Correlation of non-invasive oxygenation parameters with paO2/FiO2 ratio in patients with COVID-19 associated ARDS

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Dear Editor,

COVID-19 associated ARDS (CARDS) is defined as a new-onset respiratory failure with bilateral, non-cardiogenic pulmonary infiltrates, and a paO2/FiO2 ratio (P/F) ≤ 300 mmHg is the most severe clinical manifestation of SARS-CoV-2 infection. This condition is characterized by prolonged hospitalization, elevated mortality and a high incidence of thrombotic complications attributed to COVID-19 associated coagulopathy. Arterial blood gas (ABG) analysis, usually obtained through arterial cannulation, is needed to establish the diagnosis and follow the course of ARDS. However, COVID-19 associated coagulopathy may lead to frequent and severe thrombotic complications in the site of arterial catheter with possible detrimental consequences for the patient, such as acute limb ischemia [1]. The assessment of the reliability of non-invasive parameters to follow the course of CARDS, and their potential role in limiting arterial cannulation was the objective of our study.

We conducted a prospective study on consecutive patients admitted to COVID High Care Unit and meeting the criteria of CARDS. When performing ABGs analyses (analyzer ABL90 FLEX; Radiometer, Copenhagen DK) in order to obtain the paO2 values, we concurrently recorded the spO2 (Intellivue MX750; Philips Medical Systems International, Eindhoven NL) and the respiratory rate (RR), analogically or from ventilators (Respironics V60, Philips Medical Systems International, Eindhoven NL; SV300, Mindray Medical, Shenzhen) CN. 100 patients were included, for a total of 1000 measurements of paO2/FiO2 ratio, spo2/FiO2 (S/F) ratio and the ROX index, which is the result of S/F*1/RR. We performed a linear correlation test and a linear regression analysis between S/F and P/F ratio and between ROX index and P/F ratio (Fig. 1, Panel a).

We then divided the total measurements of P/F ratio in 3 groups, according to the Berlin definition of ARDS criteria [2]: Group 1, mild ARDS (200 < P/F ≤ 300; 49/1000 measurements); Group 2, moderate ARDS (100 < P/F ≤ 200; 522/1000 measurements); Group 3, severe ARDS (P/F ≤ 100; 429/1000 measurements). At this point, we performed linear correlation test and linear regression analysis between the aforementioned non-invasive variables and P/F ratio for each of those 3 groups. For the Group 1 (mild ARDS), neither the S/F ratio nor the ROX index significantly correlated with the P/F ratio (p = 0.206 and p = 0.217, respectively). This is likely due to the flattening of the oxygen-hemoglobin dissociation curve in its right-upper part, with non-linear increase of spO2 following a rise of the paO2 values. However, in the Group 2 (moderate ARDS) and 3 (severe ARDS) the correlation of both non invasive variables with P/F ratio was moderate/strong, and remarkably significant (Fig. 1, Panels b and c). Our study has found a strong linear correlation of S/F ratio and ROX index with P/F ratio in patients with CARDS, statistically significant analyzing both the total of 1000 measurements and the group of measurements indicative of moderate and severe CARDS.

To the best of our knowledge, only a few papers exploring the correlation between S/F and P/F ratio have been published, and none of them covering COVID-19 patients [3-5]. A recently published study has investigated the correlation between ROX index and P/F ratio in patients with SARS-CoV-2 infection, and the pooled results are consistent with our ones (R = 0.650, p < 0.001) [6]. In all the tests we performed, S/F ratio showed a better correlation than ROX index with P/F ratio; this seems likely related to a wide dispersion of RR values because of the phenomenon of silent hypoxemia, well described in CARDS [7].

The possibility to take into account the increased minute ventilation, which is a feature of COVID-19 associated respiratory failure, could represent an important perspective, as suggested by a recently published paper on the better performance of standardized paO2/FiO2 ratio versus traditional P/F in predicting in-hospital mortality [8]. However, the aim of that study was to compare the ability of these two parameters to predict the outcome, and not to evaluate the correlation of those parameters with S/F or ROX. Moreover, in the advanced stages of the disease, the progressively worsening ventilation-perfusion mismatch with increasing airway deadspace and shunt fraction, frequently causes a shift from hypocapnia to hypercapnia and a paradoxical improvement of arterial pH, which is commonly associated with a paradoxical improvement of arterial pH, which is commonly associated with a paradoxical improvement of arterial pH, which is commonly associated with a paradoxical improvement of arterial pH, which is commonly associated with a paradoxical improvement of arterial pH.

In conclusion, S/F ratio is a reliable, non-invasive, and easy to track parameter for monitoring COVID patients with moderate and severe ARDS, potentially useful in reducing the need for positioning arterial catheters and the possible consequent thrombotic complications related to COVID associated coagulopathy.

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Fig. 1. Linear correlation between spO2/FiO2 ratio and pao2/FiO2 ratio and between ROX and pao2/FiO2 ratio.

CRediT authorship contribution statement

**Giacomo Zaccagnini:** Conceptualization, Data curation, Formal analysis, Writing – original draft. **Andrea Berni:** Formal analysis, Writing – review & editing. **Filippo Pieralli:** Conceptualization, Data curation, Formal analysis, Writing – original draft.

**Declaration of Competing Interest**

The authors declare they have no conflict of interest.

**References**


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