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Recommendations on the Indications for Red Blood Cell Transfusion for the Critically Ill Child Receiving Support from Extracorporeal Membrane Oxygenation, Ventricular Assist, and Renal Replacement Therapy Devices from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative

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Abstract

OBJECTIVE—To present recommendations and supporting literature for red blood cell (RBC) transfusions in critically ill children supported with extracorporeal membrane oxygenation (ECMO), ventricular assist devices (VAD) or renal replacement therapy (RRT).

DESIGN—Consensus conference series of international, multidisciplinary experts in RBC transfusion management of critically ill children

METHODS—The panel of 38 experts developed evidence-based and when evidence was lacking, expert-based clinical recommendations as well as research priorities for RBC transfusions in critically ill children. The ECMO/VAD/RRT subgroup included six experts. We conducted electronic searches of the PubMed, Embase, and Cochrane Library (CENTRAL) databases from 1980 to May 2017, using medical subject heading terms and text words to define concepts of RBC transfusion, ECMO, VAD, and RRT. We used a standardized data extraction form to construct

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evidence tables and graded the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Recommendations developed and supporting literature were reviewed and scored by all panel members. Agreement was obtained using the Research And Development/University of California, Los Angeles (RAND/UCLA) appropriateness method.

RESULTS—For inpatients requiring ECMO, VAD, or RRT support, there was expert agreement (>80%) on five good practice statements aimed to improve accuracy and uniform reporting of RBC transfusion data in pediatric ECMO, VAD, and RRT studies and quality improvement projects; four clinical recommendations of physiologic metrics and biomarkers of oxygen delivery, in addition to hemoglobin concentration, to guide RBC transfusion, acknowledging insufficient evidence to recommend specific RBC transfusion strategies; and eight research recommendations.

CONCLUSIONS—Further research surrounding indications, risks, benefits, and alternatives to RBC transfusion in children on extracorporeal devices is clearly needed. Using a structured literature review and grading process, the TAXI panel concluded that there is currently insufficient evidence to recommend specific RBC transfusion parameters in children requiring ECMO, VAD, or RRT support.

Keywords

extracorporeal life support; ECLS; extracorporeal membrane oxygenation; ECMO; ventricular assist device; mechanical circulatory support; renal replacement therapy; dialysis; transfusion; blood; red blood cell; hemoglobin; intensive care; child; pediatric critical care; evidence-based; consensus conference

INTRODUCTION

The use of extracorporeal devices in children with cardiac, respiratory, and/or renal failure has increased significantly over the last two decades, partly driven by continued improvement in biocompatibility and safety features that allow for deployment of such devices in critically ill infants and children (1–3). With the increase in use of extracorporeal support, concern has also increased over the burden of red blood cell (RBC) transfusion in these patients as well as RBC transfusion-associated morbidity and cost.

Exposure to RBC administration in children with extracorporeal devices occurs in several ways. Neonates and small children are exposed to transfused RBCs through priming of the device at initiation of support as well as when devices need to be replaced due to thrombosis, malfunction, or other indications. Once on the device, RBCs may be transfused for active hemorrhage, which is estimated to occur in as many as one third of extracorporeal membrane oxygenation (ECMO) patients and one third of ventricular assist devices (VAD) patients (4, 5). Lastly, RBCs are often transfused in children on ECMO or VADs to maintain hemoglobin (Hb) concentrations at pre-set levels based on varied institutional practices with the presumed goal of optimizing oxygen delivery. There are no published evidence-based guidelines to direct clinicians on when to transfuse RBCs in patients supported on extracorporeal devices in the absence of active bleeding. Therefore, large variability in practice exists (6). We present recommendations for clinical practice as supported by the review of the pediatric literature on indications for RBC transfusion in critically ill children

supported with ECMO, VADs, or renal replacement therapy (RRT). Recommendations for future research are also provided.

METHODS

The details of the methodology are described elsewhere in this supplement of *Pediatric Critical Care Medicine* (7). Briefly, we searched PubMed, EMBASE, and Cochrane Library from 1980 to December 2015, with an update in May 2017, using a combination of medical subject heading terms and text words to define concepts of RBC transfusion, ECMO, VAD, and RRT. We searched references from identified articles for additional publications. Two authors reviewed all citations independently. We used a standardized data extraction form to construct evidence tables and graded the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. A panel of 38 experts from 29 academic institutions in 8 countries met over the course of two years to develop evidence-based and, when evidence was lacking, expert-based recommendations for RBC transfusion in critically ill children. Recommendations developed and supporting literature were reviewed and scored by all panel members, using the Research And Development/University of California Appropriateness Method (RAND/UCLA). All recommendations reached agreement (>80%). Final recommendations for RBC transfusion in critically ill children with ECMO, VAD, and RRT devices were divided into three categories: good practice statements, clinical recommendations, and research recommendations.

RESULTS

Using the search strategy described above, we retrieved 2782 abstracts. 81 papers were retained for the full-text evaluation, 21 papers included, among which 13 papers were selected and used in the final process to generate the following good practice statements, clinical and research recommendations, and are presented in the Supplemental Digital Content 1.

Good Practice Statements

8.1—In critically ill children on ECMO, we recommend reporting Hb concentration, rather than hematocrit, for RBC transfusion threshold algorithms. *Consensus panel expertise, 97% Agreement, n=35, median 8 (IQR 8-9)*

Rationale—Historically, most ECMO publications used hematocrit thresholds for RBC transfusions (8–15). However, in the current era, RBC transfusion research in critical care is overwhelmingly conducted using Hb (not hematocrit) thresholds, including in pediatric populations (16, 17). Using Hb to align RBC transfusion threshold reporting in ECMO patients with RBC transfusion threshold reporting in critically ill non-ECMO populations will allow on- and off-ECMO comparisons within these populations (e.g., acute respiratory distress syndrome, cardiac arrest, cardiogenic shock, etc.). Indeed, some adult ECMO centers have been reporting Hb thresholds for transfusion based on extrapolation of evidence from non-ECMO critically-ill populations (18).

8.2—In critically ill children on ECMO, we recommend measuring Hb concentration before all RBC transfusion, unless the patient experiences life-threatening bleeding. *Consensus panel expertise, 97% Agreement, n=35, median 8 (IQR 8-9)*

8.3—In critically ill children on ECMO, we recommend that adoption of blood sparing and conservation procedures and guidelines should be implemented. *Consensus panel expertise, 94% Agreement, n=35, median 8 (IQR 8-9)*

8.4—In critically ill children on ECMO, we recommend taking measures to minimize the number of donor exposures. *Consensus panel expertise, 97% Agreement, n=35, median 8 (IQR 8-9)*

8.5—In critically ill children on ECMO, we recommend that all RBC exposure within circuit prime be reported in pediatric ECMO transfusion studies and quality improvement projects. *Consensus panel expertise, 94% Agreement, n=35, median 8 (IQR 8-9)*

Rationale—It is currently not possible to combine results from multiple studies of RBC transfusion during ECMO (i.e., conduct a meta-analysis) due to variability in reporting of RBC exposure including or excluding RBC priming of ECMO circuit(s) (8–14). Furthermore, not accounting for exposure to RBCs used for priming likely underestimates the number of donor exposures for pediatric ECMO patients.

Clinical Recommendations: ECMO

8.6—In critically ill children on ECMO, we recommend using physiologic metrics and biomarkers of oxygen delivery, in addition to Hb concentration, to guide RBC transfusion. Administration of a RBC transfusion should be based on evidence of inadequate cardiorespiratory support or decreased systemic and/or regional oxygen delivery. *Weak recommendation, low quality pediatric evidence (2C), 97% Agreement, n=35, median 8 (IQR 8-9)*

Rationale—ECMO patients receive large amounts of RBCs, ranging on average from 42 ml/kg/day to up to 105 ml/kg/day (8, 9, 11, 19). The number of donor exposures in ECMO patients, therefore, ranges from a median of 1.4 to 10.9 per ECMO course (8, 12–15, 20). Indications for RBC transfusion are primarily based on expert Extracorporeal Life Support Organization (ELSO) clinical guidelines, last updated in 2013, recommending to maintain hematocrit above 40% during ECMO, in an effort to “optimize oxygen delivery while allowing the lowest reasonable ECMO circuit flow” (21). However, ECMO medical directors in a recent survey reported lower hematocrit thresholds for RBC transfusion: medians of 35% (range, 25%–40%) for pediatric-only programs and 30% (range, 20%–40%) for adult-only and mixed adult and pediatric programs (6).

Adult ECMO centers are reporting adoption of restrictive transfusion strategies based on evidence in critically ill patients, with Hb thresholds as low as 7g/dl, without adverse effects noted (18, 22). As pediatric ECMO patients were excluded from pediatric trials of restrictive vs liberal RBC transfusion strategies (16), evidence is insufficient to support a specific hemoglobin or hematocrit threshold for RBC transfusions in this population. Furthermore,

pediatric ECMO patients may have varying requirements for RBC transfusion based on age, variable physiology of the underlying disease, or mode of ECMO support (venoarterial vs venovenous). Adhering to a normal/near-normal hemoglobin/hematocrit threshold without considering adequacy of systemic and/or regional oxygen delivery (e.g., systemic oxygen saturation, mixed venous saturation, lactate, cerebral oximetry, somatic oximetry, etc.) could expose pediatric ECMO patients to unnecessary RBC transfusions. While pediatric evidence is scant, Fiser et al showed in a single center pediatric ECMO study (n=45 patients with a median of 9 RBC transfusion events per patient, range, 1–57) that a majority (>70%) of transfusions were administered when systemic mixed venous oxygen saturation was adequate (8). In the same study, the authors showed that tissue oxygenation measures, including mixed venous saturation and cerebral oximetry, were not significantly altered following RBC transfusions. Only 31/617 (5%) of RBC transfusions administered resulted in an increase in mixed venous saturation of >5%, whereas an increase in cerebral regional oxygen saturation of more than 5% was only observed in 53/617 (9%) of transfusions (8). *GRADE 2C for this recommendation was based on the pediatric literature discussed above, with downgrading for risk of bias, indirectness and residual confounding.*

8.7—In critically ill children on ECMO, there is insufficient evidence to recommend a specific RBC transfusion decision-making strategy using physiologic-based metrics and biomarkers. *Consensus panel expertise, 97% Agreement, n=35, median 8 (IQR 8-9)*

Clinical Recommendations: VAD

8.8—In critically ill children on VAD support, we recommend using physiologic metrics and biomarkers of oxygen delivery, in addition to Hb concentration, to guide RBC transfusion. Administration of a RBC transfusion should be based on evidence of inadequate cardiorespiratory support or decreased systemic and/or regional oxygen delivery. *Consensus panel expertise, 94% Agreement, n=35, median 8 (IQR 8-9)*

Rationale—There are no published prospective studies on optimal Hb and/or physiologic transfusion thresholds in critically ill children with VADs. Children with VADs were excluded from the major pediatric critical care randomized controlled trial of a restrictive vs. liberal transfusion strategy (16). AHA guidelines for mechanical circulatory support in the ambulatory and community setting emphasize the potentially detrimental role of RBC transfusion in the “bridge-to-transplant” patient due to increase in anti-HLA antibodies that could complicate donor matching, recommending that transfusion should be “targeted to symptomatic patients only” (23).

Providers are cautioned to avoid anemia in mechanical circulatory support patients, due to its association with increased morbidity and mortality in this population (23, 24). In the critical care environment, similar to ECMO patients, children with VADs receive large volumes of RBCs. Stiller et al reported that in a single center where transfusion was guided by a Hb threshold of 9 g/dl children received 17.2 ml RBCs/kg/day during the first 8 days of VAD support (20). In a different cohort, Guynes et al reported that pediatric VAD patients in a single center received 676 ml RBCs/kg/patient during the entire VAD course; of note, transfusion triggers were not reported in this study (25). With regards to ABO and HLA

sensitization, in two single center studies of pediatric mechanical circulatory support, 29% of patients developed ABO sensitization, and 43% of patients developed HLA sensitization (25, 26). The volume of transfusions was not associated with development of sensitization, but small sample sizes and retrospective design were limitations noted for both studies (25, 26).

8.9—In critically ill children on RRT support, we recommend using the smallest circuit size that will provide adequate RRT, while minimizing a driver for RBC transfusion specific to RRT (i.e., loss of blood volume that arises with circuit dysfunction/replacement of the circuit). *Consensus panel expertise, 100% Agreement, n=35, median 9 (IQR 8-9)*

Rationale—There are no published prospective studies on the optimal Hb and/or physiologic transfusion threshold for pediatric patients supported with RRT. The one way to avoid excess blood exposure is to minimize the circuit volume that has significant impact in the smaller (i.e., <20 kg) children. Presently in the U.S., the smallest RRT circuit volume is ~ 83 ml, making it a possibility to use in 10 kg children without a blood prime unless hemodynamics dictate otherwise. Outside of the U.S., approved circuit volumes range from 60 ml and miniaturized circuits are currently under study in the U.K. and Italy, with volumes of 14 ml (NIDUS) and 27 ml (CARPEDIEM). Advances in miniature circuits as small as 3 ml are ongoing in Japan (27–29). In addition to these small circuits, the volume of the vascular access (usually 2 ml for each access port) need to be considered. This group of patients presents an additional challenge in having unpredictable renal synthesis of erythropoietin to stimulate hematopoiesis, potentially complicating transfusion needs.

Research Recommendations

R8.1—In critically ill children on ECMO who are stable and not experiencing hemorrhagic shock, we recommend that Hb concentrations and correlations with physiologic indications for RBC transfusion be studied to determine minimum thresholds for safety and efficacy of RBC transfusion. *Consensus panel expertise, 97% Agreement, n=35, median 9 (IQR 8-9)*

R8.2—In critically ill children on ECMO, we recommend undertaking future studies of oxygen delivery/consumption markers (e.g., mixed venous saturation, cerebral oximetry, somatic oximetry, etc.) in patients maintained at different Hb thresholds. Such studies will aim to determine the optimal physiologic thresholds for RBC transfusion during pediatric ECMO. *Consensus panel expertise, 91% Agreement, n=35, median 9 (IQR 8-9)*

R8.3—In critically ill children who suffer from cardiac arrest pre-ECMO (i.e., extracorporeal cardiopulmonary resuscitation [ECPR]) and critically ill children with acute neurologic injury during ECMO (e.g., embolic stroke, intracranial hemorrhage, etc.), we recommend undertaking future studies for RBC transfusion strategies that optimize neuroprotection and recovery. *Consensus panel expertise, 91% Agreement, n=35, median 8 (IQR 8-9)*

R8.4—In critically ill children on ECMO, we recommend undertaking future studies of the types of RBC manipulations and attributes and their impact on outcomes (e.g., storage

duration, irradiation, leukoreduction, filtration, matching for CMV/EBV serologic status, extended minor antigen matching, washing, etc.). *Consensus panel expertise, 94% Agreement, n=35, median 8 (IQR 8-9)*

R8.5—In critically ill children on VAD support, we recommend undertaking future studies of oxygen delivery/consumption markers (e.g., mixed venous saturation, cerebral oximetry, somatic oximetry, etc.) in association with RBC transfusions and Hb concentrations. Such studies will aim to determine the optimal physiologic thresholds for RBC transfusion during pediatric VAD support. *Consensus panel expertise, 100% Agreement, n=35, median 8.5 (IQR 8-9)*

R8.6—In critically ill children on VAD/ECMO support, we recommend undertaking future studies to determine the impact of RBC transfusions on allo-sensitization, success of organ acquisition and/or risk of rejection. *Consensus panel expertise, 100% Agreement, n=35, median 8 (IQR 8-9)*

R8.7—In critically ill children on VAD support, we recommend undertaking future studies of the types of RBC manipulations and attributes and their impact on outcomes (e.g., storage duration, irradiation, leukoreduction, filtration, matching for CMV/EBV serologic status, extended minor antigen matching, washing, etc.). *Consensus panel expertise, 100% Agreement, n=35, median 8 (IQR 8-9)*

R8.8—In critically ill children on RRT support, we recommend undertaking future studies to evaluate approaches to optimize RRT length of use and hence minimize blood loss due to RRT circuit change/replacement. *Consensus panel expertise, 100% Agreement, n=35, median 8 (IQR 8-9)*

CONCLUSIONS

Using a structured literature review and grading process, the TAXI panel concluded there is currently insufficient evidence to recommend specific RBC transfusion parameters in children requiring ECMO, VAD, or RRT support. Further research surrounding indications, risk, benefits, and alternatives to RBC transfusion in children on extracorporeal devices is needed to better establish Hb and RBC-related strategies that optimize outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Barbaro RP, Paden ML, Guner YS, et al. Pediatric extracorporeal life support organization registry international report 2016. *ASAIO J.* 2017; 63:456–463. [PubMed: 28557863]
2. Burki S, Adachi I. Pediatric ventricular assist devices: Current challenges and future prospects. *Vasc Health Risk Manag.* 2017; 13:177–185. [PubMed: 28546755]
3. Kaddourah A, Goldstein SL. Renal replacement therapy in neonates. *Clin Perinatol.* 2014; 41:517–527. [PubMed: 25155724]
4. Thiagarajan RR, Barbaro RP, Rycus PT, et al. Extracorporeal life support organization registry international report 2016. *ASAIO J.* 2017; 63:60–67. [PubMed: 27984321]
5. Baumann Kreuziger L, Massicotte MP. Mechanical circulatory support: Balancing bleeding and clotting in high-risk patients. *Hematology Am Soc Hematol Educ Program.* 2015; 2015:61–68. [PubMed: 26637702]
6. Bembea MM, Annich G, Rycus P, et al. Variability in anticoagulation management of patients on extracorporeal membrane oxygenation: An international survey. *Pediatr Crit Care Med.* 2013; 14:e77–84. [PubMed: 23287906]
7. Bembea M, Valentine S, Bateman S, et al. The Pediatric Critical Care Transfusion and Anemia Expertise Initiative Consensus Conference Methodology. *Pediatr Crit Care Med.* 2018; 19 (xx Suppl): submitted.
8. Fiser RT, Irby K, Ward RM, et al. RBC transfusion in pediatric patients supported with extracorporeal membrane oxygenation: Is there an impact on tissue oxygenation? *Pediatr Crit Care Med.* 2014; 15:806–813. [PubMed: 25137550]
9. McCoy-Pardington D, Judd WJ, Knafl P, et al. Blood use during extracorporeal membrane oxygenation. *Transfusion.* 1990; 30:307–309. [PubMed: 2349629]
10. Smith A, Hardison D, Bridges B, et al. Red blood cell transfusion volume and mortality among patients receiving extracorporeal membrane oxygenation. *Perfusion.* 2013; 28:54–60. [PubMed: 22892295]
11. Henriquez-Henriquez M, Kattan J, Chang M, et al. Blood component usage during extracorporeal membrane oxygenation: Experience in 98 patients at a latin-american tertiary hospital. *Int J Artif Organs.* 2014; 37:233–240. [PubMed: 24744168]
12. Minifee PK, Daeschner CW 3rd, Griffin MP, et al. Decreasing blood donor exposure in neonates on extracorporeal membrane oxygenation. *J Pediatr Surg.* 1990; 25:38–42. [PubMed: 2299546]
13. Griffin MP, Minifee PK, Daeschner CW 3rd, et al. Benefits of a lower hematocrit during extracorporeal membrane oxygenation? *Am J Dis Child.* 1992; 146:373–374. [PubMed: 1543190]
14. Bjerke HS, Kelly RE Jr, Foglia RP, et al. Decreasing transfusion exposure risk during extracorporeal membrane oxygenation (ECMO). *Transfus Med.* 1992; 2:43–49. [PubMed: 1308462]
15. Rosenberg EM, Chambers LA, Gunter JM, et al. A program to limit donor exposures to neonates undergoing extracorporeal membrane oxygenation. *Pediatrics.* 1994; 94:341–346. [PubMed: 8065860]

16. Lacroix J, Hebert PC, Hutchison JS, et al. Transfusion strategies for patients in pediatric intensive care units. *N Engl J Med*. 2007; 356:1609–1619. [PubMed: 17442904]
17. Cholette JM, Swartz MF, Rubenstein J, et al. Outcomes using a conservative versus liberal red blood cell transfusion strategy in infants requiring cardiac operation. *Ann Thorac Surg*. 2017; 103:206–214. [PubMed: 27496630]
18. Agerstrand CL, Burkart KM, Abrams DC, et al. Blood conservation in extracorporeal membrane oxygenation for acute respiratory distress syndrome. *Ann Thorac Surg*. 2015; 99:590–595. [PubMed: 25499483]
19. Smith A, Hardison D, Bridges B, et al. Red blood cell transfusion volume and mortality among patients receiving extracorporeal membrane oxygenation. *Perfusion*. 2013; 28:54–60. [PubMed: 22892295]
20. Stiller B, Lemmer J, Merkle F, et al. Consumption of blood products during mechanical circulatory support in children: Comparison between ECMO and a pulsatile ventricular assist device. *Intensive Care Med*. 2004; 30:1814–1820. [PubMed: 15278265]
21. Extracorporeal Life Support Organization: ELSO guidelines for cardiopulmonary extracorporeal life support, version 1.3. Ann Arbor, MI: Extracorporeal Life Support Organization; 2013. <https://www.elseo.org/Resources/Guidelines.aspx> Edition
22. Voelker MT, Busch T, Bercker S, et al. Restrictive transfusion practice during extracorporeal membrane oxygenation therapy for severe acute respiratory distress syndrome. *Artif Organs*. 2015; 39:374–378. [PubMed: 25349127]
23. Cook JL, Colvin M, Francis GS, et al. Recommendations for the use of mechanical circulatory support: Ambulatory and community patient care: A scientific statement from the american heart association. *Circulation*. 2017; 135:e1145–e1158. [PubMed: 28559233]
24. Vrtovec B, Radovancevic R, Delgado RM, et al. Significance of anaemia in patients with advanced heart failure receiving long-term mechanical circulatory support. *Eur J Heart Fail*. 2009; 11:1000–1004. [PubMed: 19789404]
25. Guynes A, Delaney M, McMullan DM, et al. ABO blood group antibody levels in infants exposed to mechanical circulatory support. *ASAIO J*. 2014; 60:737–739. [PubMed: 25158885]
26. Hong BJ, Delaney M, Guynes A, et al. Human leukocyte antigen sensitization in pediatric patients exposed to mechanical circulatory support. *ASAIO J*. 2014; 60:317–321. [PubMed: 24469294]
27. Liu ID, Ng KH, Lau PY, et al. Use of HF20 membrane in critically ill unstable low-body-weight infants on inotropic support. *Pediatr Nephrol*. 2013; 28:819–822. [PubMed: 23306707]
28. Coulthard MG, Crosier J, Griffiths C, et al. Haemodialysing babies weighing. *Pediatr Nephrol*. 2014; 29:1873–1881. [PubMed: 25125229]
29. Ronco C, Garzotto F, Brendolan A, et al. Continuous renal replacement therapy in neonates and small children: development and first-in-human use of a miniaturized machine (CAPEDIEM). *Lancet*. 2014; 383(9931):1807–13. [PubMed: 24856026]

Appendix 1

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