To the Editor:

We read with great interest the recent research article, published in Critical Care: “Longitudinal changes in compliance, oxygenation and ventilatory ratio in COVID-19 versus non-COVID-19 pulmonary acute respiratory distress syndrome”, by Beloncle and collaborators [1]. We agree with their conclusion that increase in ventilatory ratio (VR) during the first week of illness is characteristic to COVID-19 ARDS and reflects its uniqueness in pathophysiology. In addition, we herein wish to propose that VR in COVID-19 ARDS may serve as a potential bedside marker reflecting clinical severity and that its longitudinal monitoring may harbor prognostic value.

In our 28-day observational study including 39 patients with critically ill COVID-19 [2], longitudinal increase in VR values were associated with failure in discontinuing respiratory support (Fig. 1). Upon predicting failure, a VR threshold of 1.56 achieved the highest predictivity with a sensitivity of 0.667 and a specificity of 0.762 on day 5 of respiratory support. Of 21 patients with a VR value lower than 1.56 on day 5, 17 had successfully extubated within 28 days from respiratory support, suggesting that longitudinal VR monitoring could predict better outcome in COVID-19. Similar findings were obtained in another research applying VR changes from day 0 to 3 of respiratory support as a prognostic indicator [3]. Although statistically insignificant, Beloncle and collaborators have also shown an apparent trend towards better prognosis for a lower VR (Table S3; mortality in “VR < 2” versus “VR ≥ 2” were 15.5% versus 30%). It would be of great interest to validate our observations in their cohort as well, by assessing longitudinally the prognostic value of VR, if sufficient data were provided. The wide variety of VR values observed along the chronological course of COVID-19 ARDS, shown in Fig. 1D, may indicate the variable responses following therapeutic interventions.

Elevation in VR, a surrogate marker of the increasing dead space fraction, is attributed to the progressive exudative damage affecting the alveoli, as well as the development of micro-embolism in the pulmonary circulation [4, 5], both known histopathological determinants of COVID-19 clinical severity. In addition to the here proposed prognostic value of VR monitoring in predicting natural history of COVID-19, future interest resides in whether longitudinal evaluation of VR may further reflect clinical response to treatment.
However, in line with the results reported by Drs. Natsuko Kaku et al., we found in patients with COVID-19 that the increase in VR from day 1 to day 7 tended to be higher in the non-survivors than in the survivors at day 28 (0.8 [0.3–1.8] vs 0.5 [0.1–0.9], \( p = 0.053 \)). This tendency was not observed in the control patients with non-COVID-19 pulmonary ARDS. High VR are known to be associated with poor outcomes in patients with non-COVID-19 ARDS [6, 7]. Even if it has to be confirmed in larger cohorts, the potential specific prognostic value of the changes in VR over time in COVID-19 associated ARDS may be consistent with the distinct evolution of clinical features observed in this population during the first week of mechanical ventilation. As highlighted in our paper, this particular evolution may be in part due to different ventilatory strategies (in particular of positive end-expiratory pressure (PEEP) titration). We agree with Drs. Natsuko Kaku et al. that whether VR changes may help the clinicians to assess the efficacy of some therapeutics as PEEP levels or prone positioning is an interesting question which remains to be addressed.
Japan. All necessary patient consent has been obtained and the appropriate institutional form has been archived.

Consent for publication
Not applicable.

Competing interests
Not applicable.

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