Luisa Tajra Carvalho[1], Pedro Vitale Mendes[1], Bruno Adler Maccagnan Pinheiro Besen[1], Marcelo Park[1]

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

1. Emergency Medicine Discipline, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo - São Paulo (SP), Brazil.

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 (DO_2) /consumption rationale (VO_2).[1] High volume ECMO centers are used to more restrictive Hb strategies, although there is no consensus on a definitive transfusion approach.[2] Conversely, some experienced centers use higher Hb thresholds for transfusion and accept oxygen arterial saturation ($SatO_2$) as low as 70% with excellent clinical outcomes.[3]

Critical illnesses are related to cellular dysfunction due to reduced DO_2 to tissues. Oxygen delivery depends on cardiac output (CO), Hb level, oxygen arterial partial pressure (PaO_2), and $SatO_2$ as in equation 1.[4]

$$DO_2 = CO \times [(Hb \times SatO_2 \times 1.36) + (0.0031 \times PaO_2)] \quad \text{Equation 1}$$

The physiological role of $SatO_2$ on DO_2 is crucial, with the oxygen bound to hemoglobin accountable for the majority of the blood's oxygen content. Additionally, because the dissolved O_2 content in plasma is negligible in normobaric conditions, it can be excluded from calculation of DO_2.[4] As the main goal of venous-venous (VV)-ECMO is to provide adequate DO_2, VV-ECMO oxygenation settings are mostly based on $SatO_2$.

While the impact of Hb levels on DO_2 in ECMO-supported patients has been previously modeled, the effect size of Hb levels on $SatO_2$ remains still unclear.[5] We used a previously described mathematical marginal multicompartmental model of systemic $SatO_2$ during femoro-jugular VV-ECMO support.[6] 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 $SatO_2$, we contrasted different scenarios related to patient and ECMO variables, such as systemic VO_2 rates, ECMO blood flow and CO, 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.

Conflicts of interest: None.

Submitted on November 21, 2021
Accepted on March 6, 2022

Corresponding author:
Luisa Tajra Carvalho
Disciplina de Emergências Clínicas
Hospital das Clínicas, Faculdade de Medicina
Universidade de São Paulo
Rua Doutor Enéas de Carvalho Aguiar, 255
Zip code: 05403-000 - São Paulo (SP), Brazil
E-mail: luisa.tajra@hc.fm.usp.br

Responsible editor: Felipe Dal-Pizzol

DOI: 10.5935/0103-507X.20220465-en

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.

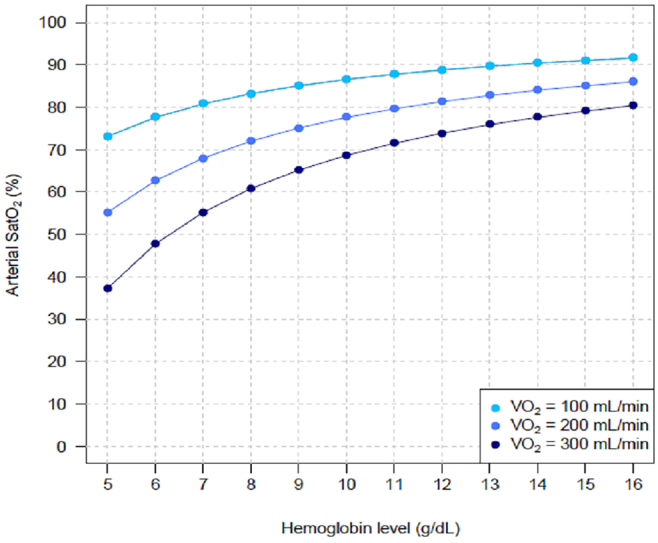

Figure 1 - Arterial oxygen saturation behavior with progressively higher hemoglobin levels under three different systemic oxygen consumptions.

The controlled variables were as follows: cardiac output = 5L/minute; extracorporeal membrane oxygenation blood flow = 3.5L/minute; partial pressure of carbon dioxide = 40mmHg; fraction of inspired oxygen with mechanical ventilator = 0.3; pulmonary shunt fraction = 0.9; and fraction of inspired oxygen with extracorporeal membrane oxygenation = 1.

$SatO_2$ - systemic arterial oxygen saturation; VO_2 - oxygen consumption.

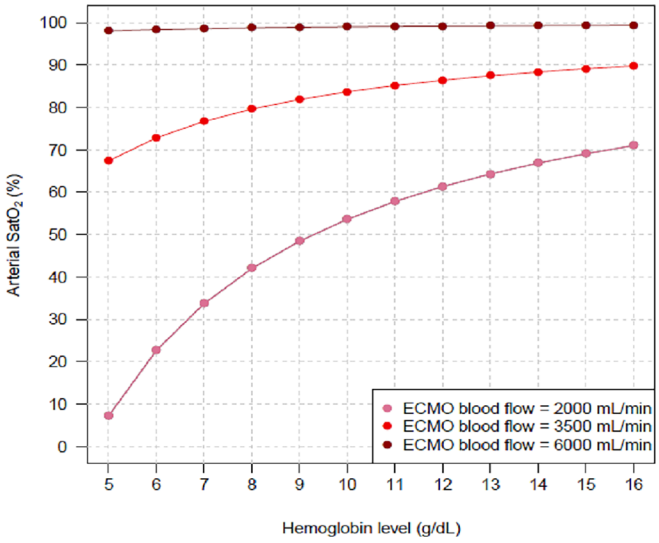

Figure 3 - Arterial oxygen saturation behavior with progressively higher hemoglobin levels under three different blood flows with extracorporeal membrane oxygenation.

The controlled variables were as follows: oxygen consumption = 300mL/minute; cardiac output = 5L/min; partial pressure of carbon dioxide = 40mmHg; fraction of inspired oxygen with mechanical ventilator = 0.3; pulmonary shunt fraction = 0.9; fraction of inspired oxygen with extracorporeal membrane oxygenation = 1.

$SatO_2$ - systemic arterial oxygen saturation; ECMO - extracorporeal membrane oxygenation.

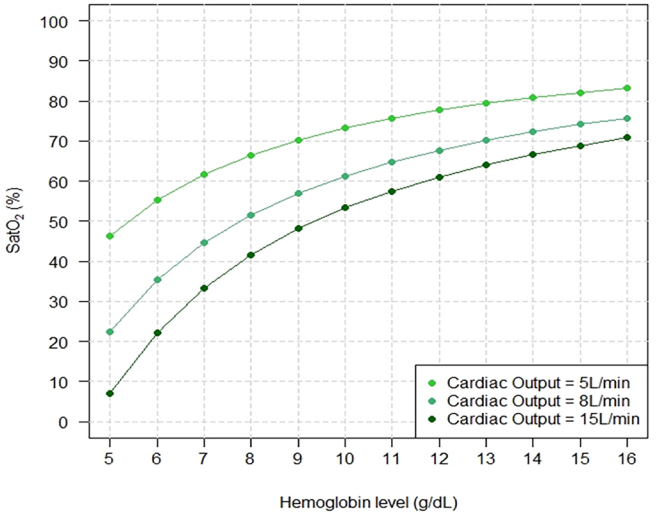

Figure 2 - Arterial oxygen saturation behavior with progressively higher hemoglobin levels under three different cardiac outputs.

The controlled variables were as follows: oxygen consumption = 300mL/minute; extracorporeal membrane oxygenation blood flow = 3.5L/minute; partial pressure of carbon dioxide = 40mmHg; fraction of inspired oxygen with mechanical ventilator = 0.3; pulmonary shunt fraction = 0.99; fraction of inspired oxygen with extracorporeal membrane oxygenation = 1.

$SatO_2$ - systemic arterial oxygen saturation.

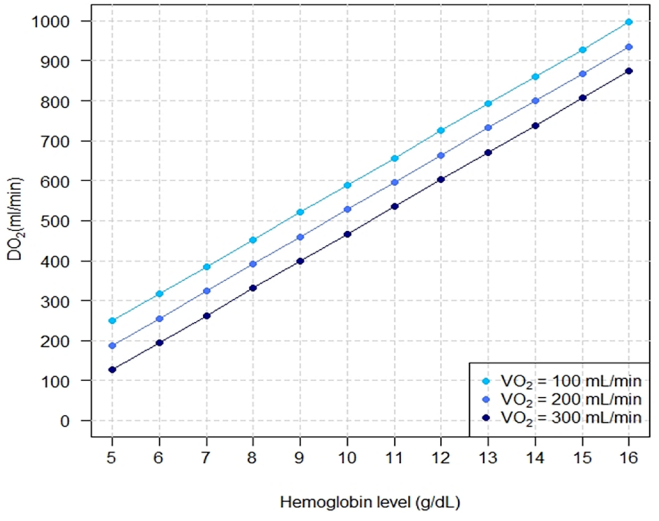

Figure 4 - Systemic oxygen delivery with progressively higher hemoglobin levels under three different systemic oxygen consumptions.

The controlled variables were cardiac output = 5L/minute; blood flow with extracorporeal membrane oxygenation = 3.5L/minute; partial pressure of carbon dioxide = 40mmHg; fraction of inspired oxygen with mechanical ventilator = 0.3; pulmonary shunt fraction = 0.9; fraction of inspired oxygen with extracorporeal membrane oxygenation = 1; systemic oxygen delivery = cardiac output x Hb x SO_2 x 1.36.

DO_2 - systemic oxygen delivery; VO_2 - oxygen consumption.

The mechanism of such Hb impact on $SatO_2$ is a matter of oxygen content. For the same VO_2, 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 $SatO_2$ 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 $SatO_2$ levels. In such cases, higher Hb thresholds could be used to allow adequacy between VO_2 and DO_2. Additionally, our mathematical model can improve the understanding of the reasoning behind findings of very low $SatO_2$ and satisfactory clinical outcomes in clinical practice.[3] 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 DO_2 and $SatO_2$. This association is modulated, at least, by the cardiac output , systemic VO_2, and ECMO blood flow.

REFERENCES

1. Cornish JD, Gerstmann DR, Null DM Jr, Smith MD, Kuehl TJ. Oxygen delivery rate and sufficiency of oxygenation during ECMO in newborn baboons. J Appl Physiol (1985). 1989;66(1):210-6.
2. Hughes T, Zhang D, Nair P, Buscher H. A systematic literature review of packed red cell transfusion usage in adult extracorporeal membrane oxygenation. Membranes (Basel). 2021;11(4):251.
3. Lindén V, Palmér K, Reinhard J, Westman R, Ehrén H, Granholm T, et al. High survival in adult patients with acute respiratory distress syndrome treated by extracorporeal membrane oxygenation, minimal sedation, and pressure supported ventilation. Intensive Care Med. 2000;26(11):1630-7.
4. Schumacker PT, Cain SM. The concept of a critical oxygen delivery. Intensive Care Med. 1987;13(4):223-9.
5. Spinelli E, Bartlett RH. Relationship between hemoglobin concentration and extracorporeal blood flow as determinants of oxygen delivery during venovenous extracorporeal membrane oxygenation: a mathematical model. ASAIO J. 2014;60(6):688-93.
6. Besen BA, Romano TG, Zigaib R, Mendes PV, Melro LM, Park M. Oxygen delivery, carbon dioxide removal, energy transfer to lungs and pulmonary hypertension behavior during venous-venous extracorporeal membrane oxygenation support: a mathematical modeling approach. Rev Bras Ter Intensiva. 2019;31(2):113-21.