Critical Care

MATTERS ARISING

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Beta-blockade in V-V ECMO

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To the Editor,

We read with great interest Staudacher et al.'s illustrative cases of beta-blocker therapy on V-V ECMO [1]. The authors' excellent work reminds us not to focus on the easily measured arterial oxygen saturation (S_aO_2) but rather on the much more physiologically important variable of delivered oxygen (DO_2). Herein, we demonstrate physiologically and mathematically that beta-blockade for a patient completely dependent on V-V ECMO will always decrease DO_2 irrespective of its effect on S_aO_2.

To illustrate this concept mathematically, there are some reasonable assumptions that must be made. The first is that ECMO effective blood flow rate (EF) are within normal operational parameters of the membrane lung and remain constant during beta-blockade. Second, that the membrane lung is well functioning such that the post-membrane lung blood oxygen saturation (S_mO_2) is 100%. Third, that the patient's lungs are non-functional and contribute no oxygenation to the blood. Finally, given the relatively small contribution of dissolved oxygen to total oxygen content, we ignore $0.03 \times P_mO_2$ in the calculation to simplify the math. With these assumptions in place, the arterial saturation on V-V ECMO equation simplifies to Eq. (1):

$$S_aO_2 = \frac{EF}{CO} \times S_mO_2 + S_vO_2\left(1 - \frac{EF}{CO}\right) + 0.03 \times P_mO_2$$
$$S_aO_2 = \frac{EF}{CO} + S_vO_2\left(1 - \frac{EF}{CO}\right) \quad (1)$$

Equation 1: Patient arterial oxygen saturation on V-V ECMO simplified

If we rewrite Eq. (1), we get Eq. (2) [2]:

$$S_aO_2 = \frac{EF + S_vO_2(CO - EF)}{CO} \quad (2)$$

Equation 2: Patient arterial oxygen saturation rewritten

Likewise, if we rewrite the Fick equation, we get Eq. (3):

$$S_aO_2 = S_vO_2 + \frac{VO_2}{13.4 \times Hgb \times CO} \quad (3)$$

Equation 3: Fick's Equation solved for S_aO_2

Equating Eqs. (2) and (3), then solving for S_vO_2, we get Eq. (4):

$$S_vO_2 = 1 - \frac{VO_2}{13.4 \times Hgb \times EF} \quad (4)$$

Equation 4: Determinants of S_vO_2

Therefore, we find that though S_vO_2 is traditionally dependent on CO, this is not necessarily true on V-V ECMO. Its covariates, CO and S_aO_2, cancel out in the idealized scenario proposed above. The only determinants of S_vO_2 on V-V ECMO, then, are VO_2, Hgb, and EF as seen in Eq. (4).

Finally, we explore the effect of beta-blockers on delivered oxygen (DO_2) with the specific question, does the increase in S_aO_2 triumph over the reduction in CO or *vis versa*?

Simplifying the DO_2 equation:

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$$DO_2 = 13.4 \times Hgb \times CO \times S_aO_2 \quad (5)$$

Equation 5: Oxygen delivery simplified
Combining Eq. (3) with Eq. (5):

$$DO_2 = 13.4 \times Hgb \times CO \times \left(S_vO_2 + \frac{VO_2}{13.4 \times Hgb \times CO}\right) = 13.4 \times Hgb \times CO \times S_vO_2 + VO_2 \quad (6)$$

Equation 6: DO_2 with relation to S_vO_2
Lastly, combining Eq. (6) with Eq. (4):

$$DO_2 = 13.4 \times Hgb \times CO \times \left(1 - \frac{VO_2}{13.4 \times Hgb \times EF}\right) + VO_2 \quad (7)$$

Equation 7: DO_2 on V-V ECMO expressed independent of S_aO_2 and S_vO_2

This final equation expresses delivery of oxygen on V-V ECMO as dependent only on hemoglobin, cardiac output, ECMO effective blood flow rate, and the body's consumption of oxygen. Introducing beta-blocker therapy, then, irrespective of its effect on S_aO_2, reduces delivery of oxygen through reduction of cardiac output if Hgb, EF, and VO_2 remains constant. While it is conceivable that beta-blocker therapy could reduce VO_2 by decreasing myocyte oxygen consumption, thereby increasing DO_2, this effect is unlikely in normal physiologic ranges because myocyte oxygen consumption is typically only 10% of total body oxygen consumption (6–8 ml/100 g/min). At maximal inotropy and chronotropy, however, myocyte oxygen consumption could become a nontrivial factor and beta-blocker therapy may have utility as an antihypertensive agent in the tachycardic patient. For the vast majority of cases, however, beta blockade is not indicated during V-V ECMO as it effectively reduces DO_2.

Abbreviations

V-V ECMO	Veno-venous extracorporeal membrane oxygenation
DO_2	Patient oxygen delivery
S_aO_2	Patient arterial oxygen saturation
EF	ECMO flow rate
S_mO_2	Post-oxygenator oxygen saturation
VO_2	Patient oxygen consumption
Hgb	Hemoglobin
P_mO_2	Partial pressure of oxygen post-oxygenator

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