

## LETTER TO THE EDITOR

# When to start spontaneous breathing in mechanically ventilated COVID-19 patients? Oxygenation index and PaO<sub>2</sub>/FiO<sub>2</sub> ratio can help

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Dear editor,

Patients with COVID-19 induced respiratory failure are initially treated with lung-protective controlled mechanical ventilation to prevent ventilator-induced lung injury.<sup>[1]</sup> Adequate timing of the switch to a support ventilation mode seems critical. Prolonged sedation and neuromuscular blocking may increase ICU-acquired weakness, whereas premature transition to spontaneous breathing may result in self-inflicted lung injury (P-SILI).<sup>[2]</sup> Currently, there are no data to predict a successful switch from controlled mechanical ventilation to spontaneous breathing in COVID-19 patients.

The oxygenation index (OI) was originally developed to measure severity of illness and predict outcome in neonatal respiratory failure. Previously, OI was also found to predict mortality in adult patients with ARDS.<sup>[3]</sup> The OI has not been used before to predict the moment of weaning from mechanical ventilation. In contrast to the PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) ratio, the OI is not only based on the fraction of inspired oxygen (FiO<sub>2</sub>) and partial pressure of oxygen in arterial blood (PaO<sub>2</sub>), but also integrates the mean airway pressure, which corresponds with static lung compliance.<sup>[4]</sup> We hypothesise that OI is a predictor for successful transition to spontaneous breathing.

## Methods

This retrospective single-centre study was performed in a closed-format 29-bed mixed ICU in a tertiary teaching hospital. All patients ≥18 years admitted to the ICU from 15 March to 30 April 2020 with PCR-confirmed COVID-19, and at least one attempt to switch from controlled mechanical ventilation to spontaneous breathing, were included in the study. The study was performed in accordance with the Declaration of Helsinki. According to applicable laws, the need for individual consent was waived by a local ethics committee.

## Protocol

All patients were treated in accordance with a local COVID-19 protocol, including haemodynamic monitoring with pulse-

contour analysis (PiCCO®, Getinge AB, Gothenburg, Sweden). In the first week of ICU admission pressure regulated volume control was the preferred ventilator setting. Sedation with midazolam/fentanyl was titrated to a Richmond Agitation-Sedation Scale level -4 to -5.<sup>[5]</sup> Additional muscle paralysis was used if deemed necessary to facilitate lung-protective ventilation with tidal volumes of 6 ml/kg ideal body weight and a driving pressure <15 cm H<sub>2</sub>O. Prone position was applied in patients with a P/F ratio <150.

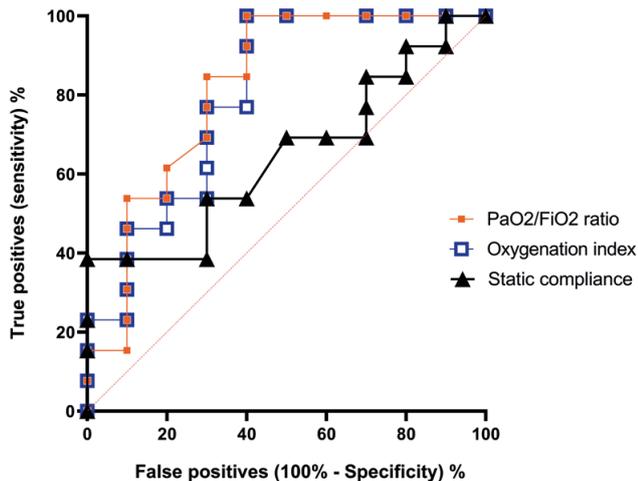
The decision to switch to spontaneous breathing was made by the attending physicians during office hours and only when an improvement was observed in a combination of compliance, P/F ratio and radiological abnormalities, together with a decrease in the extravascular lung water index (EVLW<sub>i</sub>). The attempt was regarded as unsuccessful if breathing frequency was >30/min, minute volume was >15 l/min, tidal volume >8 ml/kg ideal body weight, P<sub>0.1</sub> >5 cm H<sub>2</sub>O, presence of physical signs of respiratory distress or a decrease in P/F ratio.

## Data collection

Demographic characteristics, severity of illness scores over the first 24 hours following ICU admission and the maximum SOFA score during admission were extracted from the patient data management system (Epic®, Verona, Wisconsin, USA). C-reactive protein (CRP), EVLW<sub>i</sub>, Pulmonary Vascular Permeability Index (PVP<sub>i</sub>) and ventilation parameters, including mode of mechanical ventilation, static compliance (C<sub>stat</sub>) and P/F ratio, were recorded once daily. OI was calculated for the day of admission and prior to the moment that the first attempt to switch to spontaneous breathing was made. The formula FiO<sub>2</sub> (%) × mean airway pressure (mmHg)/PaO<sub>2</sub> (mmHg) was used for calculation.

## Statistical analysis

The Statistical Package for Social Sciences (SPSS 24 for Windows, Chicago, IL, USA) was used for statistical analysis. Comparison between the groups with a successful and an unsuccessful



**Figure 1.** ROC curves for ventilatory parameters in relation to a successful switch from controlled to support ventilation

first switch to spontaneous breathing was performed with the Mann-Whitney U test. A p value <0.05 was considered statistically significant. For distinctive variables a ROC analysis was executed to test performance and to determine an optimal cut-off value.

## Results

A total of 28 patients with COVID-19 were treated with mechanical ventilation in the ICU between 15 March and 30 April 2020. Twenty-three patients (64% male) had at least one attempt to switch from controlled mechanical ventilation to spontaneous breathing and were included in the study. The median age was 65 years [IQR 59-73] and median BMI 30.4 [IQR 25.6-33.1].

In 10 (44%) of the patients the first switch to spontaneous breathing was unsuccessful and return to pressure regulated volume control ventilation was necessary. On admission, there was no difference between groups in age, sex, BMI, comorbidities, APACHE III, SOFA score or OI and P/F ratio. Also, maximum SOFA scores during admission were similar between groups.

Time from admission to first attempt to switch to spontaneous breathing did not differ between the group with a successful first attempt and the group with an unsuccessful first attempt (median 10 [IQR 7-13] versus 9 days [IQR 6-14];  $p=0.693$ ).

On the day of the first switch, the OI and P/F ratio differed significantly between groups. The median OI in patients with a successful switch to spontaneous breathing was 5.8 [IQR 4.3-7.0] and 7.7 [IQR 5.8-8.4] in patients with an unsuccessful switch;  $p=0.015$ . Median P/F ratio was 214 [IQR 201-236] and 164 [IQR 147-206] respectively;  $p=0.008$ . The calculated AUC for the OI ROC curve was 0.80 (95% CI 0.61-0.99;  $p=0.016$ ),

with an optimal cut-off value of <7.5 (figure 1). The AUC for the P/F ROC curve was 0.82 (95% CI 0.63-1.00,  $p=0.01$ ), with an optimal cut-off value of  $\geq 168$  mmHg. There were no differences in  $C_{stat}$ ,  $EVLW_p$ ,  $PVP_i$  or CRP between groups. Furthermore, median  $C_{stat}$  did not change significantly over the first 21 days after admission.

The number of days on mechanical ventilation was significantly lower in patients who had a successful first switch to spontaneous breathing (median 10 [IQR 9-19] versus 22 days [IQR 9-34];  $p=0.004$ ).

## Interpretation

Both the OI and P/F ratio are useful parameters to predict a successful transition from pressure regulated volume control ventilation to spontaneous breathing in patients with COVID-19 induced respiratory failure. Static compliance was not different between the groups and did not change over time in this small cohort of patients.

Since there were no differences between groups in disease-severity scores or OI and P/F ratio at baseline, the longer duration of mechanical ventilation in the group with an unsuccessful first attempt might be caused by worsening of lung injury as a result of P-SILI. However, due to the retrospective nature of the study, a causal relationship between duration of mechanical ventilation and a successful switch to spontaneous breathing cannot be confirmed.

We conclude that both OI and P/F ratio may help to predict a successful switch from pressure regulated volume control ventilation to spontaneous breathing in patients with COVID-19 induced respiratory failure. Prospective confirmation of an optimal cut-off value is necessary.

## Disclosures

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