REVIEW ARTICLE

https://doi.org/10.1590/1806-9282.20230491

Prevention of catheter-related bloodstream infections in patients with extracorporeal membrane oxygenation: a literature review

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INTRODUCTION

Intravenous catheters are the most common cause of bacteremia among healthcare-related infections (HCRIs)[1,2]. Intravenous catheters are most commonly used in intensive care units (ICUs). Catheter-related bloodstream infections (CRBSIs) in ICUs increase the length of stay, morbidity, mortality, and healthcare costs[3]. Extracorporeal membrane oxygenation (ECMO), which consists of invasive cannulas, is a type of extracorporeal life support (ECLS)[4]. It is used to manage the symptoms of patients with severe but reversible cardiac and/or pulmonary dysfunction. It is also sometimes used as a bridge to heart/lung transplantation[5]. It was first used in the 1950s in pediatric patients with severe cardiorespiratory failure. However, it has been widely used in adults when it resulted in increased 6-month survival in adults with severe acute respiratory distress syndrome (ARDS) during the H1N1 compared with conventional ventilation support[6]. ECMO was used in COVID patients who developed ARDS, and the reported survival rate was 33.3%[7].

ECMO is a simple cardiopulmonary bypass system that suctions venous deoxygenated blood from a large central vein through a venous cannula (16–29 Fr), oxygenates, and then restitutes it into the arterial or venous system [cannulas (20–29 Fr)] via a centrifugal pump[8]. According to the Extracorporeal Life Support Organization (ELSO), 176,496 patients underwent ECMO/ECLS support in 2021 for cardiac, respiratory, and resuscitation purposes, with a survival rate of 54%[9]. Although ECMO improves survival rates, it also causes infections that increase morbidity and mortality.

Pathogenesis

The ECMO circuit and multiple invasive interventions disrupt the skin's protective barrier, resulting in several potential entry points for pathogenic microorganisms[10,11]. ECMO patients need central venous catheters for vasoactive drugs and arterial catheters for hemodynamic monitoring. Mechanical ventilation support, urinary catheters, abdominal or chest drainage tubes, large and wide cannulas, and membrane oxygenators increase the susceptibility to nosocomial infections[12]. HCRIs increase mortality by 38–63% in ECMO patients and negatively affect the duration of ECMO support, frequency of other complications, hospitalization length, ventilator support duration, and healthcare costs[13,14]. HCRIs in ECMO patients are defined as the development of infection 24–48 h after ECMO cannulation or 48–72 h after ECMO decannulation[15].

Catheter-related bloodstream infections in extracorporeal membrane oxygenation support

Intravenous catheters are administered to millions of patients every day, leading to an increased incidence of CRBSIs[1,3]. CRBSIs are the most common HCRIs in ECMO patients. They are associated with a mortality rate of about 25%, which is 50% in critically ill patients with cardiovascular diseases[16,17]. Sun et al. reported that 7 out of 10 patients who underwent ECMO support for longer than 10 days developed CRBSIs[18]. The risk factors for CRBSIs are extended ECMO support (250 h or more), renal failure, immunosuppression, veno-arterial ECMO, and bleeding, requiring more than 1,000 mL red blood cell transfusion[19,20]. This risk is prevalent in pediatric ECMO support for longer than 5 days[21,22]. Kutleša et al. reported that ECMO support longer than 250 h and significant bleeding episodes were independent risk factors for CRBSIs[23].

Gram-negative bacteria (44.1%), gram-positive bacteria (26.5%), and fungi (29.4%) are pathogenic agents. The strains that cause bacteremia are coagulase-negative staphylococci (17.6%), *Klebsiell*a (14.7%), *Pseudomonas* (8.8%), *Acinetobacter* (8.8%), *Stenotrophomonas maltophilia* (5.9%), *Staphylococcus aureus* (2.9%), *Micrococcus* (2.9%), *Corynebacterium bovis*

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Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on April 27, 2023. Accepted on July 22, 2023.

(2.9%), *Enterobacter cloaca* (2.9%), *Escherichia coli* (2.9%), *Candida Albicans,* and *Candida parapsilosis*[24].

Healthcare professionals should monitor ECMO patients for CRBSIs. Local erythema at cannula entry sites, purulent drainage, and positive cultures suggest the presence of CRBSIs[24,25]. However, body temperature adjustment via the ECMO system and other invasive interventions other than ECMO cannulas fall short of explaining the relationship between CRBSIs and ECMO[13,26,27]. High hemorrhagic complications during extracorporeal circulation may increase the risk of bacterial transmission from colonized sites (e.g., gut), leading to hemodynamic instability and impaired peripheral perfusion. Moreover, most infection symptoms are associated with low biocompatibility of extracorporeal circuits. This may lead to activation of the inflammatory response, leukocytosis, and ECMO circuit disruption[28].

Diagnosis

Clinical signs (e.g., fever, tachycardia, and hypotension) and lab results (e.g., C-reactive protein and procalcitonin) must be focused to diagnose CRBSIs. However, blood and catheter cultures are required for definitive diagnosis[29,30]. According to the Centers for Disease Control and Prevention, CRBSI is defined as two separate positive blood cultures for a pathogenic organism with signs of infection, including leukocytosis, leukopenia, fever, or hypothermia[31]. The most common pathogens associated with CRBSIs in ECMO are coagulase-negative staphylococci (57.9%)[3]. The most frequently reported strain types are *S. aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae, Staphylococcus epidermidis, S. aureus, E. coli, Enterobacteriaceae, Enterococcus faecium, C. albicans*, *C. parapsilosi*, and *Candida glabrata*[32-36].

Allou et al. observed bacteremia in 6 out of 10 patients (59.7%). They stated that the most frequently isolated bacteria were *Enterobacteriaceae* (38%), *Staphylococcus* spp. (28.2%), and *P. aeruginosa* (18.3%)[19]. Selçuk et al. determined that the agents in positive culture results were *Klebsiella* (8.7%), *Streptococcus* (4.8%), *Acinetobacter* (4.0%), *Enterobacter cloacae* (3.2%), coagulase-negative staphylococci (3.2%), *E. coli* (2. 4%), *Pseudomonas* (2.4%), *Serratia* (1.6%), *Citrobacter* (1.6%), *Proteus* (0.8%), *Haemophilus* (0.8%), *Listeria* (0.8%), and *Corynebacterium* (0.8%)[22].

Haneke et al. compared the results of ECMO survivors and non-survivors. They found that staphylococci (*S. aureus*, of which 22% were methicillin-resistant *S. aureus*) were the most commonly isolated bacteria in both groups. They also reported that fungi were isolated with the second-highest frequency and that most of those cases were in the non-surviving group. They detected pathogens in blood cultures, tracheal secretions, and urine. *Enterobacter* spp., *K. pneumoniae*, and *P. aeruginosa* showed a high incidence in the samples isolated from tracheal secretions[25].

Recommendations for infection control

In 2008, the ELSO issued a guideline based on ECMO-related risk factors and general principles for infection control[37]. Table 1 summarizes the strategies, staff training, surveillance practices, and preventive health measures for CRBSI prevention according to the guidelines[37]. However, there is a lack of data to guide healthcare professionals in preventing most CRBSIs and other possible complications and in the care management of ECMO patients. The data limited to the United States show variability in cannula placement and care practices performed in ECMO centers[4].

The current recommendations are only partially relevant to ECMO support. There is insufficient evidence to guide effective line fixation, dressing, and care practices to prevent decannulation and/or infection in ECMO patients. Healthcare professionals follow the guidelines to prevent intravascular catheter-related infections published by the Healthcare Infection Control Practices Advisory Committee (HICPAC) in caring for ECMO patients[31]. Within the scope of intravascular CRBSI recommendations, HICPAC guidelines include practices with a high level of evidence, such as surveillance practices, staff training, use of standard protocols and checklists, maximum aseptic technique

Table 1. Recommendations for the prevention of catheter-related bloodstream infections during extracorporeal membrane oxygenation support by the Extracorporeal Life Support Organization Infectious Disease Task Force.

1	Do not interrupt the ECMO system and avoid unnecessary interventions.
2	Needleless hubs should be used at all connections, stopcocks, and access sites in the circuit.
3	Use chlorhexidine to disinfect the parts of the ECMO system.
4	Administer only continuous infusions into the circuit to reduce the risk of transmission (e.g., heparin, vasopressors, inotropes, and narcotics).
5	To prevent cross-infection, isolate ECMO patients from other patients with multidrug-resistant organisms, heavily contaminated wounds, or severe infections.
6	Wash your hands frequently before interventions.
7	Avoid and remove unnecessary central venous catheters and invasive devices.

Table 2. Recommendations for the prevention of catheter-associated bloodstream infections in extracorporeal membrane oxygenation support.

Preparation	ECMO teams should be designated. The ECMO team must be trained in ECMO system set-up and patient management. Standard protocols/contact lists should be readily available. Antibiotics should not be used for prophylaxis because they increase antibiotic resistance.
Cannulation	Kits containing ECMO materials should be readily available. If possible, peripheral vessels should be preferred. Catheter placement should be performed under ultrasound guidance to reduce the number of mechanical complications. Maximum protective measures (e.g., mask, cap, goggles, sterile gloves, and sterile apron) should be taken. Hands should be disinfected with soap and water, alcohol-based solutions, or chlorhexidine. 5% chlorhexidine gluconate (KHG) should be used for skin antisepsis. If KHG is contraindicated, 70% alcohol solutions, isopropyl alcohol solutions, or povidone-iodine should be used. Before catheter insertion, antiseptics should be allowed to dry according to the manufacturer's recommendation. Not only the intervention site but the whole body should be covered with a sterile drape.
Post-ECMO cannulation care	Parenteral nutrition should be administered via a central venous catheter instead of administering concentrated glucose solution directly into the ECMO circuit. New vascular interventions at the site of ECMO cannulas should be avoided due to the risk of hematoma and infection. Folding of the cannula in the ECMO circuit should be prevented. Blood samples should preferably be collected from arterial catheters. Intermittent administration of drugs should be avoided. Instead, continuous infusions should be preferred. Catheter tips, needleless connectors, or injection ports should be used after wiping them with alcoholic chlorhexidine for at least 5 s. Nurse to patient ratio should be 1:1. Prophylactic antibiotics should be considered for patients with risk factors for central cannulation (immunocompromised states) or multidrug-resistant organisms.
Cannula entry site dressing	Sterile gauze or sterile, transparent, semi-permeable, or chlorhexidine dressings should be used to cover the cannulation site. If the patient is sweaty or has localized bleeding or oozing, gauze should be used until these problems are resolved. ECMO cannulas and other invasive sites should not come into contact with water. The transparent dressing should be replaced with a new one every 5–7 days (except in pediatric patients where the risk of catheter dislodgement outweighs the benefit of changing the dressing). Catheter sites should be monitored visually or by palpation when changing the dressing daily. If symptoms include tenderness at the cannula entry site and fever with no apparent source, the dressing should be removed to examine the site thoroughly.

and sterile precautions during catheterization, observation of the cannula entry site after catheterization, and dressings and collection of catheter culture after catheter removal[31]. Table 2 shows preventing CRBSIs in ECMO patients in line with the HICPAC and ELSO recommendations[11,31,32,35-39].

Glater-Welt et al. investigated standard practices for BSI prevention among national ECMO programs and reported five findings. First, most institutions use a standard approach to cannula dressings (82.9%). Second, more than half of the institutions send daily blood cultures as part of routine surveillance (34.2%). Third, healthcare professionals commonly use semi-permeable dressings to close cannulation sites (57.3%). Fourth, they use alcohol (48.2%), chlorhexidine (38.8%), and betadine (4.7%) to disinfect access ports when access to the ECMO circuit and ports is required. Fifth, more than half of healthcare professionals change cannula entry site dressings only when necessary (60.5%)[39]. Bull et al. found that cyanoacrylate tissue adhesive inhibited bacterial growth at the ECMO cannulation site. They concluded that cyanoacrylate tissue adhesive was an effective method to prevent or minimize accidental decannulation[40].

CONCLUSION

ECMO is an extracorporeal organ support in ICUs worldwide. Monitoring ECMO patients in cardiovascular surgery ICUs for CRBSIs is vital in terms of morbidity, mortality, hospitalization, and healthcare costs. Therefore, healthcare professionals should make individual and environmental adjustments, maintain aseptic conditions, and diagnose and manage signs and symptoms of infection to prevent the risk of CRBSI from the beginning to the end of ECMO support.

Researchers recommend care bundles with evidence-based practices in managing CRBSIs in ECMO patients. Cardiovascular surgeons, ICU specialists, nurses, and other healthcare professionals are responsible for implementing care bundles.

AUTHORS' CONTRIBUTIONS

HS: Conceptualization, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. **SG:** Conceptualization, Supervision, Visualization, Writing – original draft, Writing – review & editing.

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