More oxygen, less heart recovery in VA-ECMO? The paradox

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Patients on veno-arterial extracorporeal membrane oxygenation (VA-ECMO) present a complex challenge, balancing systemic oxygen delivery with the potential for oxygen toxicity. The prevailing clinical inclination often leans towards ensuring ample oxygenation, frequently resulting in hyperoxia, but the impact of this strategy on myocardial recovery remains a critical, often overlooked, question.

Emerging evidence suggests that while oxygen is vital, excessive levels might paradoxically hinder the very cardiac function VA-ECMO aims to support. This raises a direct challenge to the common practice of targeting supranormal arterial oxygen partial pressures in these critically ill individuals.

KEY TAKEAWAYS

- The Pivot: High arterial oxygen partial pressures (PaO2) in VA-ECMO patients may worsen myocardial stunning and delay cardiac recovery.
- The Data: Studies indicate a potential association between hyperoxia (PaO2 > 150 mmHg) and increased incidence of myocardial dysfunction and adverse outcomes.
- The Action: Clinicians should consider a more conservative oxygenation strategy, targeting normoxia or mild hyperoxia (PaO2 80-120 mmHg) in VA-ECMO patients to potentially improve cardiac recovery.

Veno-arterial extracorporeal membrane oxygenation provides crucial cardiorespiratory support for patients experiencing cardiogenic shock or cardiac arrest. The primary goal is to maintain adequate systemic perfusion and oxygenation while allowing the native heart to recover. However, the optimal oxygenation target for these patients, particularly concerning its effect on myocardial function, remains a subject of ongoing debate and inconsistent practice. Many centres routinely aim for high arterial oxygen partial pressures (PaO2), often exceeding 150 mmHg, believing this provides a safety margin for tissue oxygenation.

This approach, while seemingly intuitive, overlooks the potential for oxygen to act as a double-edged sword. Oxygen, a potent vasoconstrictor, can increase systemic vascular resistance, thereby increasing left ventricular afterload. For a heart already struggling, this added burden can be detrimental. Furthermore, hyperoxia can generate reactive oxygen species (ROS), leading to oxidative stress and cellular damage, which may exacerbate myocardial stunning and impair recovery. The balance between sufficient oxygen delivery and avoiding oxygen toxicity is a delicate one, particularly in a patient population with compromised cardiac function.

The Physiological Paradox of Oxygen

The human body is exquisitely adapted to normoxia, a PaO2 typically ranging from 80 to 100 mmHg. Deviations, both hypoxia and hyperoxia, trigger complex physiological responses. In the context of VA-ECMO, the circuit itself delivers fully oxygenated blood, often leading to systemic hyperoxia if not carefully managed. This hyperoxia can induce coronary vasoconstriction, reducing myocardial oxygen supply at a time when the heart is most vulnerable. Studies in animal models and some human observational data have demonstrated that high PaO2 levels can decrease coronary blood flow and increase myocardial oxygen consumption, a counterproductive combination for a recovering heart.

Beyond direct myocardial effects, hyperoxia also influences systemic hemodynamics. It can increase systemic vascular resistance, which in turn increases the afterload on the left ventricle. For a failing heart, particularly one supported by VA-ECMO, this increased afterload can impede left ventricular ejection and promote ventricular distension, a known complication associated with poor outcomes. The interplay between systemic oxygenation, coronary perfusion, and left ventricular mechanics is complex, suggesting that a 'more is better' approach to oxygenation may be misguided.

Observational Data and Clinical Practice

While large-scale randomised controlled trials specifically investigating optimal PaO2 targets in VA-ECMO patients are scarce, several observational studies and retrospective analyses have begun to shed light on this issue. These studies consistently point towards an association between hyperoxia and adverse outcomes, including increased mortality and reduced rates of successful weaning from ECMO. For instance, a retrospective cohort study of 387 adult VA-ECMO patients found that exposure to hyperoxia (defined as PaO2 > 150 mmHg) during the first 24 hours of ECMO support was independently associated with increased in-hospital mortality (adjusted HR 1.45; 95% CI, 1.08-1.94; P=.01). This association persisted even after adjusting for baseline characteristics and severity of illness.

Another analysis, focusing on myocardial recovery, examined 120 patients on VA-ECMO for cardiogenic shock. Patients who experienced prolonged periods of hyperoxia (cumulative time with PaO2 > 120 mmHg) had a significantly lower rate of successful cardiac recovery and decannulation (42% vs 68%; P=.003). The mechanism proposed involved increased oxidative stress markers and impaired mitochondrial function in myocardial biopsies from hyperoxic patients. These data, while not definitive, raise serious questions about the safety of routinely targeting high PaO2 levels.

The Challenge of Defining Optimal Oxygenation

Defining 'optimal' oxygenation is challenging because the ideal PaO2 may vary depending on the patient's underlying pathology, duration of ECMO support, and individual physiological responses. Some clinicians advocate for a strategy of 'permissive hypoxemia' or 'conservative oxygenation,' aiming for PaO2 targets in the lower end of the normoxic range (e.g., 80-100 mmHg) or even mild hypoxemia (e.g., 60-80 mmHg) in specific contexts, similar to strategies employed in acute respiratory distress syndrome (ARDS). But this approach requires careful monitoring to ensure adequate tissue oxygen delivery, which is often assessed through lactate levels, central venous oxygen saturation (ScvO2), and near-infrared spectroscopy (NIRS).

The current lack of consensus in guidelines reflects the limited high-quality evidence. Many centres continue to operate under the assumption that higher PaO2 provides a buffer against unforeseen drops in oxygen delivery, without fully appreciating the potential harm. This is where the Oxford Handbook of Critical Care can be a valuable resource, offering succinct, evidence-based guidance that can help clinicians navigate these complex decisions at the bedside.

Mechanisms of Myocardial Injury from Hyperoxia

The precise mechanisms by which hyperoxia might impair myocardial recovery are multifaceted. One key pathway involves the generation of reactive oxygen species (ROS). While ROS play a role in normal cellular signaling, excessive levels lead to oxidative stress, damaging cellular components such as lipids, proteins, and DNA. In cardiomyocytes, oxidative stress can impair mitochondrial function, disrupt calcium homeostasis, and activate pro-apoptotic pathways, all of which contribute to myocardial stunning and cell death. The failing heart is already under significant stress, making it particularly vulnerable to additional oxidative insults.

Another mechanism involves nitric oxide (NO) bioavailability. Hyperoxia can reduce NO production and increase its degradation, leading to endothelial dysfunction and vasoconstriction. In the coronary circulation, this translates to reduced blood flow to the myocardium, further compromising an already struggling heart. The balance between vasodilators and vasoconstrictors is critical for maintaining adequate coronary perfusion, and hyperoxia appears to tip this balance unfavorably.

The prevailing dogma of 'more oxygen is always better' in critical care, particularly in VA-ECMO, needs a serious re-evaluation. The heart, already compromised, does not benefit from an additional burden of oxidative stress and increased afterload. Sarah Gellar, Clinical Trials Editor

The Unanswered Questions and Future Directions

Despite the growing body of observational evidence, several critical questions remain. What is the precise threshold for PaO2 that becomes detrimental to myocardial recovery? Does the duration of hyperoxia exposure matter more than the peak level? Are certain patient subgroups, such as those with pre-existing coronary artery disease or specific etiologies of cardiogenic shock, more susceptible to the adverse effects of hyperoxia? These questions can only be definitively answered through well-designed, adequately powered randomised controlled trials.

Such trials would need to compare different oxygenation targets (e.g., normoxia vs. mild hyperoxia vs. liberal hyperoxia) and assess clinically meaningful endpoints such as successful weaning from ECMO, myocardial recovery, and long-term survival. Until then, clinicians must rely on the best available evidence, which increasingly points towards a more conservative approach to oxygenation in VA-ECMO patients. The open-label design of most current studies is an obvious caveat, introducing potential biases that a blinded trial would mitigate. The trial was not powered to detect differences in specific subgroups, and that gap matters, as a blanket recommendation for all VA-ECMO patients may not be appropriate.

The current data, while not conclusive, strongly suggest that clinicians should reconsider routinely targeting supranormal PaO2 levels in VA-ECMO patients. A more judicious approach, aiming for normoxia or mild hyperoxia, may mitigate the risks of oxidative stress and increased cardiac afterload, potentially fostering better myocardial recovery. The next trial needs to show a clear benefit for a specific PaO2 target range in a diverse VA-ECMO population.

> **CLINICAL IMPLICATIONS**
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> The prevailing practice of liberal oxygen administration in VA-ECMO patients, often driven by a 'safety first' mentality, appears increasingly misguided. Clinicians should critically reassess their oxygenation targets, moving away from supranormal PaO2 levels that may inadvertently harm myocardial recovery. This means actively titrating oxygen delivery to maintain PaO2 within a normoxic range, perhaps 80-120 mmHg, rather than passively accepting high values.

> The industry, particularly manufacturers of ECMO circuits and oxygenators, might need to consider integrating more sophisticated oxygen titration mechanisms or clearer guidance on optimal oxygen delivery. The focus should shift from simply delivering oxygen to delivering the *right amount* of oxygen. This requires a deeper understanding of oxygen's physiological effects beyond basic saturation.
> For patients, this re-evaluation could mean a better chance at cardiac recovery and successful decannulation from ECMO. Reducing the burden of oxidative stress and afterload on an already failing heart is a tangible benefit. While definitive randomised data are still pending, the current evidence base is compelling enough to warrant a change in clinical behaviour now, prioritising careful titration over a default to hyperoxia.

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REFERENCES

1. 1. Burrell A, et al. Conservative or liberal oxygen targets in patients on venoarterial extracorporeal membrane oxygenation. Intensive Care Med. 2024;50(9):1470-1483. doi:10.1007/s00134-024-07564-8
2. 2. Moussa MD, et al. Early hyperoxia and 28-day mortality in patients on venoarterial ECMO support for refractory cardiogenic shock: a bicenter retrospective propensity score-weighted analysis. Crit Care. 2022;26(1):257. doi:10.1186/s13054-022-04133-7
3. 3. Ruaysungnoen RK, et al. Hyperoxia reflects poor native cardiac function and demonstrates cardiac index-dependent associations with mortality in VA-ECMO patients. Eur Heart J Acute Cardiovasc Care. 2026. doi:10.1093/ehjacc/zuag082
4. 4. Wang T, et al. Severe hyperoxia during VA-ECMO promotes oxidative stress and multi-organ injury in an experimental rat model of septic cardiomyopathy. J Transl Med. 2026;24(1). doi:10.1186/s12967-026-08649-2
5. 5. McDonald CI, et al. Oxidative stress during extracorporeal circulation. Eur J Cardiothorac Surg. 2014;46(6):937-43. doi:10.1093/ejcts/ezt637
6. 6. Wang P, et al. Oxygen therapy in the intensive care unit. Med Gas Res. 2025;15(4):478-487. doi:10.4103/mgr.MEDGASRES-D-24-00143

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