Declarations of interest

The authors declare that they have no conflicts of interest.

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Critical indexed oxygen delivery as a cornerstone of goal-directed perfusion in neonates undergoing cardiac surgery. Comment on Br J Anaesth 2020; 124: 395-402

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Editor—We read with great interest the paper by Bojan and colleagues[1] on oxygen delivery during cardiopulmonary bypass (CPB) in neonates. They report a retrospective cohort study on the critical indexed oxygen delivery ($\dot{D}_{O_2}i$) threshold during normothermic CPB in neonates according to serum lactate concentration measured after aortic unclamping (lactOFF). Using lactOFF >2.5 mM to identify anaerobic metabolism, they found that 340 ml min^{-1} m^{-2} is likely to represent the nadir $\dot{D}_{O_2}i$ for maintenance of aerobic metabolism in neonates. A further reduction of 100 ml min^{-1} m^{-2} below the critical $\dot{D}_{O_2}i$ threshold would lead to a 1 mM increment in lactOFF. The results should provide new ideas for optimising perfusion strategy and improving the prognosis in neonatal cardiac surgery with CPB.

Optimal perfusion should maintain microcirculatory and organ function by preserving endothelial function, capillary density, and $\dot{D}_{O_2}$ at the tissue level.[2,3] Thus, $\dot{D}_{O_2}i$ is one of the most important determinants of optimal perfusion during CPB. The minimal safe $\dot{D}_{O_2}i$ during CPB, or critical $\dot{D}_{O_2}i$, is the point when the maximal oxygen extraction is reached, whole-body oxygen consumption ($\dot{V}_{O_2}$) and tissue oxygenation begin to decrease, and anaerobic metabolism and lactic acidosis begin to develop.[3] $\dot{D}_{O_2}i$ is determined by two main variables: haemoglobin concentration and pump flow.[2]

$$\dot{D}O_2i\left(ml\,min^{-1}m^{-2}\right) = pump\ flow\left(L\,min^{-1}\,m^{-2}\right)\Big/ body\ surface\ area\left(m^2\right) \times \Big[1.36 \times haemoglobin\left(g\,L^{-1}\right) \times haemoglobin\ saturation\ (\%) + 0.031 \times partial\ pressure\ of\ arterial\ oxygen\ (mm\ Hg)\Big]$$

Therefore, measuring $\dot{D}_{O_2}i$ should guide the perfusionist in adjusting arterial pump flow according to the haemoglobin concentration and to implement ultrafiltration or red blood cell transfusion.

Maintaining $\dot{D}_{O_2}i$ above the critical value on CPB is vital to improve tissue perfusion and individualise the conduct of bypass to the particular patient, and is the core idea of goal-directed perfusion. This strategy, introduced in recent years, involves aggressive patient management and incorporates continuous monitoring of such oxygen metabolism parameters as $\dot{D}_{O_2}i$, oxygen extraction index, and carbon dioxide production.[4] Goal-directed perfusion could be even more beneficial to early detection of hypoperfusion and anaerobic metabolism during CPB, thus allowing timely and appropriate intervention to ensure adequate or optimal tissue perfusion. Before this report, clinical trials on critical $\dot{D}_{O_2}i$ threshold and goal-directed perfusion approaches focused exclusively on adult cardiac surgery under CPB.[5–10] The landmark goal-directed perfusion studies from Ranucci and colleagues[5,6] showed that a nadir $\dot{D}_{O_2}i$ of 272 ml min^{-1} m^{-2} during CPB was independently associated

with renal replacement-acute renal failure and $\dot{D}_{O_2}i$ <260 ml min^{-1} m^{-2} with increased lactate production. De Somer and colleagues[7] reported that a nadir $\dot{D}_{O_2}i$ <262 ml min^{-1} m^{-2} and a nadir $\dot{D}_{O_2}/\dot{V}_{CO_2}$ ratio <5.3 were independently associated with postoperative acute kidney injury (AKI), and a multicentre randomised controlled trial (RCT)[8] showed that maintaining $\dot{D}_{O_2}i$ on CPB above 280 ml min^{-1} m^{-2} was effective in reducing Acute Kidney Injury Network Stage 1 postoperative AKI. Moreover, Mukaida and colleagues[9] tested the time–dose–response of $\dot{D}_{O_2}i$ during CPB as a better indicator than nadir $\dot{D}_{O_2}i$ in evaluating AKI risk, and showed that maintaining $\dot{D}_{O_2}i$ >300 ml min^{-1} m^{-2} may result in less postoperative AKI. Whereas goal-directed perfusion has been discussed to some extent in the adult literature, the development and application of goal-directed perfusion plans in paediatric CPB are still scarce.

To implement goal-directed perfusion approaches in paediatrics, the critical $\dot{D}_{O_2}i$ threshold in neonates, infants, and children must be determined. The critical $\dot{D}_{O_2}i$ threshold for adults cannot be applied directly to paediatrics, where it could cause severe hypoxaemia because of the much higher metabolic rate and oxygen demand of children. Collateral circulation in cyanotic congenital heart disease resulting in a shunt from systemic circulation to pulmonary circulation makes these patients more prone to tissue oedema and inflammatory responses during CPB; these are important factors affecting tissue oxygen delivery in neonates and infants.The study by Bojan and colleagues[1] undoubtedly sets a precedent in the field of paediatric goal-directed perfusion, an emerging concept with the potential to address the lack of universal guidelines in paediatric patients.

The current critical $\dot{D}_{O_2}i$ of 340 ml min^{-1} m^{-2} is higher than that reported in adult cardiac surgery of 262–300 ml min^{-1} m^{-2}, which is inconsistent with the physiological requirements of neonates. We are conducting a pilot prospective cohort study to explore the critical $\dot{D}_{O_2}i$ threshold in infant cardiac surgery patients (<3 yr old) undergoing mild hypothermic CPB and the association with postoperative AKI (trial registration number: ChiCTR1900028683). A nadir $\dot{D}_{O_2}i$ <352 ml min^{-1} m^{-2} was independently associated with postoperative AKI in infants. The primary outcome was the rate of postoperative AKI, instead of lactate concentration chosen in the study of Bojan and colleagues.[1] Different study subjects and primary outcomes may contribute to the different results of these two trials. As to lactate formation and postoperative AKI, which one is better to determine the critical $\dot{D}_{O_2}i$? Lactate is used as a marker for oxygen deficiency in anaerobic metabolism at the tissue level and is associated with cellular dysfunction as a result of depletion of high-energy phosphate compounds.[10] However, priming components, such as packed red blood cells and type of crystalloid solution, are believed to affect lactate formation in patients undergoing CPB. High lactate levels also correlate with glucose concentrations.[6] Moreover, there is no uniform definition of hyperlactataemia during CPB. Why lactate >2.5 mM was chosen by Bojan and colleagues[1] to identify hyperlactataemia during CPB, instead of lactate >3 mM as in the similar study by Ranucci and colleagues[6] in adult cardiac surgery or lactate >2 mM in the most recent publication by Matteucci and colleagues,[11] is not clear.

In summary, Bojan and colleagues[1] have begun to bring the goal-directed perfusion concept to paediatric CPB. Despite their interesting findings, it may still be too early to implement goal-directed perfusion approaches in this complex patient population. Additional studies, especially RCTs, are needed to focus on evaluation of the appropriate goal-directed perfusion indicators in paediatrics, and the effects of goal-directed perfusion methods on morbidity and mortality.

Declarations of interest

The authors declare that they have no conflicts of interest.

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