Diagnosing Nosocomial Infections During Pediatric Extracorporeal Membrane Oxygenation

KEYWORDS: biomarkers; extracorporeal life support; inflammatory markers; sepsis; surveillance cultures

Erika R. O'Neil, MD[1,2]
Joseph E. Marcus, MD[2,3]
Graeme MacLaren, MBBS, MSc, FELSO, FCCM[4,5]

Nosocomial infections are one of the most frequent complications of extracorporeal membrane oxygenation (ECMO) and are associated with increased mortality (1). Bloodstream infections present a particular problem because of the risk of biofilm formation and the clinical challenges associated with cannula and circuit exchanges in this patient population (2). With their significant impact on patient outcomes, nosocomial infections on ECMO must be promptly recognized to ensure adequate treatment with antimicrobials and effective source control. Diagnosing these infections, however, can be difficult. Clinical and laboratory markers typically used to diagnose infections, such as WBC count, temperature dysregulation, or hemodynamic instability, are altered on ECMO due to the properties of both the ECMO circuit and the patient's underlying immune response to foreign material and critical illness (3). Furthermore, there are no widely accepted standardized definitions of infections during ECMO, and guidelines to diagnose and treat these infections do not yet exist (4). Given the grave consequences of missing a bloodstream infection in an ECMO patient, surveillance cultures are frequently collected to help diagnose these infections as early as possible (5, 6).

In this issue of *Pediatric Critical Care Medicine*, Schmoke et al (7) evaluated the use of daily surveillance blood cultures in neonatal and pediatric ECMO patients. In 111 patients, they reviewed 1059 surveillance blood cultures, which yielded only a 3% positivity rate. Similar to previous studies (1, 8–10), they found that surveillance cultures to diagnose bloodstream infections in ECMO patients are low-yield and this ultimately led to their center stopping the practice.

The study by Schmoke et al (7) highlighted the disadvantages of obtaining daily blood cultures and the potential costs associated with this practice. The authors calculated a direct cost-saving of $18,551 annually by stopping surveillance cultures. However, the indirect cost savings may be even greater if the price of additional antibiotic days, complications of broad-spectrum antibiotics, and nursing time are considered. The authors were also transparent about other drawbacks to obtaining surveillance blood cultures, such as the possibility of false positives from contamination that may expose patients to unnecessary antimicrobial administration, especially when using a definition as broad as any positive blood culture to indicate infection. Previous studies have suggested contamination rates as high as 3% in patients receiving ECMO (8). Blood loss from phlebotomy is another disadvantage, which in this population

DOI: 10.1097/PCC.0000000000003723

can directly lead to the need for blood transfusions and their associated risks (11). Additionally, the increased frequency of accessing a central or arterial line for cultures carries the risk of introducing infection.

This study had several limitations. First, the authors stated that all seven patients (of 111) with positive blood cultures also had clinical and laboratory markers of infections, suggesting that one could rely solely on clinical signs and biomarkers to detect infection. However, these signs and biomarkers are altered on ECMO and the authors did not comment on whether the patients with negative blood cultures lacked these changes (1). Additionally, they did not exclude other reasons for changes in clinical or laboratory markers, such as steroids leading to leukocytosis or inflammation from the interaction of blood with a nonbiological interface (2, 3, 12). Third, understandably in this population, small amounts of blood (3 to 5 mL) were collected for these cultures. Knowing that the sensitivity of blood cultures increases with the amount collected, this volume may have been insufficient to reliably detect infection (13). Finally, the authors did not describe infection control and prevention practices and antimicrobial prophylaxis strategies at their center, which may have had a significant impact on the yield of surveillance blood cultures.

Despite these limitations, the study by Schmoke et al (7) highlighted the ongoing challenges in diagnosing infections on ECMO, and the authors should be commended for using direct evidence to change their clinical practice. Addressing the lack of standardized definitions of infection on ECMO faced by this study, the ECMO "Core Elements Needed for Trials Regulation and Quality of Life" Academic Research Consortium recently created infection adverse event definitions in pediatric and neonatal ECMO to help provide clinicians and researchers with a common language (14). These definitions combine positive cultures with clinical and laboratory makers within a timeframe related to ECMO. Building upon a foundation of standardized definitions, clinicians can better track infections during ECMO and future studies can perhaps identify what clinical signs or laboratory markers are helpful in the early detection of infections.

In addition to standardized definitions, transparent reporting of practices across international ECMO centers through medical societies such as the Extracorporeal Life Support Organization will help determine strategies to decrease the burden of infectious complications. These data collected on center practices can then leverage the design, implementation, and study of evidence-based care bundles. ECMO infection prevention care bundles could target cannulation techniques or focus on the daily maintenance or access of the circuit (3). Until these best practices are determined, ECMO studies should transparently report their local protocols regarding infection control and prevention. Furthermore, ECMO centers should also create local care bundles to fit their institutions and patient populations with goals to minimize poor screening tests (e.g., daily surveillance cultures), implement infection prevention practices, and avoid unnecessary antimicrobials.

Ultimately, standardized definitions, transparent reporting, and the development of care bundles through international collaboration should improve outcomes for our patients on ECMO. In the meantime, there is accumulating evidence that daily surveillance cultures during ECMO are an unnecessary waste of time and money and that the practice should be abandoned.

1 *United States Air Force, Department of Pediatrics, Brooke Army Medical Center, San Antonio, TX.*

2 *Uniformed Services University of Health Sciences, Bethesda, MD.*

3 *United States Air Force, Infectious Diseases Service, Department of Medicine, Brooke Army Medical Center, San Antonio, TX.*

4 *Antimicrobial Stewardship Program, Division of Infectious Diseases, Department of Medicine, National University Hospital, Singapore.*

5 *Cardiothoracic ICU, National University Hospital, Singapore.*

The authors have disclosed that they do not have any potential conflicts of interest.

REFERENCES

1. MacLaren G, Schlapbach L, Aiken A: Nosocomial infections during extracorporeal membrane oxygenation in neonatal, pediatric, and adult patients: A comprehensive narrative review. *Pediatr Crit Care Med* 2020; 21:283–290
2. Marcus JE, Shah A, Peek GJ, et al: Nosocomial infections in adults receiving extracorporeal membrane oxygenation: A review for infectious diseases clinicians. *Clin Infect Dis* 2024; 79:412–419
3. Vazquez-Colon Z, Marcus JE, Levy E, et al: Infectious diseases and infection control prevention strategies in adult and pediatric population on ECMO. *Perfusion* 2024 Jun 11. [online first]

4. Sweet LM, Marcus JE: A systematic review of variability in the reporting of extracorporeal membrane oxygenation-associated infections and recommendations for standardization. *Am J Infect Control* 2024; 52:1209–1214
5. Farrell D, MacLaren G, Schlapbach LJ: Infections on extracorporeal life support in adults and children: A survey of international practice on prevention, diagnosis, and treatment. *Pediatr Crit Care Med* 2019; 20:667–671
6. Glater-Welt LB, Schneider JB, Zinger MM, et al: Nosocomial bloodstream infections in patients receiving extracorporeal life support: variability in prevention practices: A survey of the extracorporeal life support organization members. *J Intensive Care Med* 2016; 31:654–669
7. Schmoke N, Clark E, Nemeh C, et al: Daily surveillance blood cultures in children supported with extracorporeal membrane oxygenation: Single-center, retrospective cohort study, 2021–2023. *Pediatric Crit Care Med* 2025; 26:e447–e453
8. De Roux Q, Renaudier M, Bougouin W, et al: Diagnostic yield of routine daily blood culture in patients on venoarterial extracorporeal membrane oxygenation. *Crit Care* 2021; 25:241
9. Kaczala GW, Paulus SC, Al-Dajani N, et al: Bloodstream infections in pediatric ECLS: Usefulness of daily blood culture monitoring and predictive value of biological markers. The British Columbia experience. *Pediatr Surg Int* 2009; 25:169–173
10. Elerian LF, Sparks JW, Meyer TA, et al: Usefulness of surveillance cultures in neonatal extracorporeal membrane oxygenation. *ASAIO J* 2001; 47:220–223
11. Dalton HJ, Reeder R, Garcia-Filion P, et al; *Eunice Kennedy Shriver* National Institutes of Child Health and Human Development Collaborative Pediatric Critical Care Research Network: Factors associated with bleeding and thrombosis in children receiving extracorporeal membrane oxygenation. *Am J Respir Crit Care Med* 2017; 196:762–771
12. Ryerson LM, Annich G, Batchinsky A, et al: Adverse effects of extracorporeal life support. *In*: *Extracorporeal Life Support: The ELSO Red Book*. Sixth Edition. MacLaren G, Brodie D, Lorusso R, Peek G, et al (Eds). Ann Arbor, MI, ELSO, 2022, pp 97–111
13. Lamy B, Dargère S, Arendrup MC, et al: How to optimize the use of blood cultures for the diagnosis of bloodstream infections? A state-of-the art. *Front Microbiol* 2016; 7:697
14. Alexander PMA, Di Nardo M, Combes A, et al; Extracorporeal Life Support Organization (ELSO): Definitions of adverse events associated with extracorporeal membrane oxygenation in children: Results of an international Delphi process from the ECMO-CENTRAL ARC. *Lancet Child Adolesc Health* 2024; 8:773–780