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LETTER TO THE EDITOR

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Comment on: "A novel 'shunt fraction' method to derive native cardiac output during liberation from central VA ECMO" by Lim, HS

We have read with interest the case report by Lim and his recent review of the Fick principle on veno-arterial extracorporeal membrane oxygenation (VA ECMO).[1,2] We are delighted that the measurement of native cardiac output during extracorporeal support found its successful way to the bedside. Still, we wonder how our work on the subject has gone unnoticed.[3–6] We therefore take the liberty to offer some comments. Lim's method to create a right-to-left shunt by turning off sweep gas flow on the ECMO is not novel. Instead, it represents a special case of our modified Fick principle during VA ECMO. This concept, published in 2020, provides a general solution to the problem.[4]

Based on principles of mass balance, we derived the relationship between content differences over the ECMO and the lung and their respective blood flows[4]:

$$\dot{Q}_{LUNG} = \dot{Q}_{ECMO} * \frac{(\Delta_{v-pm}O_2 - \Delta_{ao-v}O_2)}{(\Delta_{ao-v}O_2 - \Delta_{v-LA}O_2)} \quad (1)$$

Q stands for blood flow, $\Delta_{ao-v}O_2$ is the absolute veno-aortal O_2 content difference, resulting from total body oxygen consumption ($\dot{V}O_{2\ Total}$), $\Delta_{v-LA}O_2$ is the absolute veno-left atrial O_2 content difference, resulting from lung oxygen uptake ($\dot{V}O_{2\ Lung}$), and $\Delta_{v-pm}O_2$ is the absolute veno-post membrane O_2 content difference, resulting from ECMO oxygen uptake ($\dot{V}O_{2\ ECMO}$).[4] We derived this equation for CO_2, but based on principles of mass balance, it must be true for oxygen consumption and uptake, albeit with changing negative or positive signs. Assuming proportionality between the content differences and the respective gas exchange, Equation (1) results in the following relationship ($\dot{V}O_2$: oxygen transfer)[4]:

$$\dot{Q}_{Lung} = \frac{\dot{Q}_{ECMO} * |\dot{V}O_{2\ Lung}|}{|\dot{V}O_{2\ ECMO}|} \quad (2)$$

Equation (2) is similar to the proposed method by Lim (Equation 3), where k is a classical representation of the Fick principle (Equation 4; sO_2: saturation)[1]:

$$\dot{Q}_{LUNG} = \frac{\dot{Q}_{ECMO} * k}{(1 - k)} \quad (3)$$

$$k = \frac{sO_{2\ Aorta} - sO_{2\ Pulmonaryartery}}{sO_{2\ leftatrium} - sO_{2\ Pulmonaryartery}} \quad (4)$$

Equation (3) can be rearranged as follows:

$$\frac{\dot{Q}_{ECMO}}{\dot{Q}_{LUNG}} = \frac{(1 - k)}{k} = \frac{1}{k} - 1 \quad (5)$$

We can prove that Equation (5) can be derived from Equation (1) by substituting the differences between oxygen content with saturation differences and assuming a difference of zero over the artificial lung, as sweep gas is turned off in Lim's special case[1] (Equations 6–12; sO_2 pulmonary artery represents mixed venous conditions, and freely dissolved oxygen content is disregarded):

$$\Delta_{v-pm}O_2 = sO_{2\ postmembrane} - sO_{2\ Pulmonaryartery} \quad (6)$$

$$\Delta_{ao-v}O_2 = sO_{2\ Aorta} - sO_{2\ Pulmonaryartery} \quad (7)$$

$$\Delta_{v-LA}O_2 = sO_{2\ leftatrium} - sO_{2\ Pulmonaryartery} \quad (8)$$

$$\text{Rearranging Equation (1)}: \frac{\dot{Q}_{ECMO}}{\dot{Q}_{LUNG}} = \frac{(\Delta_{ao-v}O_2 - \Delta_{v-LA}O_2)}{(\Delta_{v-pm}O_2 - \Delta_{ao-v}O_2)} \quad (9)$$

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$$\text{Equations (6)-(8) inEquation (9)}: \frac{\dot{Q}_{ECMO}}{\dot{Q}_{LUNG}} = \frac{sO_{2\ Aorta} - sO_{2\ Pulmonaryartery} - (sO_{2\ leftatrium} - sO_{2\ Pulmonaryartery})}{sO_{2\ postmembrane} - sO_{2\ Pulmonaryartery} - (sO_{2\ Aorta} - sO_{2\ Pulmonaryartery})} \tag{10}$$

In the special case of no sweep gas flow:

$$sO_{2\ postmembrane} - sO_{2\ Pulmonaryartery} = 0 \tag{11}$$

$$\text{Equations (11) and (4) inEquation (10)}: \frac{\dot{Q}_{ECMO}}{\dot{Q}_{LUNG}} = \frac{sO_{2\ Aorta} - sO_{2\ Pulmonaryartery} - (sO_{2\ leftatrium} - sO_{2\ Pulmonaryartery}}{-(sO_{2\ Aorta} - sO_{2\ Pulmonaryartery})}$$
$$= \frac{sO_{2\ leftatrium} - sO_{2\ Pulmonaryartery}}{sO_{2\ Aorta} - sO_{2\ Pulmonaryartery}} - \frac{sO_{2\ Aorta} - sO_{2\ Pulmonaryartery}}{sO_{2\ Aorta} - sO_{2\ Pulmonaryartery}} = \frac{1}{k} - 1 \tag{12qed}$$

Our approach represents a generalized solution to the problem without the restriction of turning off sweep gas flow. Our method was theoretically derived, tested in a small pilot study,[4] and further elucidated in a bench study.[5] Then, we assessed the method on 16 animals with varying conditions, such as high dead space and shunt fractions.[6] This integral assessment, which has meticulously documented gas exchange during VA ECMO in the blood and gas phases of the native and artificial lungs, incorporating over 1500 blood gas analyses, has proven that a modified Fick principle is feasible. Monitoring of gas exchange estimates native cardiac output with acceptable precision and accuracy.[6] Based on our work, we conclude the following and would like to highlight certain limitations regarding Lim's method.[1]

First, our method does not limit itself to states of no sweep gas flow (i.e. building an artificial right–left shunt). It also estimates cardiac output with clinically adequate bias and accuracy when extracorporeal gas exchange is present. This may allow continuous monitoring of native cardiac output at all stages of ECMO therapy.[4–6] The concept proposed by Lim maximizes the content differences between the extracorporeal circuit and the native cardiopulmonary unit and may therefore improve accuracy.

Second, our previous experimental data demonstrate that both venous and arterial differential hypoxia are present during VA ECMO.[6] While differential hypoxia on the arterial side is a known phenomenon (e.g. Harlequin or North–South), venous differential hypoxia is as common and important to managing patients on VA ECMO, albeit less often recognized.[3,7] The method is only accurate if and only if the inlet and outlet conditions of both the ECMO and the native lung are perfectly mixed; that is, there is no venous and arterial differential hypoxia.[5,6] Lim acknowledges the limitations of venous oxygen differences but suggests assuming a pulmonary vein (or left atrial) saturation of 100% to obviate the need for direct blood sampling and advises caution for critically ill patients with his assumption. Our data confirm that left atrial saturation cannot be assumed to be 100% in healthy lungs, let alone in states of shunt.[6]

In conclusion, Lim's approach is a modification of our method and therefore shares the limitations we have assessed extensively. Alternative approaches to the assessment of native cardiac output during VA ECMO may include modified thermodilution, which would also allow the evaluation of right ventricular performance.[8] We highly welcome further studies within the field of gas exchange and extracorporeal support and commend Lim for his work.

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