Review Article on Pediatric Heart

Cardiopulmonary bypass in neonates and infants: advantages of high flow high hematocrit bypass strategy—clinical practice review

Karthik Ramakrishnan[1,2]^, Tk Susheel Kumar[3], Umar S. Boston[1,2], Jerry Allen[1], Christopher J. Knott-Craig[1,2]

[1]Division of Pediatric Cardiovascular Surgery, LeBonheur Children's Hospital, Memphis, TN, USA; [2]Department of Surgery, University of Tennessee Health Sciences Center, Memphis, TN, USA; [3]Division of Surgery, NYU Langone Hospital, New York, NY, USA

Contributions: (I) Conception and design: K Ramakrishnan, CJ Knott-Craig; (II) Administrative support: None; (III) Provision of study materials or patients: J Allen; (IV) Collection and assembly of data: J Allen; (V) Data analysis and interpretation: K Ramakrishnan, CJ Knott-Craig, US Boston, TS Kumar; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Christopher J. Knott-Craig, MD, FACS. Division of Pediatric Cardiovascular Surgery, LeBonheur Children's Hospital, 49 N Dunlap St., Memphis, TN 38105, USA; Department of Surgery, University of Tennessee Health Sciences Center, Memphis, TN, USA. Email: cknottcr@uthsc.edu.

Abstract: Cardiopulmonary bypass is an integral and indispensable part of surgical repair of congenital heart defects. While the complications and morbidity secondary to the use of cardiopulmonary bypass has decreased considerably, there remains a significant incidence of clinically relevant renal and neurological injury. To provide more physiological delivery of oxygenated blood to the end-organs, our center has been successfully using a high-flow, high hematocrit cardiopulmonary bypass strategy since 2006. The essential components of this strategy include maintaining high flows (typically 200 mL/kg/min in neonates, 150–175 mL/kg/min in older infants weighing <10 kg, and 2.6 L/min/m^2 in older children) throughout the duration of cardiopulmonary bypass irrespective of patient temperature, as well as maintaining a hematocrit of at least 32% on cardiopulmonary bypass. The incidence of post-operative acute kidney injury (around 3%) and clinical acute neurological events (<1%) with this strategy is considerably less when compared to other contemporary publications using the conventional cardiopulmonary bypass strategy. In this review, we discuss the rationale behind our approach and present evidence to support the high-flow, high-hematocrit strategy. We also discuss the practical aspects of our strategy and describe the adjuncts we use to derive additional benefits. These adjuncts include the use of a hybrid pH/alpha stat strategy during cooling/rewarming, aggressive use of conventional ultrafiltration during cardiopulmonary bypass, a terminal hematocrit of 40–45%, and avoidance of milrinone and albumin in the early peri-operative period. This results in a very low incidence of post-operative bleeding, facilitates chest closure in the operating room even in most neonates, helps in reducing the need for post-operative blood product transfusion and helps in achieving a favorable post-operative fluid balance early after surgery.

Keywords: Cardiopulmonary bypass; pediatric; infants; neonates; congenital heart disease

Submitted Feb 15, 2023. Accepted for publication Jun 30, 2023. Published online Jul 17, 2023.
doi: 10.21037/tp-23-94
View this article at: https://dx.doi.org/10.21037/tp-23-94

^ ORCID: 0000-0003-4042-4679.

Introduction

The first ever clinical application of cardiopulmonary bypass for repair of congenital cardiac defects was conducted by John Gibbon Jr in 1953. The early years of cardiopulmonary bypass were characterized by the use of in-house built crude hardware that were expensive, bulky and complicated to operate (1). This was associated with high mortality and morbidity even for repair of simple congenital heart defects. Over the last several decades, there have been tremendous improvements in hardware technology as well as understanding of cardiopulmonary physiology that has made open heart surgery safer. This has translated into improvements in outcomes and a drastic reduction in mortality, especially in neonates and infants. Despite these advances, there is a significant incidence of post-operative elevated serum lactate levels, renal dysfunction and neurodevelopmental sequelae (2-6). Certain aspects of pediatric cardiopulmonary bypass are well standardized. There is little variation, if any, in the hardware component of pediatric cardiopulmonary bypass. The bypass tubings, cannulae and oxygenators are each available in different sizes suitable for the smallest of neonates to older children and teens. The physiological aspect and the actual conduct of cardiopulmonary bypass, however, varies among institutions. Over five decades of clinical experience has led to the practice of what we henceforth refer to as the conventional or traditional way of conducting pediatric cardiopulmonary bypass. In brief, this includes a lower flow rate tailored to patient temperature on bypass, the use of minimum accepted safe hematocrit (hematocrit equals temperature) level on bypass and the liberal use of blood and blood products after cessation of cardiopulmonary bypass. In contrast, our institution has adopted a high-flow, high-hematocrit strategy to mitigate the effects of inadequate oxygen delivery [cardiac output times oxygen carrying capacity (7)], and to facilitate a smooth post-bypass course. This review will elaborate on the benefits of our strategy and the outcomes we have achieved over the last 15 years.

Conventional cardiopulmonary bypass strategies

The primary purpose of cardiopulmonary bypass is to provide adequate oxygen delivery to the end-organs that closely mimick native cardiac output. In children, the normal cardiac index ranges between 3.5 and 5 L/min/m^2 (8). Normal cardiac output in neonates and infants ranges between 200 to 350 mL/kg/min (9,10). Conventional cardiopulmonary bypass strategies typically use flows of 2.4 L/min/m^2 which translates to around 150 mL/kg/min for neonates. The description of conventional cardiopulmonary bypass is based on what is published in literature (11-14) and in textbooks of cardiopulmonary bypass and cardiac surgery (Principles of Cardiopulmonary Bypass-Gravlee, Comprehensive Surgical Management of Congenital Heart Disease-Jonas, Pediatric Cardiac Surgery-Mavroudis and Backer). These flows are considerably lower than normal cardiac output but are still considered 'adequate' to provide adequate systemic oxygen delivery during general anesthesia. The flows are further reduced based on the patient's temperature with flows of 1.6 L/min/m^2 used at a temperature of 28 ℃ and 1.0 L/min/m^2 used at temperatures lower than 25 ℃. These numbers are based mainly on decades of clinical experience to achieve a balance between providing adequate oxygen deliveries to all vital organs while avoiding the potential theoretical consequences of hyper perfusion. The hematocrit in the traditional approach is maintained around 25% and not higher based on publications from the Boston hematocrit trials (15). Ultrafiltration, both conventional and modified are used but are more focused on volume removal and if hemoconcentration is a target, the hematocrit goal is set at 35% (16). Administration of calcium prior to separating off cardiopulmonary bypass or use of calcium infusion as an inotrope is not routinely practiced in this approach. Blood products including platelets, fresh frozen plasma and cryoprecipitate are administered along with or soon after administration of protamine. Milrinone is often used in the early post-operative period to prevent post-operative low cardiac output syndrome (17).

High flow, high hematocrit strategy: rationale and practice

The high incidence of renal dysfunction after pediatric cardiac surgery prompted a rethink in the way we conduct cardiopulmonary bypass. For the past 16 years or so our cardiopulmonary bypass strategy at LeBonheur Children's Hospital, Memphis, Tennessee has primarily been based on providing higher than 'standard' flows to provide better end-organ perfusion. Although the exact origin of this strategy is unclear, it partly stems from the senior author's (CJKC) experience way back prior to at least 2002 with the use of this strategy in the adult population with excellent neurological outcomes (18). *Table 1* lists the essential differences between the conventional approach and the

Table 1 Basic differences between conventional CPB and high-flow; high-hematocrit CPB

Parameters on CPB	Conventional	High-flow; high-hematocrit
Minimum flows at normothermia (older infants and children)	2.4 L/min/m^2	2.6–3.0 L/min/m^2
Minimum flows for neonates	150 mL/kg/min	175–200 mL/kg/min
Flows between 26–30 ℃	1.6–2 L/min/m^2 or 100 mL/kg/min	2.6 L/min/m^2 or 150–175 mL/kg/min
Lowest hematocrit on CPB	25%	32%
Hematocrit while coming off CPB	30%	40–45%[†]

[†], higher hematocrit for single ventricle palliations. CPB, cardiopulmonary bypass.

Table 2 Desired flows on cardiopulmonary bypass with high-flow; high-hematocrit strategy

Patient weight	Full flow
<2.5 kg	200 cc/kg
2.5 to 3.5 kg	175 cc/kg
>3.5 to 10 kg	150 cc/kg
>10 kg	2.6 L/min/m^2

high-flow strategy and is further elaborated here. The pump is primed with a balanced solution of Plasmalyte, fresh frozen plasma and packed red blood cells to achieve a post-dilutional hematocrit of >32%. The total prime volume is usually not more than 140 mL. In addition, 125 mL/kg of mannitol is added to the bypass circuit. 3/16 tubing sizes are used for flows less than 600 mL/min. The length of the tubing is also minimized as much as possible. Full flow rates are calculated based on weight (*Table 2*). It is typically around 175 mL/kg/min for neonates, 150 mL/kg for infants, and a cardiac index of >2.6 L/min/m^2 for those >10 kg. To achieve and maintain these flows, appropriately sized venous cannulae are chosen. We prefer to use plastic tipped right-angled venous cannulae. As a rough guide, the following cannula size/flow rate is used to decide on the size of the cannula to be used. A 10 F venous cannula can flow up to 250 mL/min, a 12 F can flow 450 mL/min, a 14 F can flow up to 600 mL/min and a 16 F can flow up to 900 mL/min. For example, if a neonate needs a flow of 600 mL/min, then a combination of 10 F (250 mL/min) and 12 F (450 mL/min) will be used. The cannulae are positioned in the respective vena cavae and vacuum assist is used if needed. The heart should be completely empty once both venous cannulae are placed and full bypass flows are achieved. In some instances, circulatory arrest is utilized at deep hypothermia to facilitate repair (some examples include atrial septal defect closure during arterial switch operation, aortic arch reconstruction, and selected total anomalous pulmonary venous return repairs). The flows are maintained during cooling, even at profound hypothermia (15 degrees). Cooling to deep hypothermia is carried out over a minimum of 20 min. Flows are reduced at deep hypothermia to 50 mL/kg/min prior to ceasing cardiopulmonary bypass for circulatory arrest. A pH strategy is used during cooling. Just prior to circulatory arrest on deep hypothermia, the excess carbon dioxide is washed off. Alpha stat strategy is used during rewarming. Conventional ultrafiltration is used to maintain a hematocrit of >32% on bypass. During the rewarming phase, conventional ultrafiltration is used to raise the hematocrit to 40% (45% for single ventricle palliation) before weaning off bypass. Prior to separating off bypass, 400 mg of calcium chloride (600 mg for older children), is administered through the bypass circuit. In neonates and infants, an infusion of calcium chloride (5–10 mg/kg/h) with an infusion of Dopamine (3–5 μg/kg/min) is initiated prior to separation from bypass. Protamine is administered along with 10 mL/kg of platelets for patients undergoing deep hypothermia. Surgical bleeding spots are sought only after administration of protamine and platelets. Additional blood products are used, if necessary, but our experience shows that they are needed only in the rarest of rare cases. We do not use milrinone in the immediate post-operative period (usually the first 24 to 48 h) since it is a potent vasodilator and is associated with renal injury (17,19). We also avoid the use of albumin for the first 24 h. The volume of distribution of albumin, like those in critically ill patients, may be higher in the post cardiopulmonary bypass period, thereby contributing to third spacing and interstitial edema often encountered in these neonates (20). We prefer to use fresh frozen plasma or crystalloids like normal saline for volume replacement, or packed red blood cells if the hematocrit is low.

Outcomes of high-flow, high hematocrit strategy

Some of our outcomes with our strategy has been previously published. The incidence of post-operative acute kidney injury with our strategy was first reported in 2016 (21). In this study, 102 neonates and young infants who underwent open heart surgery with or without circulatory arrest were analyzed. The overall incidence of post-operative acute kidney injury was 11%, with none of the patients having advanced renal failure. At the time of publication this incidence of post-operative acute kidney injury was much lower than contemporary cohorts using conventional bypass (22,23). The mean intra-operative lactate in this study was 1.59 and 1.74 mmol/dL at 24 and 48 h. This led to a prospective bi-institutional comparative study directly comparing the high-flow strategy with the conventional strategy (24). Over a one-year period, all neonates and infants undergoing open heart surgery were prospectively enrolled at our center and at a reputable nationally recognized high-volume center using the conventional bypass approach. The incidence of post-operative acute kidney injury in the high-flow cohort was significantly lower (3.3% *vs.* 15.4%, P<0.03). Lower flows on cardiopulmonary bypass as well as lower hematocrit at the end of bypass were the only significant factors associated with post-operative acute kidney injury. The conventional group utilized 30% more packed red blood cells in the prime and on pump, and 60% more fresh frozen plasma than our high flow cohort. The high-flow cohort showed significantly better and consistent fluid balance in the first 72 h after operation. The high flow cohort also had a greater proportion of primary chest closures in the operating room (3% *vs.* 26%).

We have also recently reported an analysis of post-operative acute clinical neurological events with the use of our strategy (25). Seven hundred and fourteen children who underwent open heart surgery at our center were included in the study. The incidence of post-operative acute clinical neurological event was less than 1%. This again compares favorably with historical and contemporary data using the same diagnostic criteria (2.4–6%) (26,27).

Apart from preserving renal and neurological function, there are several other advantages to the high-flow, high-hematocrit strategy. A higher post-bypass hematocrit makes the blood more viscous. This prevents blood from seeping out through the needle holes and facilitates hemostasis. Reduced bleeding also helps in avoiding post-bypass blood product transfusion and facilitates primary chest closure even in complex newborns. In our experience the time from separation from bypass to the end on skin closure averaged 61 min for patients undergoing deep hypothermia. Higher hematocrit also increases oxygen delivery, maintains cardiac output, prevents secondary end-organ injury, helps maintain favorable post-operative fluid balance, and in general ensures a smooth post-operative period with faster recovery. This unpublished data was presented at the annual meeting of the Congenital Heart Surgeons' Society in 2018. Eighty-one consecutive neonates undergoing open heart surgery with the use of deep hypothermia and circulatory arrest between 2012 and 2018 were included for analysis. Forty-two patients underwent Norwood operation, 30 had an arterial switch, 16 underwent repair of truncus arteriosus and 12 had repair of interrupted aortic arch. Chest was primarily closed in 75% of this patient cohort. Only a fraction of the Norwood patients had their chest left open. 4/81 (5%) or needed additional cryoprecipitate or platelets for bleeding. The median number of blood products used in the operating room (including the priming volume) was 1 unit each of packed red blood cells, fresh frozen plasma and platelets. The average time to close the chest from cessation of bypass was 61 min.

High-flow strategy also results in low intra-operative and post-operative lactate levels indicating a global benefit in maintaining end-organ perfusion. In our most recent analysis, 155 neonates and infants who underwent open heart operation over the last 2 years (January 2021 to October 2022) were included (*Table 3*). The primary aim was to look at the serum lactate levels during and after surgery. The median age of this cohort was 3 months [interquartile range (IQR), 3] and the median weight was 4.6 kg (IQR, 2.7). 19% of the patients were in STAT 4 (n=19, 12%) or 5 (n=11, 7%) mortality categories. The median baseline hematocrit was 37% (IQR, 10%), hematocrit on bypass was 33% (IQR, 4%), and the hematocrit soon after coming off bypass was 43 (IQR, 6). Serum median lactate levels on bypass was 1.47 mmol/dL (IQR, 2), immediate post-bypass was 1.37 mmol/dL (IQR, 2), 24 h post-bypass was 0.92 mmol/dL (IQR, 0.7), and 48 hours post-bypass was 0.8 mmol/dL (IQR, 0.7) (*Figure 1*). The lactate clearance, calculated as (initial lactate-delayed lactate)×100/initial lactate as described by Ladha *et al.* with a cut-off greater than 10% indicating adequate lactate clearance (28) was 12% in the first 6 h and 28% in the first 24 h. The incidence of acute kidney injury, as defined by the Kidney Disease Improving Global Outcomes (KDIGO) criteria (29) was 9% (14/155), with 2/155 (1.3%) in advanced renal failure or stage 3 renal

Table 3 Characteristics and outcomes of the high-flow; high-hematocrit strategy (n=155)

Variables	Values
STAT categories	
STAT 1	55 (35%)
STAT 2	41 (26%)
STAT 3	29 (19%)
STAT 4	19 (12%)
STAT 5	11 (7%)
Age (months)	3 (IQR, 3)
Weight (kg)	4.6 (IQR, 2.7)
Hematocrit on bypass	33% (IQR, 4)
Post-bypass hematocrit	43% (IQR, 6)
Incidence of acute kidney injury (stage 3)	2 (1.3%)
Incidence of stroke	1 (<1%)
Incidence of hemolysis	0 (0%)
Low cardiac output syndrome	12 (7.7%)
Lactate clearance by day 1	28% (IQR, 52%)
Lactate levels on day 1 (mmol/dL)	0.92 (IQR, 0.7)
Vasoactive inotropic score (day 0)	5 (IQR, 3.5)
Vasoactive inotropic score (day 1)	4 (IQR, 8)
Vasoactive inotropic score (day 2)	0 (IQR, 6)

IQR, interquartile range.

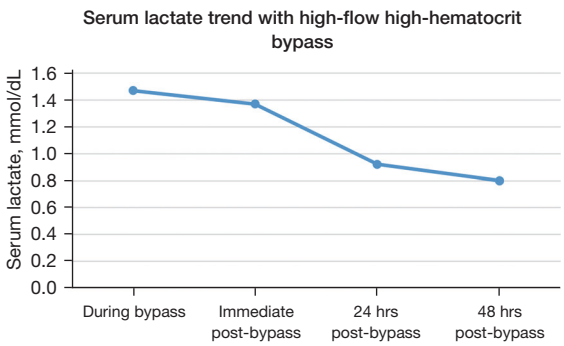

Figure 1 Peri-operative serum lactate.

failure. This included patients who needed extracorporeal life support (2/155—1.3%). None of the patients needed renal replacement therapy (including peritoneal dialysis). The adequacy of cardiac output is mainly determined by physical examination, serial lactate levels, arterial blood gas (base deficit) and end-organ function (urine output, serum creatinine, near infra-red spectroscopy, liver function tests). Mixed venous oxygen saturations are measured when the adequacy of cardiac output is equivocal. The incidence of persistent or new onset low cardiac output in our cohort was 7.7% (12/155). This compares favorably with the 25% incidence of low cardiac output reported in literature (30). The median vasoactive inotropic score (VIS) was 5 (IQR, 3.5) on the day of surgery, 4 (IQR, 8) on post operative day one and 0 (IQR, 6) on post-operative day 2. Most patients in our cohort were off inotropes within 48 to 72 h after surgery. There was no documented incidence of hemolysis. The incidence of new post-operative stroke was less than 1% (1/155) and 6/155 (3.9%) showed evidence of post-operative ventricular dysfunction that subsequently resolved. Primary chest closure was achieved in 140/155 (90%) with all open chests in the STAT 4/5 categories. The low lactate levels in the peri-operative period, adequacy of lactate clearance, low VIS, low incidence of low cardiac output syndrome and preservation of end-organ function attests to the success of our bypass strategy.

Discussion

The principal objective of cardiopulmonary bypass is to ensure adequate oxygen delivery (DO_2) to the vital organs during the conduct of open-heart surgery. The critical DO_2 necessary to preserve end-organ metabolism and prevent end-organ dysfunction following cardiopulmonary bypass has not been determined. The widely used current practice of providing a cardiac index of 2.2–2.4 L/min/m^2 at normothermia is based on the normal cardiac output estimated in an anesthetized adult with a normal hematocrit (31). Flows are further reduced at lower temperature based on the concept of temperature co-efficient (Q_{10}- the ratio of metabolic rates at two temperatures separated by 10 ℃). The

limitation of this strategy is evident by the high incidence of post-operative acute kidney injury and neurological injury (21,22,26,27,32). The lower oxygen delivery likely plays a role in precipitating acute kidney injury (33). Acute kidney injury has been noted in neonates even after operations without cardiopulmonary bypass. There are multiple factors that leads to acute kidney injury after cardiac surgery. Multi-institutional data from 22 north American centers revealed an estimated incidence of 54% (range, 27% to 86%) (34). A subsequent study also estimated the incidence of acute kidney injury in this cohort to be as high as 38% (35). Thus, cardiopulmonary bypass alone may not be a factor in determining the incidence of post cardiac surgical acute kidney injury. However, our own results and studies from other centers do indicate that the way cardiopulmonary bypass is conducted plays an important role in mitigating renal injury (7). A cumulative time spent below the critical oxygen delivery of 350 mL/min/m^2 is associated with acute kidney injury after cardiopulmonary bypass in children (7). Oxygen delivery to the tissues depend on two critical factors—the cardiac output and the hematocrit. The amount of oxygen delivered (DO_2) is the product of the cardiac output and the amount of oxygen carried in the blood (31). DO_2 can thus be optimized by increasing the flows on cardiopulmonary bypass (i.e., the 'cardiac' output) as well as by maintaining a higher hematocrit. This lays the physiologic foundation for high-flow, high-hematocrit cardiopulmonary bypass.

The concept of high-flow high-hematocrit has been known for a since the early 2000s (14,36). However, its application has not gained popularity due to the lack of systematic studies. Our long experience of over a decade and robust data from our patient population attests to the safety and efficacy of the high-flow high-hematocrit strategy. This approach has now been validated by other groups. A recent publication from Cincinatti Children's hospital reported a significantly lower incidence of acute kidney injury with the use of higher flows on cardiopulmonary bypass (37). In addition to the low incidence of post-operative end-organ dysfunction, our strategy also results in normal intra-operative and post-operative serum lactate levels. Serum lactate levels are a direct indicator of adequacy of systemic perfusion. It has prognostic significance too, with higher levels associated with prolonged and complicated hospital course (4). Thus, the lower lactate levels achieved with our strategy translates to better outcomes.

Contrary to the expectation that maintaining a higher hematocrit requires more exposure to more blood products, our use of blood products is not any greater. We are able to achieve this with the use of tailored smaller sized circuits, lower pump prime volume, use of adequately sized cannulae and generous use of ultrafiltration on bypass. Strategies have been described to avoid or minimise blood transfusion in neonates undergoing open heart procedures (38,39). The trade-off in these strategies has been accepting a lower hematocrit. With our strategy we have been able to minimize the use of donor blood while at the same time maintain a higher hematocrit. A higher terminal hematocrit also has a hemostatic effect, and this results in a lower post-operative transfusion requirement thereby balancing out the overall use of blood products.

Overall, there still seems to be a wide variation in the practice of pediatric perfusion. Recent evidence has emerged that a minimum threshold of oxygen delivery is necessary to preserve end organ function (7,33). Our results with high-flow, high-hematocrit strategy has shown promising outcomes with a low incidence of complications. This has also been adopted with modifications by other centers over the years (14,37). Prospective studies with well-defined protocols can further define the safety and efficacy of this approach. These studies can focus on more intense monitoring of end organ perfusion and a more careful evaluation of potential complications to overcome the limitations of a limited retrospective analysis.

Conclusions

High-flow; high-hematocrit bypass strategy is easily adaptable and has several advantages. The key benefits are preservation of renal and neurological function, ability to achieve hemostasis without the need for a lot of additional blood products, lesser duration of operation, higher chance of primary chest closure, stable and favorable post-operative fluid balance, and faster post-operative recovery.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Antonio F. Corno and Jorge D. Salazar) for the column "Pediatric Heart" published in *Translational Pediatrics*. The article has undergone external

peer review.

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-23-94/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-23-94/coif). The column "Pediatric Heart" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Stoney WS. Evolution of cardiopulmonary bypass. Circulation 2009;119:2844-53.
2. Sharma A, Chakraborty R, Sharma K, et al. Development of acute kidney injury following pediatric cardiac surgery. Kidney Res Clin Pract 2020;39:259-68.
3. Arslanoğlu E, Kara KA, Yiğit F, et al. Neurological complications after pediatric cardiac surgery. The Cardiothoracic Surgeon 2021;29:19.
4. Basaran M, Sever K, Kafali E, et al. Serum lactate level has prognostic significance after pediatric cardiac surgery. J Cardiothorac Vasc Anesth 2006;20:43-7.
5. Desplanque L, Hamaide-Defrocourt F, Berkia I, et al. Lactate clearance in infants undergoing surgery for congenital heart disease. Artif Organs 2019;43:54-9.
6. Kanazawa T, Egi M, Shimizu K, et al. Intraoperative change of lactate level is associated with postoperative outcomes in pediatric cardiac surgery patients: retrospective observational study. BMC Anesthesiol 2015;15:29.
7. Hayward A, Robertson A, Thiruchelvam T, et al. Oxygen delivery in pediatric cardiac surgery and its association with acute kidney injury using machine learning. J Thorac Cardiovasc Surg 2023;165:1505-16.
8. Cattermole GN, Leung PY, Ho GY, et al. The normal ranges of cardiovascular parameters measured using the ultrasonic cardiac output monitor. Physiol Rep 2017;5:e13195.
9. Hudson I, Houston A, Aitchison T, et al. Reproducibility of measurements of cardiac output in newborn infants by Doppler ultrasound. Arch Dis Child 1990;65:15-9.
10. Walther FJ, Siassi B, Ramadan NA, et al. Pulsed Doppler determinations of cardiac output in neonates: normal standards for clinical use. Pediatrics 1985;76:829-33.
11. Hirata Y. Cardiopulmonary bypass for pediatric cardiac surgery. Gen Thorac Cardiovasc Surg 2018;66:65-70.
12. Whiting D, Yuki K, DiNardo JA. Cardiopulmonary bypass in the pediatric population. Best Pract Res Clin Anaesthesiol 2015;29:241-56.
13. Pouard P, Bojan M. Neonatal cardiopulmonary bypass. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2013;16:59-61.
14. Corno AF. What are the best temperature, flow, and hematocrit levels for pediatric cardiopulmonary bypass? J Thorac Cardiovasc Surg 2002;124:856-7; author reply 857.
15. Wypij D, Jonas RA, Bellinger DC, et al. The effect of hematocrit during hypothermic cardiopulmonary bypass in infant heart surgery: results from the combined Boston hematocrit trials. J Thorac Cardiovasc Surg 2008;135:355-60.
16. Ziyaeifard M, Alizadehasl A, Massoumi G. Modified ultrafiltration during cardiopulmonary bypass and postoperative course of pediatric cardiac surgery. Res Cardiovasc Med 2014;3:e17830.
17. DiNardo JA, Nasr VG. Milrinone Administration and Pediatric Cardiac Surgery: Beloved but Sadly Misunderstood. J Cardiothorac Vasc Anesth 2021;35:2079-81.
18. Yuh WT, Knott-Craig CJ, Tilak MD. Cognitive outcomes following cardiopulmonary bypass. JAMA 2002;287:3078; author reply 3078-9.
19. Amin K, Bastani B. Incidence of Acute Renal Failure Associated with Milrinone. Journal of Pharmacy Technology 2005;21:21-4.
20. Crystalloid, colloid, albumin? BMJ 1998;317. doi: https://doi.org/10.1136/bmj.317.7153.0.
21. Kumar TK, Allen Ccp J, Spentzas Md T, et al. Acute Kidney Injury Following Cardiac Surgery in Neonates and

Young Infants: Experience of a Single Center Using Novel Perioperative Strategies. World J Pediatr Congenit Heart Surg 2016;7:460-6.
22. Piggott KD, Soni M, Decampli WM, et al. Acute Kidney Injury and Fluid Overload in Neonates Following Surgery for Congenital Heart Disease. World J Pediatr Congenit Heart Surg 2015;6:401-6.
23. Park SK, Hur M, Kim E, et al. Risk Factors for Acute Kidney Injury after Congenital Cardiac Surgery in Infants and Children: A Retrospective Observational Study. PLoS One 2016;11:e0166328.
24. Tadphale SD, Ramakrishnan K, Spentzas T, et al. Impact of Different Cardiopulmonary Bypass Strategies on Renal Injury After Pediatric Heart Surgery. Ann Thorac Surg 2021;111:1374-9.
25. Chakraborty A, Ramakrishnan K, Buyukgoz C, et al. Incidence of Acute Neurological Events in Neonates and Infants Undergoing Cardiac Surgery Using a High-Hematocrit/ High-Flow Bypass Strategy. World J Pediatr Congenit Heart Surg 2023;14:375-9.
26. Bell JL, Saenz L, Domnina Y, et al. Acute Neurologic Injury in Children Admitted to the Cardiac Intensive Care Unit. Ann Thorac Surg 2019;107:1831-7.
27. Menache CC, du Plessis AJ, Wessel DL, et al. Current incidence of acute neurologic complications after open-heart operations in children. Ann Thorac Surg 2002;73:1752-8.
28. Ladha S, Kapoor PM, Singh SP, et al. The role of blood lactate clearance as a predictor of mortality in children undergoing surgery for tetralogy of Fallot. Ann Card Anaesth 2016;19:217-24.
29. Sutherland SM, Byrnes JJ, Kothari M, et al. AKI in hospitalized children: comparing the pRIFLE, AKIN, and KDIGO definitions. Clin J Am Soc Nephrol 2015;10:554-61.
30. Chandler HK, Kirsch R. Management of the Low Cardiac Output Syndrome Following Surgery for Congenital Heart Disease. Curr Cardiol Rev 2016;12:107-11.
31. Murphy GS, Hessel EA 2nd, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. Anesth Analg 2009;108:1394-417.
32. Tanyildiz M, Ekim M, Kendirli T, et al. Acute kidney injury in congenital cardiac surgery: Pediatric risk-injury-failure-loss-end-stage renal disease and Acute Kidney Injury Network. Pediatr Int 2017;59:1252-60.
33. Gao P, Jin Y, Zhang P, et al. Nadir oxygen delivery is associated with postoperative acute kidney injury in low-weight infants undergoing cardiopulmonary bypass. Front Cardiovasc Med 2022;9:1020846.
34. Gist KM, Blinder JJ, Bailly D, et al. Neonatal and Paediatric Heart and Renal Outcomes Network: design of a multi-centre retrospective cohort study. Cardiol Young 2019;29:511-8.
35. Sasaki J, Rodriguez Z, Alten JA, et al. Epidemiology of Neonatal Acute Kidney Injury After Cardiac Surgery Without Cardiopulmonary Bypass. Ann Thorac Surg 2022;114:1786-92.
36. Durandy Y, Hulin S, Lecompte Y. Normothermic cardiopulmonary bypass in pediatric surgery. J Thorac Cardiovasc Surg 2002;123:194.
37. Reagor JA, Clingan S, Gao Z, et al. Higher Flow on Cardiopulmonary Bypass in Pediatrics Is Associated With a Lower Incidence of Acute Kidney Injury. Semin Thorac Cardiovasc Surg 2020;32:1015-20.
38. Naguib AN, Winch PD, Tobias JD, et al. A single-center strategy to minimize blood transfusion in neonates and children undergoing cardiac surgery. Paediatr Anaesth 2015;25:477-86.
39. Boettcher W, Dehmel F, Redlin M, et al. Cardiopulmonary Bypass Strategy to Facilitate Transfusion-Free Congenital Heart Surgery in Neonates and Infants. Thorac Cardiovasc Surg 2020;68:2-14.

Cite this article as: Ramakrishnan K, Kumar TS, Boston US, Allen J, Knott-Craig CJ. Cardiopulmonary bypass in neonates and infants: advantages of high flow high hematocrit bypass strategy—clinical practice review. Transl Pediatr 2023;12(7):1431-1438. doi: 10.21037/tp-23-94