The hemoglobin level impact on arterial oxygen saturation during venous-venous-extracorporeal membrane oxygenation support of acute respiratory distress syndrome patients: a mathematical marginal approach

TO THE EDITOR

Hemoglobin (Hb) levels in the range of 7 - 14g/dL have been targeted in extracorporeal membrane oxygenation (ECMO)-supported acute respiratory distress syndrome (ARDS) patients. There is an association between low Hb levels and prolonged duration of mechanical ventilation and bleeding episodes. In contrast, higher Hb levels are associated with lower ECMO blood flow, increased hemolysis, and increased costs. Current transfusion strategies are mostly based on individual judgment, derived mainly from oxygen delivery (DO2) /consumption rationale (VO2). High volume ECMO centers are used to more restrictive Hb strategies, although there is no consensus on a definitive transfusion approach. Conversely, some experienced centers use higher Hb thresholds for transfusion and accept oxygen arterial saturation (SatO2) as low as 70% with excellent clinical outcomes.

Critical illnesses are related to cellular dysfunction due to reduced DO2 to tissues. Oxygen delivery depends on cardiac output (CO), Hb level, oxygen arterial partial pressure (PaO2), and SatO2 as in equation 1.

\[ \text{DO2} = \text{CO} \times \left[ \text{Hb} \times \text{SatO2} \times 1.36 \right] + \left( 0.0031 \times \text{PaO2} \right) \]

Equation 1

The physiological role of SatO2 on DO2 is crucial, with the oxygen bound to hemoglobin accountable for the majority of the blood’s oxygen content. Additionally, because the dissolved O2 content in plasma is negligible in normobaric conditions, it can be excluded from calculation of DO2. As the main goal of venous-venous (VV)-ECMO is to provide adequate DO2, VV-ECMO oxygenation settings are mostly based on SatO2.

While the impact of Hb levels on DO2 in ECMO-supported patients has been previously modeled, the effect size of Hb levels on SatO2 remains still unclear. We used a previously described mathematical marginal multicompartamental model of systemic SatO2 during femoro-jugular VV-ECMO support. This model accounts for recirculation proportional to ECMO blood flow and systemic, native lung and artificial lung compartments. To assess the effect of Hb level on systemic SatO2, we contrasted different scenarios related to patient and ECMO variables, such as systemic VO2 rates, ECMO blood flow and CO2, to highlight the dynamic care required by such patients. The behavior of dual lumen bicaval and femoro-femoro (venous-venous) configurations are probably similar but with a slightly increased recirculation.

The R free source software was used for the mathematical modeling and graphical buildings. The script of the model is freely accessible on the website.
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Figure 1 shows the results of Hb level influence on SatO$_2$ under three different VO$_2$ levels. Figure 2 shows the same impact under fixed VO$_2$ and different COs, while figure 3 shows the same impact under fixed VO$_2$ and CO but with different ECMO blood flows. Figure 4 shows the linear relationship between Hb levels and DO$_2$.

The results of these mathematical marginal simulations were compatible with increased SatO$_2$ and DO$_2$ when the Hb levels were higher. Other bedside physiological variables interacted with the relationship between Hb level and SatO$_2$; hence, our findings reflect that for a fixed Hb level, a higher VO$_2$, higher CO, and lower ECMO blood flow were associated with more severe hypoxemia.
The mechanism of such Hb impact on SatO₂ is a matter of oxygen content. For the same VO₂, CO, and ECMO blood flow, a higher Hb level provides a higher arterial oxygen content; therefore, the residual venous oxygen content will also be increased, resulting in a higher venous oxygen saturation and consequently a higher SatO₂ after oxygenation through the native and artificial lungs.

The reported relationships are not intended to have a predictive role in clinical circumstances, since the model was constructed to reflect associations between the studied variables in a hypothetical steady state. Despite these limitations, our findings reflect important physiological concepts that can be incorporated into the rationale of managing severely hypoxemic patients on VV-ECMO support.

Among patients undergoing ECMO support, extremely hypoxemic circumstances are not an uncommon scenario, and intensivists may need to accept very low SatO₂ levels. In such cases, higher Hb thresholds could be used to allow adequacy between VO₂ and DO₂. Additionally, our mathematical model can improve the understanding of the reasoning behind findings of very low SatO₂ and satisfactory clinical outcomes in clinical practice. However, it remains fundamental to emphasize the possible deleterious effects of severe hypoxemia with the installation of pulmonary hypertension and right ventricular dysfunction, in addition to long-term cognitive effects.

In conclusion, higher levels of Hb are associated with increased DO₂ and SatO₂. This association is modulated, at least, by the cardiac output, systemic VO₂, and ECMO blood flow.

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