Journal of Intensive Care Medicine
1-6

DOI: 10.1177/0885066616641383
jic.sagepub.com
SAGE

Physiology of Gas Exchange During ECMO for Respiratory Failure

Robert H. Bartlett, MD[1]

Abstract

Management of gas exchange using extracorporeal membrane oxygenation (ECMO) in respiratory failure is very different than management when the patient is dependent on mechanical ventilation. All the gas exchange occurs in the membrane lung, and the arterial oxygenation is the result of mixing the ECMO blood with the native venous blood. To manage patients on ECMO, it is essential to understand the physiology described in this essay.

Keywords

ECMO, respiratory failure, oxygenation, gas exchange

With conventional ventilation, all the venous return (the cardiac output) goes through the right ventricle (RV), lungs, and into the left atrium and ventricle. CO_2 removal is achieved by regulating ventilator rate, volume, and inspiratory and expiratory pressure (the minute ventilation). Oxygenation is achieved by matching inflated alveoli to blood flow (controlling Fio_2, inspiratory and expiratory pressure, patient position, hemoglobin concentration, and cardiac output). If a patient on mechanical ventilation becomes hypercarbic or hypoxemic, the response is to increase the ventilator settings (more minute ventilation, inflating pressure, or FiO_2) and to decrease metabolism by paralysis or cooling.

With extracorporeal membrane oxygenation (ECMO), most of the venous return blood goes to the ECMO circuit, through the membrane lung, and is returned to the aorta (VA [venoarterial]) or right atrium (VV [venovenous]) where it mixes with the venous blood that did not go through the ECMO circuit. Oxygenation is controlled by blood flow and the oxygen-carrying capacity (which depends on the hemoglobin concentration and the oxyhemoglobin saturation of the venous [inlet] blood). CO_2 removal is controlled by sweep gas flow (the minute ventilation) and by blood flow. If a patient on ECMO becomes hypercarbic or hypoxic, the correct response is to solve the problem with ECMO and not with settings on the mechanical ventilator. However, these phenomena are often not well understood by treating physicians who are accustomed to solving gas exchange problems with the mechanical ventilator. This report describes the physiology and management of gas exchange during ECMO.

Basic Oxygen Kinetics

The oxygen in blood is the amount bound to hemoglobin plus the amount dissolved in plasma. These are measured as % saturation (Hb [g/dL] × % saturation × 1.34 ml/O_2/g) and O_2 (Po_2 × 0.003 ml/mm Hg/dL). Bound plus dissolved oxygen is the oxygen content (ml/dL). Oxygen content is difficult to measure directly so is usually not reported on printouts from the blood gas machine, but it is the most important (perhaps the only important) measurement of oxygen in blood. In clinical practice, the amount of dissolved oxygen is less than 1% of the content, so it is often ignored. The relation of these 3 measurements is shown in Figure 1. Notice that there is twice as much oxygen in normal blood with an O_2 content of 20 ml/dL than in anemic blood with a content of 10 mL/dL, even though the saturation and Po_2 are the same in both samples.[1]

The amount of oxygen delivered to metabolizing tissue is the oxygen content in arterial blood times the blood flow (cardiac output), called the oxygen delivery (DO_2). For an adult, the normal DO_2 is 600 ml/min/m^2 (20 ml/dL × 30 dL/min/m^2). The normal oxygen consumption at rest is 120 ml/min/m^2, abbreviated as Vo_2. These phenomena are described in Figure 2. The DO_2 is controlled by homeostatic mechanisms to be 5 times Vo_2, so in a resting adult, 20% of the available oxygen is used for metabolism, leaving 80% in the venous blood. Therefore, the normal arterial oxygen of a patient breathing air is Po_2 90 mm Hg, saturation 100%, and O_2 content 20 ml/dL and the normal venous oxygen is Po_2 40 mm Hg, saturation 80%, and content 16 ml/dL. The Vo_2 increases with exercise, catecholamines, and sepsis. The DO_2 adjusts to Vo_2,

[1] Department of Surgery, University of Michigan, Ann Arbor, MI, USA

Received November 16, 2015, and in revised form March 1, 2016.
Accepted for publication March 7, 2016.

Corresponding Author:
Robert H. Bartlett, ECLS Laboratory, University of Michigan, B560 MSRB II, 1150 W Medical Center Drive, Ann Arbor, MI 48109, USA.
Email: robbar@umich.edu

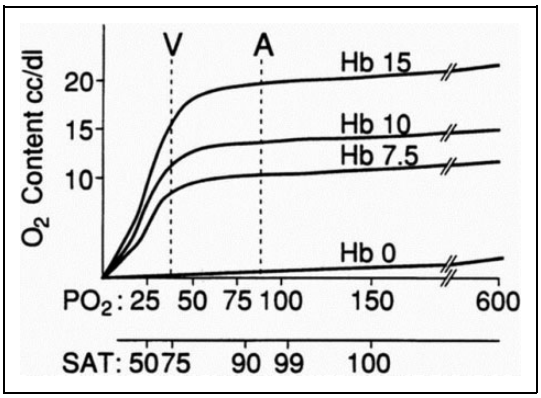

Figure 1. O_2 in blood. Of the 3 methods of describing oxygen in blood, oxygen content is the most important. Oxygen content depends on the amount of hemoglobin, and it is not described by the P_{O_2} or saturation of arterial (A) or venous (V) blood.

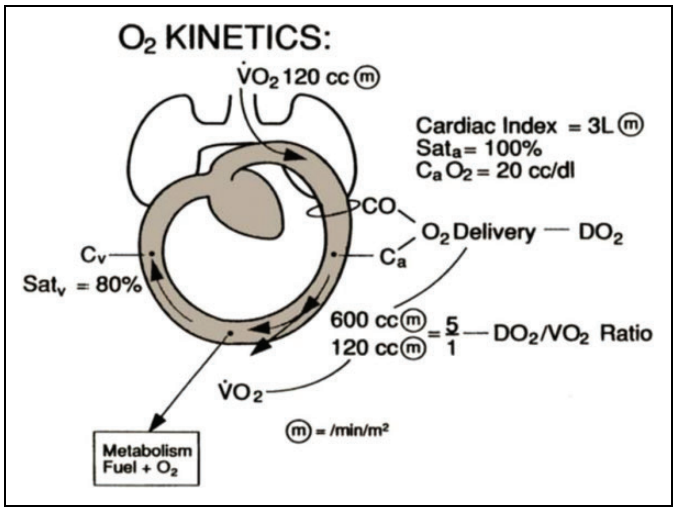

Figure 2. DO_2:V_{O_2} homeostasis: normal adult values are shown.

maintaining the ratio at 5:1. If the DO_2 is decreased compared to V_{O_2} (eg, in low cardiac output or anemia or hypoxemia), V_{O_2} continues at the same rate, more oxygen is extracted per dL of flow, and there is less oxygen in venous blood. Normal aerobic metabolism continues. However, when the DO_2 is less than twice V_{O_2}, oxygen supply is inadequate to maintain aerobic metabolism and anaerobic metabolism results, producing lactic acid rather than CO_2. DO_2:V_{O_2} ratio less than 2:1 leads to supply dependency systemic acidosis and organ failure (Figure 3). A goal of managing any critically ill patient is to maintain DO_2:V_{O_2} close to normal (5:1). So it is important to know the V_{O_2} and DO_2 when planning management. With ECMO, we have the ability to control DO_2 regardless of native lung function.[2]

During ECMO, blood from the extracorporeal circuit mixes with blood that follows the normal pattern of circulation (the native venous flow). Understanding DO_2, V_{O_2}, and gas exchange during ECMO requires understanding of the consequences of mixing 2 blood flows of different oxygen content.[3]

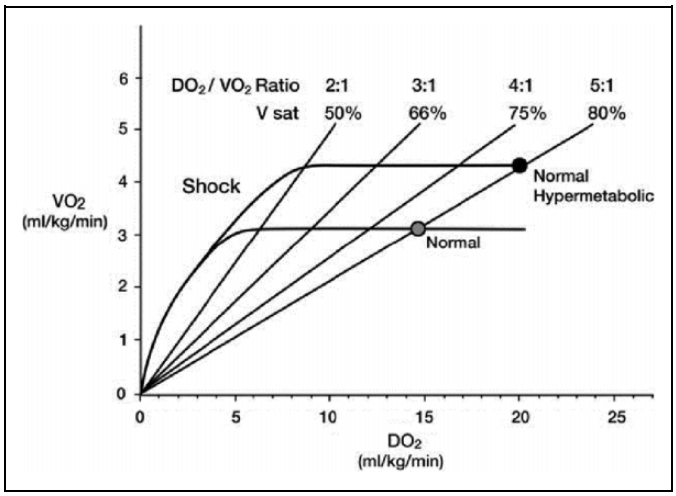

Figure 3. DO_2:V_{O_2} relationships. Normally DO_2 is autoregulated (by cardiac output and rate) to be 5 times V_{O_2} (because of low cardiac output or anemia or both) anaerobic metabolism and supply dependency (shock) occurs.

When VA access is used for cardiac failure, lung function is usually normal and the patient is managed at low ventilator settings or extubated and breathing spontaneously. Mixing of the ECMO flow with native venous flow is not important for discussion of gas exchange. The following discussion is about ECMO for respiratory failure. Respiratory ECMO support can be VA, but it is usually VV.

In venovenous access, the mixing occurs in the right atrium. With VV access, some of the venous return will go through the native heart and lungs and some will go through the circuit; the ratio is determined by the total venous return compared to the extracorporeal flow. Typically 60% to 80% of the venous return goes through the circuit, but this is limited by the flow through the drainage cannula at typical suction pressure of −100 cm/H_2O. With VV access, fully saturated and oxygenated perfusate blood mixes with desaturated venous blood in the right atrium and RV. That mixed blood proceeds through the (nonfunctioning) lungs, left ventricle, and into the aorta, so the arterial saturation and Pa_{O_2} will reflect the relative amount of oxygenated blood from the circuit and deoxygenated venous blood. The circuit flow is usually at maximum, so the P_{O_2} and saturation of the mixture are dependent on the ratio between circuit flow and total flow. At constant ECMO flow, when the cardiac output (hence the venous return) increases, the arterial saturation will decrease, even though the same total amount of oxygen is supplied to the patient (this discussion assumes that there is no recirculation between the ECMO inflow and outflow blood).

Oxygenation

To illustrate the principles, the discussion begins with the assumption that there is no native lung gas exchange (which is often the case in ECMO patients). In a membrane lung (and in the native lung), oxygenation is a much greater problem than CO_2 removal, so the initial focus is on oxygenation. The circuit and blood flow are planned for total oxygen supply (V_{O_2}) at

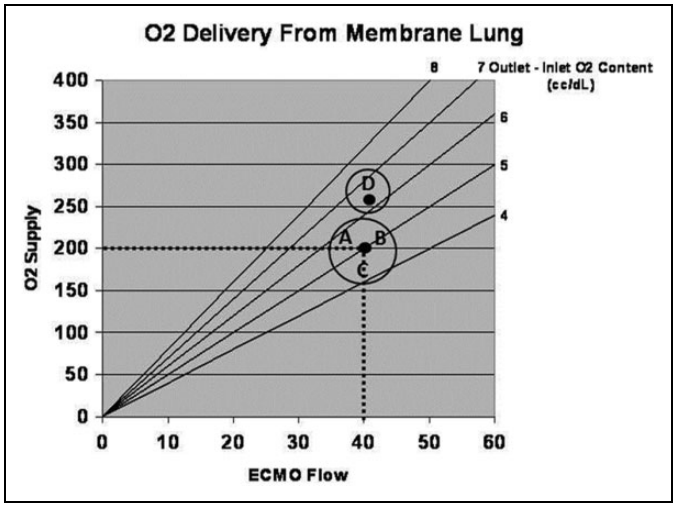

Figure 4. Oxygen supplied by the membrane lung. The points describe the situation in stable VV physiology, example 1, point A; increased cardiac output, example 2, point B; anemia, example 3, point C; increased metabolism, example 4, point D.

rest or during moderate exercise. This is 120 ml/min/m^2 (3 ml/kg/min) or 250 to 300 ml of oxygen/min for average adults. The membrane lung must be large enough to transfer this amount of oxygen (all devices on the market can do this). The oxygen supply from the membrane lung is dependent on the blood flow, the hemoglobin concentration, and the difference between the outlet minus inlet O_2 content. Because the outlet blood is typically 100% saturated and P_{O_2} is over 500 mm Hg, the dissolved oxygen can be as much as 10% of the oxygen content. Membrane lung oxygen supply over a range of outlet–inlet contents and flows are shown in Figure 4.

Relation of Extracorporeal Oxygenation to Systemic Oxygen Delivery

Assuming that there is no native lung function, the systemic arterial content, saturation, and P_{O_2} will result from mixing the flow of oxygenated blood from the membrane lung with the flow of venous blood that passes into the RV, not into the ECMO drainage cannula (referred to as the native venous flow). The amount of oxygen in systemic arterial blood is the result of the mixture of these 2 flows. These relationships are shown in Figure 5.

Calculations Related to Mixing 2 Flows

When 2 blood flows of different oxygen contents mix, the resultant oxygen content is the average of the amount of oxygen in each of the 2 flows (not the average of the P_{O_2}). The amount of oxygen contributed by each flow is the oxygen content (in ml/dL) in the blood times the flow rate (in dL/min). The equation summarizing these events is in Figure 6. The same calculation can be done using saturation rather than oxygen content. This calculation is done for simplicity and is not an exact representation of the amount of oxygen content but it is

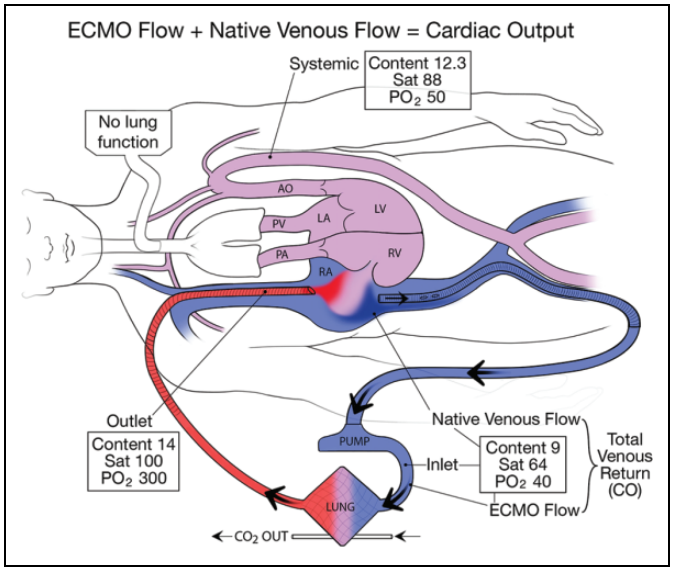

Figure 5. VV access: mixing extracorporeal membrane oxygenation (ECMO) flow and native venous in the right atrium.

Mixing 2 Blood Flows of Different O_2 Content (C_1 and C_2)

The resultant O_2 content (C_3) is the sum of each content x flow divided by total flow

$$\frac{C_1 \times \text{Flow}_1}{\text{Total Flow}} + \frac{C_2 \times \text{Flow}_2}{\text{Total Flow}} = C_3$$

In VVECMO, assuming no native lung function:
C1 and F1 are extracorporeal content and flow
C2 and F2 are the venous content and the native venous flow
The equation can be solved for cardiac output and native venous flow

$$\text{Total Flow} = \text{Flow}_1 \frac{(C_1 - C_2)}{C_3 - C_2} = \text{Cardiac Output}$$

$$\text{Flow}_2 = \text{Total Flow} - \text{Flow}_1 = \text{Native Venous Flow}$$

Figure 6. Equation describing the mixing of blood flows of different O_2 content.

useful at the bedside (Figure 7). Note that these are averages of the amount of oxygen delivered by each flow, not averages of the saturations or contents. The combinations of flow and oxygen (expressed as saturation) variations are shown in Figure 8. Of the variables in the equation, all are known except the flow of venous blood that does not go through the extracorporeal circuit (the native venous flow). The native venous flow can be back calculated from the systemic arterial oxygen content. The total venous return (cardiac output) is the sum of the native venous and circuit flow.

Systemic Arterial P_{O_2}, Saturation, and Content During ECMO

In the following examples, 1 variable is changed while others are held constant to illustrate the principles. Clinically, all these variables may change simultaneously and at different rates. For simplicity of the examples, we assume no

Mixing 2 Blood Flows in VV ECMO: Example 1

Using O_2 Content:

$$\frac{14 \times 4}{4 + F_2} + \frac{9 \times F_2}{4 + F_2} = 12.3 \text{ cc/dL}$$

$$\text{Cardiac Output} = \frac{4(14-9)}{(12.3-9)} = 6 \text{ L/min}$$

$$\text{Native Venous Flow} = 6 - 4 = 2 \text{ L/min}$$

Using O_2 Saturation:

$$\frac{100 \times 4}{4 + F_2} + \frac{64 \times F_2}{4 + F_2} = 90\%$$

$$\text{Cardiac Output} = \frac{4(100-64)}{(90-64)} = 6 \text{ L/min}$$

$$\text{Native Venous Flow} = 6 - 4 = 2 \text{ L/min}$$

Figure 7. The mixing equation using the values in example 1, using O_2 content and saturation. Calculation using O_2 content is the most accurate, but calculation with saturation is close enough for bedside management.

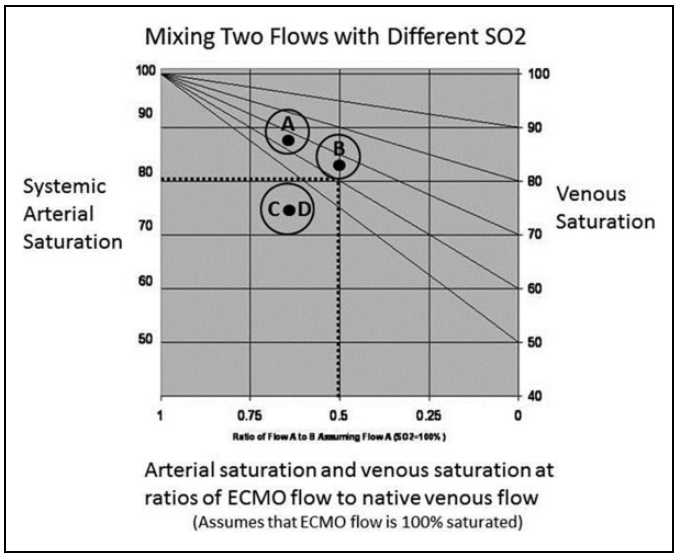

Figure 8. Mixing of extracorporeal membrane oxygenation (ECMO) flow with native venous flow. Example 1 point A; example 2, point B; example 3, point C; and example 4, point D.

native lung function and approximate the points on the graphs. We do not account for dissolved oxygen in calculation of O_2 content, although it can be significant when the Po_2 is over 300.

Example 1—Typical VV physiology: Suppose the extracorporeal flow for an adult with no lung function is 4 L/min and the systemic Po_2 is 50 mm Hg, saturation 88%, and O_2 content 12.3 ml/dL. The Hb is 10.5 g/dL, and the venous blood saturation is 64%. The patient's oxygen consumption is 200 ml/min. The oxygen content of blood leaving the membrane lung is determined primarily by the concentration of hemoglobin. At hemoglobin concentration of 10.5 g/dL and 64% saturation, the drainage (inlet) O_2 content is 9 ml/dL and the outlet content at 100% saturation is 14 ml/dL. The amount of oxygen supplied to the patient is the outlet minus inlet content (which is 5 ml/dL) times the flow (40 dL/min) equals 200 ml oxygen supplied per minute. The native venous flow is calculated at 2 L/min (per equation in Figure 6), so the cardiac output is 6 L/min (native plus circuit venous flow). The O_2 content of native venous blood is the same as the drainage content (9 ml/dL). The oxygen content of the arterial (mixed) blood is 12.3 ml/dL. The complete equation is 40 dL/min $\times$ 14 c/dL divided by 60, plus 20 dL/min $\times$ 9 ml/dL divided by 60 $=$ 12.3 ml/O_2/dL (corresponding to a Po_2 of approximately 50 mm Hg). The calculation using saturation is 4 L/min $\times$ 100% divided by 6 plus 2 L/min $\times$ 70% divided by 6, which yields a systemic arterial saturation of 88% (point A in Figures 4 and 8)

DO_2 is the arterial content (12.3 ml/dL) $\times$ 60 dL/min $=$ 738 ml/O_2/min. DO_2–Vo_2 ratio is 3.64.

Example 2—Increased cardiac output at fixed ECMO flow: If, in the same patient, the cardiac output (venous return) increases to 8 L/min and the circuit flow is fixed at 4 L/min, there will more native venous return at 64% saturation mixing with the fully saturated ECMO flow. The systemic arterial content will decrease to 11.5, and the saturation will decrease to 84% corresponding to Po_2 of 45 mm Hg. The total amount of oxygen going to the patient is the same (200 ml/min), but the systemic saturation and Po_2 are lower. The systemic oxygen delivery is 920 ml/min. The DO_2–Vo_2 is 4.6. There has been a gain in systemic oxygen delivery because of the higher cardiac output, despite a decrease in arterial saturation and content. If the patient's systemic oxygen consumption is 200 ml/min, systemic oxygen delivery is perfectly adequate and full aerobic metabolism is supported, even though the arterial Po_2 is 45 mm Hg and arterial saturation is 84%. No changes are required, but the intensive care unit staff needs to understand that the hypoxemia does not require intervention. Understanding this concept can be difficult when the plan is to keep the arterial saturation over 90% (point B in Figures 4 and 8).

Example 3—Anemia: The patient in example 1 is moderately anemic (Hb 10.5 g%) but stable. Suppose the hemoglobin suddenly drops to 8 g%. The venous drainage is fixed at 4 L/min by the resistance of the drainage cannula, and cardiac output is 6 L/min. The outlet content at 100% saturation is 10.7. The amount of oxygen supplied by the membrane lung is the outlet content (10.7 ml/dL) minus the inlet content (9 ml/dL) times the flow (40 dL/min). The O–I (output oxygen

content minus input oxygen content) difference is 1.7 ml/dL. At 4 L/min flow, the membrane lung is supplying only 68 ml/min. The native venous flow is still 20 dL/min, and content is 9 ml/dL. The arterial content goes from 11.5 to 9.8, the arterial saturation to 80%, and the DO_2 has gone from 738 to 588 ml/min. This results in a DO_2–VO_2 ratio of 2.9 (assuming no difference in metabolic rate). However, since only 68 ml of oxygen is being added per minute and the oxygen consumption is 200 ml/min, venous (inlet) content and saturation decrease quickly. When the inlet content falls to 5.7 (saturation 50%), the membrane lung O–I difference is 5 ml/dL and the oxygen supplied is 200 ml/min. The mixture of the fully saturated blood at 40 dL/min and the 50% saturated native venous flow results in arterial saturation of 75% and arterial content 9 ml/dL. The systemic oxygen delivery is 540 ml/min, and the DO_2–VO_2 ratio is 2.7. The patient can remain in steady state with arterial saturation 75% and venous saturation 50%, but any further decrease in hemoglobin or increase in metabolic rate will result in supply dependency and lactic acidosis (point C in Figures 4 and 8).

Example 4—Increased metabolic rate: Suppose the patient in example 1 becomes hypermetabolic (VO_2 = 250 ml/min). The size of the venous cannula determines that the circuit flow is at maximum at 4 L/min so the circuit oxygen delivery is limited to 200 ml/min. The cardiac output is 6 L/min. Going through the same arithmetic, the patient will fall behind at the rate of 50 ml of oxygen per minute, and venous content and saturation will steadily decrease (eg, 70%-45%). As venous saturation and content decrease, the oxygenator will still increase the outlet saturation to 100% and oxygen content to 14 ml/dL, so the circuit outlet minus inlet, oxygen difference (oxygen supply) will go up as the venous saturation goes down (eg, from 5 to 6). Systemic saturation will decrease because the saturation and content of the native venous blood going through the heart and lungs will decrease. At venous content 7.5, the O–I content difference is 6.5 and the oxygen supplied is 260 ml/min. Steady state is reached with arterial saturation at about 75% and PaO_2 35 mm Hg. The DO_2–VO_2 is 2.1, and any increase in activity will lead to anaerobic metabolism that will produce lactate rather than CO_2 and lactic acidosis results. In time, this will lead to multiple organ failure and death (point D in Figures 4 and 8).

How can systemic oxygen delivery be increased in examples 3 and 4? Turning up the ventilator FiO_2 or airway pressure will not help. Furthermore, the whole objective is to avoid increasing FiO_2 and pressure from the mechanical ventilator. There are 4 alternatives. The first is to increase the hemoglobin concentration to normal (8 or 10.5-15 g/dL) so systemic oxygen delivery goes to 930 ml/min, arterial saturation at 6 L/min returns to 95%, venous saturation goes to 80%, and the patient is stable and well supported. The DO_2–VO_2 is 4.6. The second alternative is to increase the suction or add another cannula and increase the circuit flow to 5 L/min. The DO_2 is 792, and the DO_2–VO_2 is 3.9. The third alternative for example 4 is to paralyze and cool the patient decreasing the VO_2 back to 200 ml/min. A fourth is to add another membrane lung to increase the gas exchange surface, but O_2 supply is still limited by the blood flow, so this will not help.

The risks of transfusion are minor compared to inadequate DO_2 and death. Increasing the flow without changing the hemoglobin increases the blood surface exposure. Increasing the suction raises the possibility of cavitation resulting in hemolysis, and a high return pressure at higher flows runs the risk of circuit blowout. In general, the lower the blood flow the lower the risk. Adding another membrane lung will not increase oxygen supply because oxygenation depends on flow, not on membrane surface area. Paralyzing and cooling the patient risks prolonged supine position, risks neuropathy, prevents spontaneous breathing, and prevents neurologic assessment. The whole benefit to extracorporeal support is to manage the patient awake, breathing, and active. So in this example, transfusion to a normal hemoglobin level is the way to solve the problem.[4]

Oxygenation Summary

The combination of venous access cannula, membrane lung size, and hemoglobin concentration should be planned to match or exceed resting VO_2 (120 ml/m^2/min for adults). The membrane lung will supply the most oxygen at a normal hemoglobin (15 g/dL). All the important variables related to blood flow and oxygenation can be measured or calculated. It is essential to know the patient's oxygen consumption and systemic oxygen delivery to decide the best way to manage the extracorporeal circuit. Hypoxemia (PaO_2 40-60, SaO_2 70-90) always occurs with venovenous support and is adequate to maintain normal oxygen delivery. If systemic oxygen delivery falls to a critical level (near twice consumption), circuit oxygen supply must be increased by (1) transfusing to a higher hemoglobin or (2) adding additional venous drainage access to increase the flow. There is a trade-off of risk between transfusion and increasing circuit flow, which favors transfusion of red blood cells. Membrane lungs function optimally at a normal hematocrit.

CO_2 Removal

CO_2 production is equal to O_2 consumption (when the respiratory quotient is 1), so the amount of CO_2 exchanged per minute is essentially the same as the amount of oxygen (120 ml/min/m^2 for adults). Because CO_2 is much more soluble and diffusible in blood than O_2, CO_2 clearance will exceed oxygenation in any circumstance, so all the circuit management is based on oxygenation. If CO_2 clearance is the only or the major goal, much lower blood flow can be used and hemoglobin concentration is not important. The amount of CO_2 elimination is a function of the gradient between the inlet PCO_2 (typically 50 mm Hg) and the sweep gas (0) and the sweep gas flow. The systemic PCO_2

is the result of mixing circuit outlet blood (P_{CO_2} typically 30 mm Hg) with native flow (typically 45 mm Hg). Unlike oxygenation, measuring or calculating the actual amount of CO_2 exchanged by the circuit is not critical; the sweep gas is simply adjusted to maintain the desired systemic P_{CO_2} (typically 40 mm Hg).

One phenomenon unique to ECMO is the effect of water accumulation on the gas side of the membrane lung. This is the only circumstance in which CO_2 clearance is less than oxygenation. The reason is that fibers filled with water loose the gradient for CO_2 transfer, but the water is full of oxygen so oxygenation continues.

ECMO Management When the Native Lung Is Recovering

All the preceding discussions describe a situation when there is no native lung function. As the native lung begins to recover, some oxygen and CO_2 exchange will occur. The effect will be to improve systemic arterial oxygenation and Pa_{CO_2} with no change in the extracorporeal flow rate and hemoglobin. It is tempting to increase ventilator settings and Fi_{O_2} in order to take advantage of this recovery, but this may add to lung injury and delay lung recovery. Rest settings are continued, and when arterial P_{CO_2} drops below 40, the sweep gas to the membrane lung can be proportionally decreased. When the systemic arterial saturation exceeds 95%, the extracorporeal flow can be gradually decreased (changing the ratio of circuit to native venous flow). When native lung function is sufficient for total patient support, ECMO can be discontinued. Because reestablishing vascular access in ECMO can be difficult, it is wise to continue ECMO support for a day or 2 beyond this point to allow more lung recovery, unless there is a pressing reason to take the patient off ECMO (systemic bleeding or central nervous system complications).

Managing VV ECMO Based on These Principles

1. Plan the circuit based on the best estimation of the metabolic rate (adults, 3-4 ml/kg/min for both O_2 and CO_2) and the drainage flow, which can be achieved from the largest drainage cannula (or cannulas) that can be placed. Plan for total support, realizing that there may be some native lung function and total support may not be necessary. For a septic 80-kg adult, you will need 5 L/min flow and an oxygenator with rated flow over 5 L/min to supply 300 ml O_2/min.
2. On ECMO, go to the highest flow to determine the maximum capacity, then turn down the ventilator to rest settings (Fi_{O_2} 0.3, continuous positive airway pressure 15-20 cm H_2O) and wean off the vasoactive drugs. The hypermetabolism will decrease to baseline. The lungs may go to total consolidation. Adjust the sweep gas to keep the Pa_{CO_2} 40 mm Hg.
3. When the patient is stable (usually 6-12 hours), determine the variables of O_2 kinetics, using the formulas and nomograms described above. If oxygen supply is adequate (DO_2:V_{O_2} over 3), no changes are necessary. If the oxygen supply is more than adequate (DO_2:V_{O_2} over 5), turn down the flow until the ratio is 4. If oxygen supply is inadequate (DO_2:V_{O_2} under 3) and the patient is anemic, transfuse to a higher hemoglobin (12-14 g%). This will result in arterial saturation around 90% and venous saturation around 65% (DO_2–V_{O_2} 3-4).
4. Manage the patient based on continuous venous and arterial saturation monitoring. Plot the position on Figure 8 frequently. Calculate the variables if oxygen supply seems excessive or inadequate.
5. When the native lung begins to recover (the arterial saturation is >95%), turn down the flow, keeping the venous saturation >70%. When the flow is half of total venous return, start trials off ECMO at modest ventilator settings.

Conclusion

Understanding the basic physiology of blood oxygenation and oxygen delivery in relation to consumption is elementary in any patient in respiratory failure. With ECMO, we can control many of these variables that are difficult to control with conventional care. With that ability and understanding, we can manage severe respiratory failure without the damaging effects of mechanical ventilation. Treating anemia is often necessary for optimal management. Correct use of ECMO in the VV mode often results in arterial saturation less than 90% and Pa_{O_2} less than 50 mm Hg. Intensive care unit staff may need to be educated to understand why this level of oxygenation is adequate, even desirable, when patients with respiratory failure are managed with ECMO.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. West J. *Respiratory Physiology. The Essentials*. 6th ed. Baltimore, MD: Lippincott Williams and Wilkins; 1999.
2. Bartlett RH. *Critical Care Physiology*. Ann Arbor, MI: Scholarly Publishing Office, University of Michigan; 2010.
3. Bartlett RH. Physiology of ECLS. In: Van Meurs KP, Lally KP, Peek G, Zwischenberger, eds. *ECMO: Extracorporeal Cardiopulmonary Support in Critical Care*. 3rd ed. Ann Arbor, MI: Extracorporeal Life Support Organization; 2005:5-27.
4. Spinelli E, Bartlett RH. Relationship between hemoglobin concentration and extracorporeal blood flow as determinants of oxygen delivery during VV-ECMO: a mathematical model. *ASAIO J*. 2014;60(6):688-693.