



# Predictors of Worsening Oxygenation in COVID-19

Jee Youn Oh, M.D., Ph.D. 

Division of Pulmonary Allergy and Critical Care Medicine, Department of Internal Medicine, Korea University Guro Hospital, Seoul, Republic of Korea

The spread of coronavirus disease 2019 (COVID-19) has resulted in a pandemic, leading to a sudden and substantial increase in the use of medical resources worldwide<sup>1</sup>. Although the key characteristic of COVID-19 is that most patients have a mild clinical course, some patients demonstrate rapid deterioration to respiratory failure<sup>2</sup>. Thus, it is important to triage and stratify the risk of COVID-19 patients in order to optimize the distribution of medical resources and prevent progression<sup>3</sup>. Worsening oxygenation is the key finding that forecasts severe cases<sup>4</sup>, but investigating biomarkers for worsening oxygenation is still an unmet medical need in COVID-19 patients.

Hahm et al.<sup>5</sup> retrospectively evaluated the factors associated with worsening oxygenation in patients with non-severe COVID-19 pneumonia. Quantitative analysis of computed tomography (CT) using artificial intelligence (AI) tools as well as laboratory findings such as C-reactive protein (CRP), ferritin, lactic dehydrogenase (LDH), and lower lymphocyte counts were predictors of worsening oxygenation. Although this was a retrospective, single-center study involving a small number of patients with non-severe pneumonia, it synthetically analyzed the factors known to be associated with deterioration including comorbidities, pro-inflammatory cytokines, and CT findings using AI tools, and provided an automatic and objective estimation of the disease burden.

Previous studies have reported that age and underlying

diseases may be risk factors for COVID-19 patients requiring oxygenation, which is a well-known risk factor for other pneumonia<sup>6</sup>. Particularly for COVID-19, some patients progress to hypoxemia rapidly at approximately 1–2 weeks after onset, likely not due to the cytopathic activity of the virus, but due to the cytokine storm, as evidenced by increased proinflammatory cytokines<sup>7</sup>. Thus, inflammatory markers such as CRP, procalcitonin levels, neutrophil-lymphocyte ratio, and the rate of change of CRP have been reported to predict the progression of COVID-19<sup>8</sup>. Subsequently, more critical COVID-19 patients release procoagulant autoantibodies and markers associated with cytokine-mediated tissue damage and organ failure, and these are reported markers predicting severe COVID-19 or poor outcomes of COVID-19<sup>9</sup>. Elevated D-dimer levels, LDH, troponin I, and thrombocytopenia in patients with severe COVID-19 have also been reported, suggesting that a hypercoagulable state may contribute to the severity of illness and mortality<sup>10</sup>.

In non-severe cases, chest CT is pivotal in predicting prognosis<sup>11,12</sup>. Chest quantitative CT has a promising role in the early diagnosis of COVID-19 and provides new metrics for predicting clinical outcomes<sup>13</sup>. The binding of coronavirus spike protein to angiotensin-converting enzyme II receptor increases pulmonary capillary permeability and causes diffuse opacities in CT<sup>14</sup>. CT could reflect the early pathogenesis of COVID-19 inflammation, even though chest radiography could not detect the abnormalities<sup>15</sup>. In fact, CT severity score is associated with inflammatory levels, and CT severity score on admission is an independent risk factor for early deterioration<sup>16</sup>. Moreover, the rapid improvement of AI has enabled the automatic quantification of lesions and the prediction of outcomes more precisely.

There have been thousands of reports on biomarkers for predicting outcomes of COVID-19 with various parameters, diverse clinical severities, and outcomes. In particular, many studies have dealt with mortality predictors for severe COVID-19 cases<sup>4,10,17</sup>. However, rather than predicting mortality for initially critical patients, Hahm et al.<sup>5</sup> investigated the scoring of non-severe patients on potential rapidly worsening oxygenation, which would be a more useful tool in regions where non-severe cases are more prevalent due to mass surveillance

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## Address for correspondence: Jee Youn Oh, M.D., Ph.D.

Division of Pulmonary Allergy and Critical Care Medicine, Department of Internal Medicine, Korea University Guro Hospital, 148 Gurodong-ro, Guro-gu, Seoul 08308, Republic of Korea

Phone: 82-2-2626-3192, Fax: 82-2-2626-1166

E-mail: happymaria0101@hanmail.net

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screening<sup>18</sup>. More accurate, simple, and easily applicable tools for predicting worsening oxygenation in COVID-19 for initial risk stratification and medical resource arrangement are needed.

## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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