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Commentary: Is perfusate arterial oxygen tension the best barometer of inflammation following cardiopulmonary bypass for congenital heart surgery?

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Exposure to cardiopulmonary bypass, with its attendant activation of the inflammatory and coagulation cascade, is inevitable for a patient undergoing congenital heart surgery. Optimal perfusion requires management of physiologic variables such as mean arterial blood pressure, hematocrit level, flow rate, temperature, oxygen delivery (DO_2), pH, and arterial carbon dioxide tension/arterial oxygen tension (PaO_2) management.¹ The ultimate goal is to deliver a healthy, long-term survivor without gross organ dysfunction.

One of the components of DO_2 is PaO_2 . During cardiopulmonary bypass, PaO_2 is measured as the oxygen tension in the perfusate (Ppao_2). In this issue of *the Journal*, Liu and associates² have conducted an elegant study of the effects of Ppao_2 on children (>1 month) and young adults (<18 years) from different geographic locations (and thusly, altitude) across China. The cohort was separated into 2 groups based on the patients' low- or high-altitude residence. The primary outcome, occurrence of severe systemic inflammatory response syndrome (SIRS), was nearly identical (18.27% vs 18.79% for low- vs high-altitude, respectively). However, upon a detailed look at the secondary outcomes, patients at greater altitudes had longer hospital length of stay and in-hospital mortality (despite the fact that overall

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CENTRAL MESSAGE

Controlled reoxygenation rather than hyperoxygenation is beneficial in mitigating the inflammatory response, especially in cyanotic patients.

mortality in this cohort of >6300 patients was a remarkable 0.35%).

With steady ascent in altitude, a multitude of physiologic changes occur, chief among those are enhanced oxygen delivery and uptake, allowing the process of adaptation, or acclimatization. Acclimatization was not accounted for, and it is unknown whether these patients had their surgery performed at a center with an altitude different from where they reside. Furthermore, these adaptive changes start to occur at or above altitudes of >1500 m above sea level.³ It is difficult to conceive that said adaptations have occurred at the authors' chosen altitude threshold of 500 m. Moreover, this lower threshold may introduce an "altitude bias" that precludes correctly interpreting their results, especially when others⁴ have found equal surgical outcomes at greater altitudes when compared with outcomes at sea level. Lastly, without the preoperative oxygen saturation levels, the gradual oxygen saturation decline seen with decrease in barometric pressure with greater altitudes⁵ could not be analyzed.

The range of Ppao_2 , to which patients of both groups were exposed, was 250 to 350 mm Hg, a number that other investigators,⁶ including previous work from the same group,⁷ would define as hyperoxia. Ultimately, using complex statistics, the authors found that a Ppao_2 threshold of >310 mm Hg for low-altitude patients and >350 mm Hg for high-altitude patients was associated with a high probability of development of severe SIRS. Based on these findings, the authors recommend keeping Ppao_2 <365 mm Hg for all patients.

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Hyperoxia is injurious to the homeostasis of patients with cyanosis and by no means inconsequential. Specific perfusion details, such as flow rate goal or transfusion triggers that impact DO_2 , were not described. Although not studied by Liu and associates,² other investigators have showed the effects of hyperoxia in the inflammatory response leading to SIRS, in particular: (1) complement activation, interleukin (IL)-6, IL-8, IL-10, or cortisol levels representing whole body inflammation⁸; (2) release of troponin-I reflecting myocardial cell damage and oxidative stress⁹; (3) protein S-100 (cerebral damage); and (4) alpha-glutathione S-transferase (hepatic cell damage). The release of these key markers has been shown to be mitigated by controlled reoxygenation rather than hyperoxygenation, with maximum clinical benefit for univentricular hearts.⁹ By that rationale, controlled reoxygenation rather than hyperoxygenation makes physiologic sense, particularly for single-ventricle (who are in a constant-state of hypoxemia) and cyanotic bi-ventricular patients (whom hypoxemia tends to fluctuate).

In summary, the impact of inflammation in patients undergoing congenital heart surgery can't be underestimated. Ppao_2 plays a small, albeit important role, especially when controlled reoxygenation is selectively used for cyanotic and single-ventricle patients.

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