected patients. Of the three scoring systems analyzed, the National Early Warning Score (NEWS) measured at the time of hospital admission was best able to predict critical outcome, defined in this study as admission to the intensive care unit (ICU) or death, with critically ill patients defined similarly. We believe that these definitions should be modified.

These definitions of critical outcome and critically ill patients would result in a target group with heterogeneous characteristics, including not only patients with severe coronavirus disease 2019 (COVID-19) but patients with other conditions. The outbreak of COVID-19 may result in a selection bias, as some critically ill patients may not be admitted to the ICU because of a shortage of ICU beds. Actually, some critical patients using high flow oxygen were in the general ward, and some elderly patients who died from conditions other than COVID-19 were not actively treated and had do-not-resuscitate (DNR) orders.

In addition, these definitions of critical outcomes and critically ill patients do not include timing. Admission to the ICU care and death was assumed to occur within 28 days after initial hospitalization because 28-day mortality rates were measured. In another study evaluating the National Early Warning Score 2 (NEWS2) in 3,869 patients, the primary outcome was defined as patient status 14 days after symptom onset, with patients categorized as those who were transferred to the ICU or died (WHO-COVID-19 Outcomes Scale scores of 6–8) and those who were not transferred and did not die (scores of 3–5) within a specific time after symptom onset.[2]

Third, the definitions of critical outcomes and critically ill patients cited by Jang et al. were too broad. We found it unusual that the definition of critical outcome did not include acute respiratory distress syndrome or respiratory failure. A study showing an association between hypoxemia and mortality in 140 COVID-19 patients defined disease severity according to

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proposed Chinese guidelines for COVID-19 associated pneumonia.[3] In that study, critical outcome was defined as COVID-19 associated pneumonia along with a requirement for intubation due to respiratory failure, shock, or multiple organ dysfunction requiring ICU admission.

Therefore, in this paper, we believe that critical outcomes and critical patients should be defined more specifically and accurately, and in reference to time of evaluation.

The study by Jang et al. was important, showing that NEWS can predict the progression of COVID-19 patients to ICU care or death. Several components of NEWS, including hypoxemia, oxygen saturation, and respiratory rate, are therefore important factors predicting whether or not COVID-19 patients will progress to critical condition. Our findings, in a tertiary hospital located in the same area as the hospital described in the study by Jang et al., were similar. Of 131 patients aged ≥ 18 years who were hospitalized for COVID-19, 13 patients (9.9%), all of whom were hospitalized for hypoxemia, were admitted to the ICU. Five patients (3.8%) died within 28 days, with all having DNR orders. Of these five patients, only one was admitted to the ICU, whereas the other four died while on high flow oxygen therapy in the general ward because there was no room in the ICU. As the outbreak progressed rapidly, admission to the ICU was very difficult. Of the 13 patients admitted to the ICU, three (23.1%) showed slow improvements in hypoxemia while on high flow oxygen therapy, but did not require a ventilator. In addition, of the 118 patients in the general ward, 12 (10.2%) used more than 40% of fraction of inspired oxygen (FiO_2) in the ward. NEWS scores at the time of hospitalization differed significantly in non-critical and critical patients (2.6 ± 2.6 vs. 8.2 ± 3.3, $P < 0.001$). Although there was no between-group difference in blood pressure, respiratory rate, and body temperature, oxygen saturation ($P < 0.001$) and supplemental oxygen ($P = 0.001$) differed significantly. That is, blood pressure, body temperature, and respiratory rate at the time of hospitalization did not significantly differ between critical and non-critical COVID-19 patients.

We fully agree with Jang et al. that severe COVID-19 infection is accompanied frequently by silent hypoxemia. Therefore, oxygen saturation may be reduced despite comfortable breathing, making it necessary to continuously monitor oxygen saturation by pulse oximetry. Our patients who required ventilator therapy were characterized by 'rapid desaturation,' with a median time from desaturation to application of maximum FiO_2 being only 7.5 hours (interquartile range, 3.5–15.3 hours).

As mentioned in the limitations of the paper by Jang et al., the inability to perform arterial blood gas analysis in many patients with COVID-19 prevented measurements of their arterial oxygen pressure (PaO_2). It was therefore difficult to analyze the ability of SOFA and PaO_2/FiO_2 (PF ratio) to predict the likelihood of critical illness. Because of this, we suggest using an alternative to oxygen saturation/FiO_2 (SF ratio).[4]

In conclusion, exacerbation of hypoxia and reduction in saturation, as well as the NEWS scale, are important predictors of outcome in patients with COVID-19.

REFERENCES

1. Jang JG, Hur J, Hong KS, Lee W, Ahn JH. Prognostic accuracy of the SIRS, qSOFA, and NEWS for early detection of clinical deterioration in SARS-CoV-2 infected patients. *J Korean Med Sci* 2020;35(25):e234. PUBMED | CROSSREF

2. Carr E, Bendayan R, Bean D, Stammers M, Wang W, Zhang H, et al. Evaluation and improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study. https://www.medrxiv.org/content/10.1101/2020.04.24.20078006v3. Updated 2020. Accessed July 8, 2020.
3. Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association between hypoxemia and mortality in patients With COVID-19. *Mayo Clin Proc* 2020;95(6):1138-47.
PUBMED | CROSSREF
4. Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB, et al. Comparison of the SpO2/FIO2 ratio and the PaO2/FIO2 ratio in patients with acute lung injury or ARDS. *Chest* 2007;132(2):410-7.
PUBMED | CROSSREF

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The Author's Response: Prognostic Accuracy of the SIRS, qSOFA, and NEWS for Early Detection of Clinical Deterioration in SARS-CoV-2 Infected Patients

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We thank the authors of the comment for their interest in our article entitled "Prognostic Accuracy of the SIRS, qSOFA, and NEWS for Early Detection of Clinical Deterioration in SARS-CoV-2 Infected Patients" published in the *Journal of Korean Medical Science*.[1] The authors concerned that our definition of critical outcomes might create heterogeneity. In our study of 110 patients hospitalized with coronavirus disease 2019 (COVID-19), 13 (11.8%) required intensive care unit (ICU) care. Six (5.5%) died within 28 days (two had do-not-resuscitate orders in place). One of these patients refused ICU care. Five of the 18 acute respiratory distress syndrome (ARDS) patients were not considered to be critical because they did not die or receive ICU care. I fully agree that hypoxemia and ARDS affect the prognosis of COVID-19 patients. However, not all ARDS patients die or require ICU care. Patients with mild ARDS do not necessarily need intensive care; the fatality rate is not high. In our center, if ICU care is required but we lack beds, we transfer patients to a university hospital in another area. Such patients were excluded from analysis. Therefore, the selection bias that concerns the authors is unlikely to be significant.

The authors also concerned that our definition of critical outcomes was too broad and "unusual". However, our definition is not unusual. Carr et al.[2] used the National Early Warning Score 2 (NEWS2) instrument to evaluate 3,869 patients in terms of primary

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outcomes (severe disease, thus a need for ICU care or death), as did we. In the Ana-COVID study evaluating whether Anakinra was a useful treatment for patients with severe COVID-19 disease, a "severe" outcome was defined as either a need for ICU care or death, as in our study.[3] A nationwide Chinese analysis defined any of ICU admission, a need for ventilation, or death, as a serious adverse outcome.[4] We evaluated the predictive utilities of existing scoring systems employing indicators of clinical deterioration including ARDS, septic shock, a need for ICU care, 28-day mortality, and critical outcomes (a need for ICU care or death). In short, we defined a "critical outcome" appropriately.

In terms of the timing of clinical assessment, other study did not address this issue.[5] To be clear, all clinical outcomes were assessed within 28 days of hospitalization (as the authors correctly assumed).

Few reports have explored whether existing scoring systems usefully predict the clinical outcomes of COVID-19-infected patients. Gidari et al.[6] found that the NEWS2 score at the time of admission well predicted the need for later ICU admission; the thresholds were 5 and 7. Hu et al.[5] emphasized the need for rapid scoring of COVID-19 patients. The Rapid Emergency Medicine Score accurately predicted in-hospital mortality.[5] We found that the NEWS score at admission was at least as accurate as the SIRS and qSOFA scores in terms of predicting ARDS, septic shock, a need for ICU care, 28-day mortality, and critical outcomes. Therefore, even if critical outcomes (including ARDS and septic shock) are redefined, the predictive superiority of the NEWS instrument will not be affected. Future, large cohort studies are required to compare the utilities of the various scoring systems that evaluate different clinical outcomes.

We thank the editor-in-chief of the *Journal of Korean Medical Science* and all readers interested in our research. We thank the authors of the comment for sharing their data; we admire their efforts to treat COVID-19 infections effectively.

REFERENCES

1. Jang JG, Hur J, Hong KS, Lee W, Ahn JH. Prognostic accuracy of the SIRS, qSOFA, and NEWS for early detection of clinical deterioration in SARS-CoV-2-infected patients. *J Korean Med Sci* 2020;35(25):e234. PUBMED | CROSSREF
2. Carr E, Bendayan R, Bean D, Stammers M, Wang W, Zhang H, et al. Evaluation and improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study. https://www.medrxiv.org/content/10.1101/2020.04.24.20078006v3. Updated 2020. Accessed July 8, 2020.
3. Huet T, Beaussier H, Voisin O, Jouveshomme S, Dauriat G, Lazareth I, et al. Anakinra for severe forms of COVID-19: a cohort study. *Lancet Rheumatol* 2020;2(7):e393-400. CROSSREF
4. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J* 2020;55(5):2000547. PUBMED | CROSSREF
5. Hu H, Yao N, Qiu Y. Comparing rapid scoring systems in mortality prediction of critically ill patients with novel coronavirus disease. *Acad Emerg Med* 2020;27(6):461-8. PUBMED | CROSSREF
6. Gidari A, De Socio GV, Sabbatini S, Francisci D. Predictive value of National Early Warning Score 2 (NEWS2) for intensive care unit admission in patients with SARS-CoV-2 infection. *Infect Dis (Lond)* 2020:1-7. PUBMED | CROSSREF