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REVIEW ARTICLE

Pharmacological Research Agenda on Adult Extracorporeal Membrane Oxygenation Using the Delphi Method: A Position Paper of the Extracorporeal Membrane Oxygenation Pharmacology Network

OBJECTIVES: Extracorporeal membrane oxygenation (ECMO) is a critical intervention for patients with severe cardiac or respiratory failure. However, pharmacological management for ECMO-supported patients presents unique challenges due to alterations in drug pharmacokinetics and pharmacodynamics induced by the ECMO circuit and underlying critical illness. This position paper identifies key research priorities in ECMO pharmacology using a structured Delphi consensus process and provides a focused review of current evidence and knowledge gaps to inform future research and clinical practice.

DATA SOURCES: An international panel of 25 ECMO pharmacology experts from 13 countries representing the ECMO Pharmacology Network contributed to this position paper. Literature was reviewed to summarize current evidence and identify knowledge gaps in ECMO pharmacology.

STUDY SELECTION: The Delphi process involved iterative, anonymous voting by the expert panel to propose key research priorities. Items selected were based on their perceived importance to improving clinical outcomes and advancing pharmacological management in ECMO-supported patients.

DATA EXTRACTION: Key research priorities were identified, and a detailed literature review was conducted for each, focusing on pharmacokinetics/pharmacodynamics, related therapeutic challenges, and knowledge gaps. Future research directions were outlined.

DATA SYNTHESIS: Six critical ECMO pharmacotherapy research priorities were identified: 1) pharmacokinetics/pharmacodynamics reporting, 2) interactions between ECMO and renal replacement therapy, 3) antimicrobial dosing, 4) analgesia and sedation for pain and agitation, 5) sedation and neuromuscular blocking agents for increased work of breathing, and 6) anticoagulation. The review for the key research priorities highlighted substantial gaps in the existing literature, emphasizing the need for comprehensive studies addressing these issues to enhance pharmacotherapy in ECMO patients, improve clinical outcomes, and contribute to the development of evidence-based guidelines for this complex population.

CONCLUSIONS: ECMO presents unique challenges to drug pharmacokinetics and pharmacodynamics, complicating pharmacotherapy in critically ill patients. Further research addressing identified gaps is essential to develop evidence-based treatment strategies and enhance patient outcomes.

KEYWORDS: extracorporeal membrane oxygenation; network; pharmacodynamics; pharmacokinetics; position paper

Diana Morales Castro, MD[1]
Abdulrahman Abdullah Al-Fares, MD[2]
Gianluca Paternoster[3]
Haifa Lyster, PhD[4]
Benjamin Hohlfelder, PharmD[5]
Julian Arias Ortiz, MD[6]
Mohd Hafiz Abdul-Aziz, PhD[7]
Daniel Herr, MD[8]
Rawan Alraish, MD[9]
Andrés Ferre Contreras, MD[10]
Marcela Palavecino, PharmD[11]
Luigi Milella, PharmD[12]
Kevin Watt, MD[13]
Afrah Alkazemi, PharmD[14]
Federico Carlos Carini, MD[15]
Jason A. Roberts, PhD[16,17,18,19]
Jordi Riera del Brio, MD[20,21]
Alba Pau Parra, MD[22]
Vivek Kakar, MD[23,24]
Pauline Dureau, MD[25]
Marc-Alexandre Duceppe, PharmD[26,27]
Mark Alm, MSc[28]
Stephanie Cha, MD[29]
Kiran Shekar, PhD[30]
Amy L. Dzierba, PharmD[31]
on behalf of the Extracorporeal Membrane Oxygenation Pharmacology Network (ECMOPharm Net)

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KEY POINTS

Question: What are the key pharmacological research priorities in adult extracorporeal membrane oxygenation (ECMO) patients?

Findings: Using a Delphi consensus process with international experts, six key priorities were identified: pharmacokinetics/pharmacodynamics reporting, interactions with renal replacement therapy, antimicrobial dosing, sedation and analgesia for pain and agitation, sedation and neuromuscular blocking agents for increased work of breathing, and anticoagulation.

Meaning: Addressing these priorities through focused research will help optimize drug therapy, improve patient outcomes, and support the development of evidence-based guidelines for pharmacological management in critically ill adults supported by ECMO.

Extracorporeal membrane oxygenation (ECMO) is a life-saving intervention for cardiac and/or respiratory failure (1–4). While the use of ECMO has exponentially increased over the past decade, it only provides temporary support and does not address the underlying cause of organ failure (1, 5–8). Patients on ECMO often receive vasopressors and inotropes for shock management, neuromuscular blocker agents (NMBAs), sedatives and analgesics for comfort and tolerance of supportive therapies, antimicrobials for infections, and other drugs to manage their comorbidities (9). Given that these drugs are essential for addressing the underlying pathologic processes, interactions between the ECMO circuit and pharmacotherapy may hinder the patient's ability to recover (7, 10, 11).

Pharmacokinetics studies the changes in drug concentrations over time due to absorption, distribution, metabolism, and excretion, while pharmacodynamics focuses on the magnitude of the response elicited by drug concentration at the action site (12, 13). In patients supported with ECMO, pharmacokinetics and pharmacodynamics are influenced by a complex interplay of patient-specific factors such as critical illness, organ dysfunction and the inflammatory response, ECMO circuit characteristics, including the type of ECMO support (venovenous vs. venoarterial ECMO), circuit surface area and oxygenator type, among others, and drug physicochemistry such as lipophilicity, protein binding, molecular weight (**Fig. 1**) (11, 15–19). Given the dynamic nature of these variables and the lack of high-quality comparative data, it remains difficult to quantify the independent impact of each factor for different drugs. Since 2017, experts identified drug pharmacokinetics, pharmacodynamics, and innovative pharmacologic strategies in ECMO-supported patients as one of the top ten research priorities for the next decade (20). However, pharmacokinetics data from ex vivo studies and clinical trials have yielded conflicting results, with adult clinical studies often constrained by factors such as limited sampling, single-center analysis, and a scarcity of comprehensive clinical pharmacokinetics/pharmacodynamics studies (13, 16, 17, 21). Considering the large number of drugs used in clinical practice, many questions about proper dosing in adult patients supported with ECMO remain unanswered (10, 11, 22). The primary purpose of this position paper is to reach a consensus on research priorities in ECMO pharmacology based on the expert opinions of physicians, academics, ECMO specialists, pharmacists, and allied healthcare workers using a Delphi process and provide a focused literature review of current knowledge and existing gaps for each priority.

METHODS

Panel Members Selection

An organizing committee (D.M.C., K.S., A.L.D.) convened a panel of international experts under the auspices of the ECMO Pharmacology Network. ECMOPharmn Net (ecmopharmnet.org) is a nonprofit international collaboration dedicated to advancing ECMO pharmacology knowledge globally. Panel members were selected based on their expertise in ECMO pharmacology, which was demonstrated through their publication records, experience in guidelines development, and recognition as international experts. To ensure diversity and overcome disparities in the generation of medical research, the selection process considered sex, profession, and geography. Although the expert panel primarily included ECMO pharmacology researchers, most were also practicing critical care clinicians. Their clinical uncertainties observed at the bedside shaped

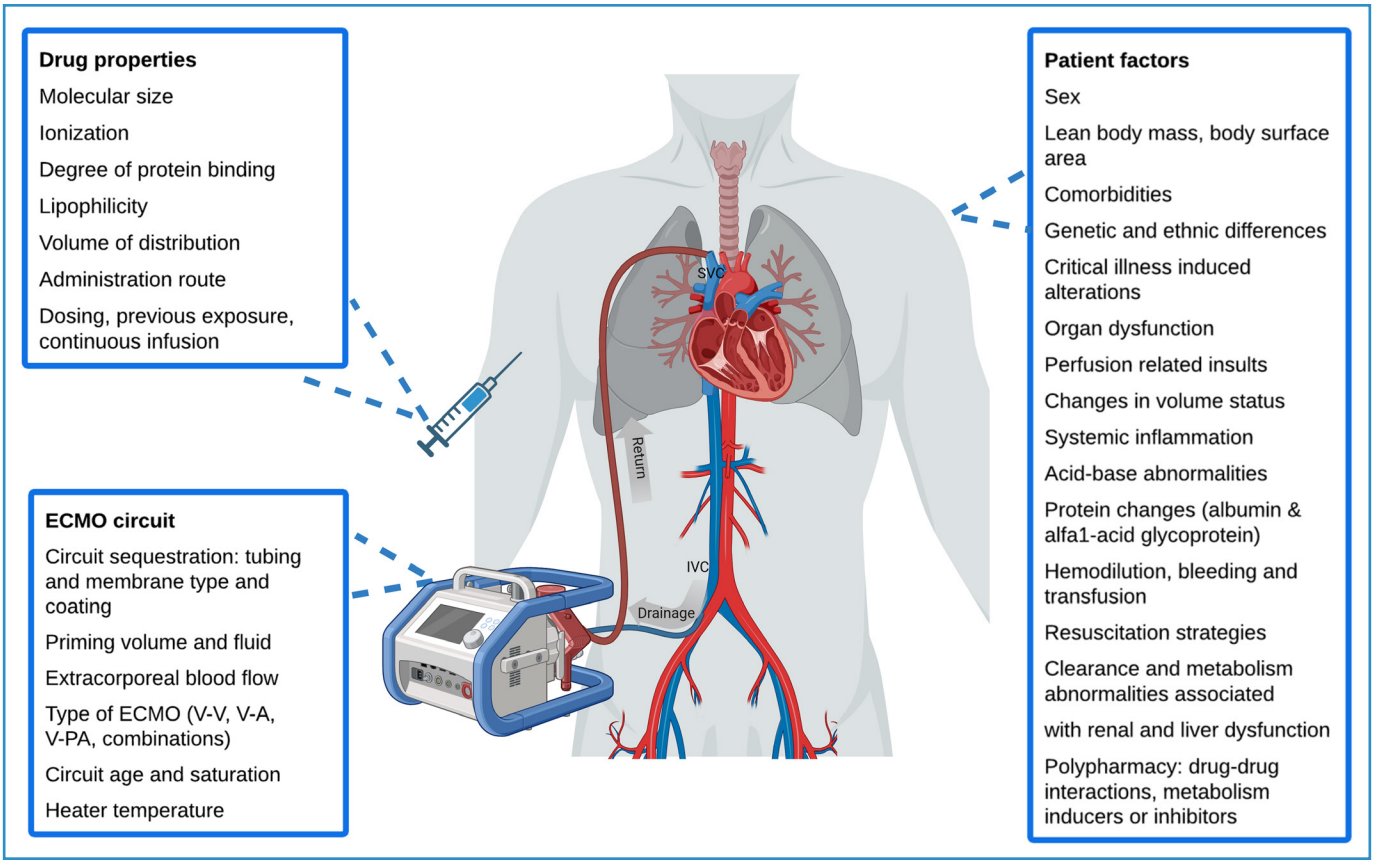

Figure 1. Multifactorial determinants of pharmacokinetics and pharmacodynamics in extracorporeal membrane oxygenation (ECMO)-supported patients (14). IVC = inferior vena cava, SVC = superior vena cava, V-A = venoarterial, V-V = venovenous, V-PA = veno-pulmonary artery.

the formulation of relevant research priorities shaped the formulation of relevant research priorities.

Delphi Process

A Delphi process was conducted to reach consensus on research priorities in ECMO pharmacology, with the results reported in accordance with the Conducting and Reporting Delphi Studies guidelines (**Supplemental Table 1**, https://links.lww.com/CCM/H772) (23, 24). Each panel member was asked to submit research-related items that could advance the understanding of ECMO pharmacology. The organizing committee reviewed and consolidated the responses, merging similar topics and categorizing them into a list. Surveys were then built on the Google Forms platform and distributed via email. The iterative voting process was conducted anonymously to ensure confidentiality.

In the first round, the panel members voted on the extended list of research priorities using a multiple-choice question format. The priorities were selected for the second round based on a voting threshold of over 40%. Subsequently, the experts were divided into working groups to create narrative reviews for these second-round priorities, drawing on systematic analyses of the medical literature, national and international guidelines, and expert opinions. During this round, the panel members refined the priorities, made necessary semantic adjustments, and combined certain statements based on the group's feedback, thereby narrowing the priorities lists. In the third round, the narrowed list of priorities was subjected to further voting for consensus using a 7-point Likert-scale. The voting process concluded with the fourth round to confirm the stability and robustness of the consensus.

Consensus, Robustness, and Stability

Consensus for the research priorities was defined as over 70% of panel agreement (scores 5–7). Median (interquartile range) was used to express the responses' central tendency and dispersion, with robustness

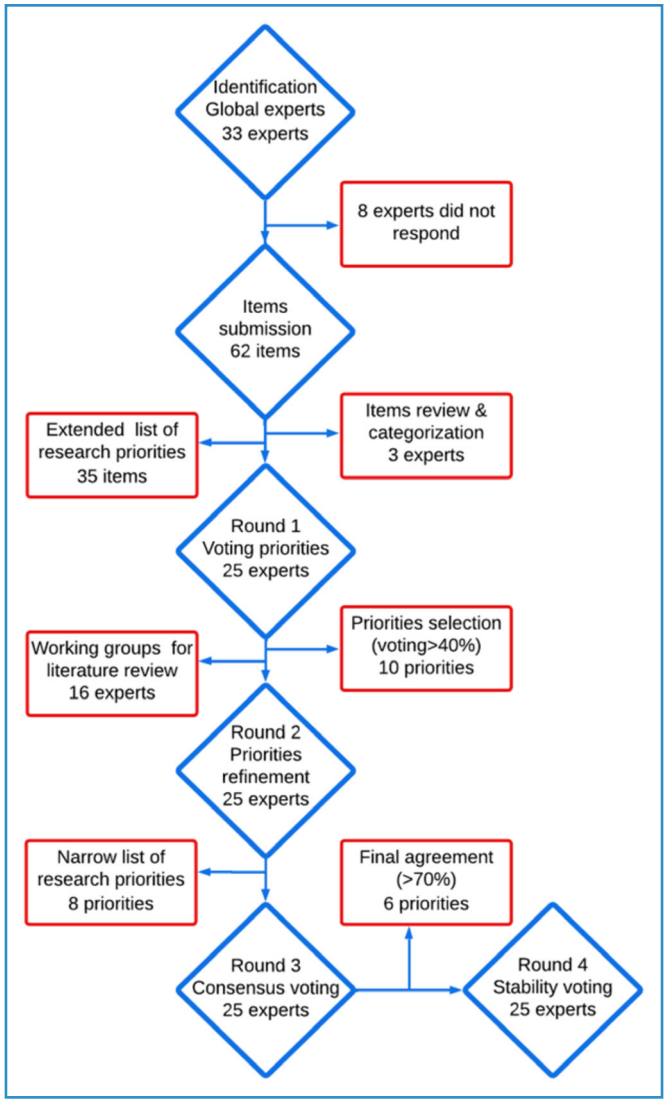

Figure 2. Flowchart of the Delphi process.

measured by a median of greater than or equal to 6 (for agreement) in the Likert-scale questions. Stability was assessed to identify the need for further iterations. Using Kruskal-Wallis tests the responses of two consecutive rounds was performed for each Liker-scale question, with stability defined as *p* value of greater than or equal to 0.05 (25).

Research Priorities

Research priorities meeting consensus, robustness, and stability were included in the position paper. A qualitative thematic analysis was performed for the questions on each research priority to be addressed by future studies. The experts reviewed and approved the article's final version before submission for publication.

RESULTS

Of the 33 experts identified, 25 experts from 13 countries across four continents (America, Europe, Asia, and Oceania) participated in the Delphi process and completed all rounds (**Supplemental Fig. 1**, https://links.lww.com/CCM/H772). The Delphi process was conducted in four rounds between April 2024 and October 2024 (**Fig. 2**). The experts suggested 62 research priorities that were refined and grouped into 35 items (**Fig. 3**). Ten topics reached the threshold for the first round and were selected for the literature review and the subsequent rounds. During this round, the panel members refined the priorities, made necessary semantic adjustments (e.g., simplifying "analgesia and sedation for pain and agitation" and leaving delirium to "antipsychotics for delirium"), and combined or excluded items based on group feedback. After statement combinations and semantic modifications, eight research priorities were identified, of which six achieved consensus, robustness, and stability (**Table 1**; and **Supplemental Delphi material**, https://links.lww.com/CCM/H772). These six research priorities are discussed below. Following the final Delphi round, the organizing committee performed a thematic analysis of the expert responses and a literature review to develop the research questions listed in **Table 2**. These questions represent structured areas of uncertainty and clinical need, validated by panel consensus, and are intended to guide focused investigations.

DISCUSSION

The Delphi process yielded the final research priorities that formed the foundation of this position paper. Table 2 summarizes the qualitative thematic analysis for the questions on each research priority to be addressed by future studies.

Pharmacokinetic/Pharmacodynamic Reporting

The focus of pharmacokinetics reporting has traditionally relied on detailed model descriptions rather than their practical applications (26). Understanding the relationship between pharmacokinetics changes and target pharmacodynamics responses is crucial for developing optimal dosing regimens for ECMO-supported patients. In addition, non-ECMO models in critically ill patients are necessary to accurately

distinguish the derangements caused by ECMO vs. those resulting from critical illness itself. Ensuring homogeneity in sample timing is critical for future studies to mitigate differences in pharmacokinetics/pharmacodynamics aberrations during different stages of ECMO support and critical illness (27, 28).

To enhance the standardization of pharmacokinetics/pharmacodynamics studies in ECMO,

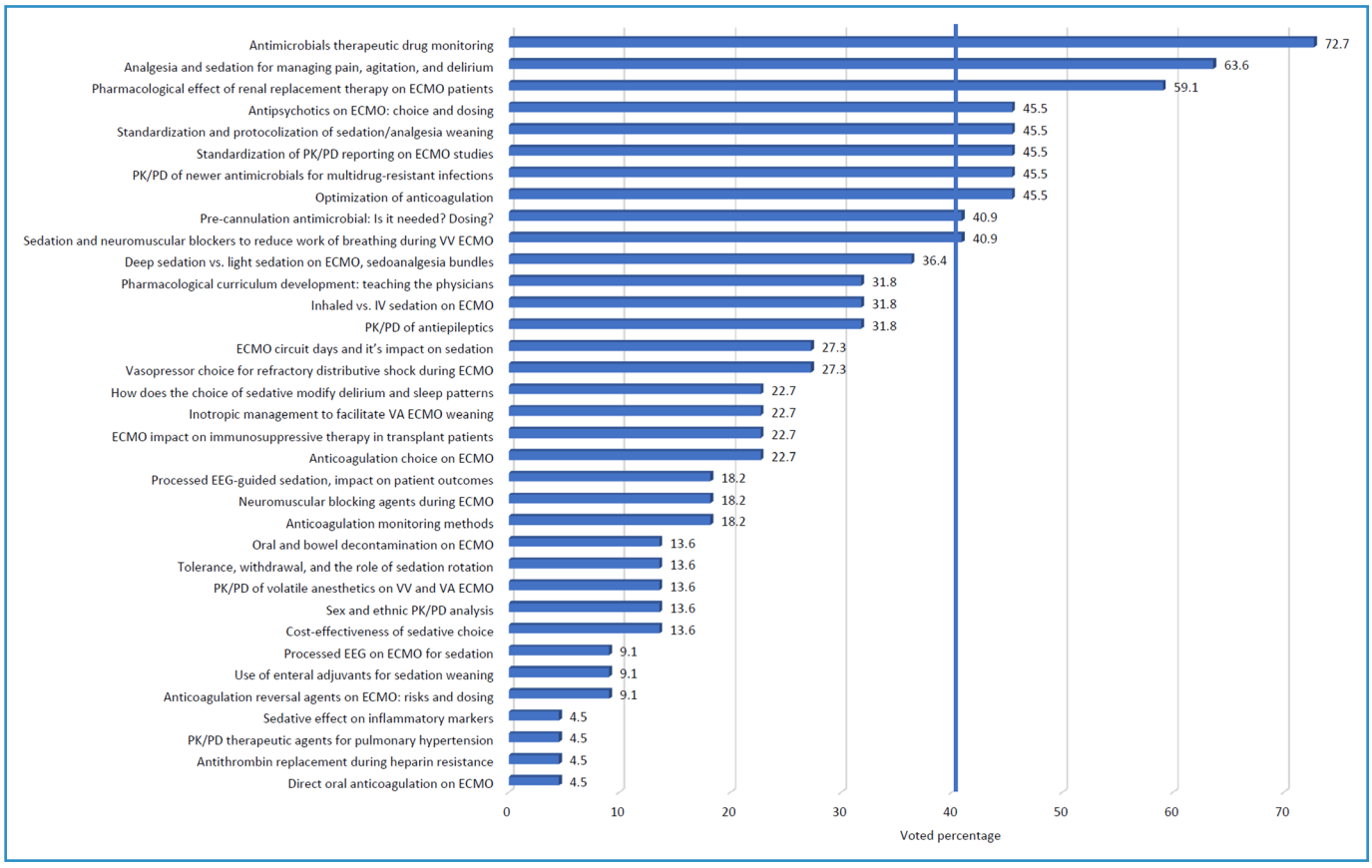

Figure 3. Refined research priorities and round one voting results. ECMO = extracorporeal membrane oxygenation, EEG = electroencephalography, PK/PD = pharmacokinetics/pharmacodynamics, VA = venoarterial, VV = venovenous.

TABLE 1.
Final Consensus and Stability of the Delphi Process

Research Priority	Agree (%)	Neutral (%)	Disagree (%)	Median (IQR)	Stability *p*
Pharmacokinetic/pharmacodynamic reporting	96	0	4	7 (6–7)	0.7
Interactions with renal replacement therapy	84	12	4	6 (6–7)	0.4
Pre-cannulation antibiotic prophylaxis	68	20	12	5 (4–7)	0.7
Antimicrobial dosing	92	4	4	7 (7–7)	0.4
Analgesia and sedation for pain and agitation	100	0	0	7 (6–7)	0.4
Sedation and neuromuscular blocking agents for increased work of breathing	84	12	4	6 (5–7)	0.4
Antipsychotics for delirium	68	24	8	5 (4–6)	0.6
Anticoagulation	92	8	0	7 (6–7)	0.9

IQR = interquartile range.

TABLE 2.
Essential Questions to Be Addressed by Future Studies in Extracorporeal Membrane Oxygenation Pharmacology

Research Priority	Questions to Be Addressed
PK/PD reporting	What is the relationship between PK changes and target PD responses for commonly used drugs to optimize dosing regimens?
Interactions with RRT	How does the interaction between RRT and ECMO affect PK/PD?
	Does the RRT configuration with the ECMO (directly integrated vs. separate) affect PK/PD differently?
	How do different RRT modalities affect ECMO-PK/PD?
Antimicrobial dosing	What is the impact of different dosing or infusion strategies on antimicrobial effectiveness?
	Is there cost-effectiveness in therapeutic drug monitoring implementation?
	Can we explore the link between antimicrobial exposure and clinical outcomes?
Analgesia and sedation for pain and agitation	When is the optimal time to start weaning sedation and analgesia?
	Can enteral agents be used to minimize the need for continuous sedative and analgesic infusions and promote light sedation?
	Are there sedation strategies that could promote cellular recovery or diminish organ damage?
	Will using objective monitoring strategies (e.g., processed electroencephalogram) result in less sedative doses or facilitate sedation weaning?
Sedation and NMBAs for increased work of breathing	What sedatives should be used during paralysis? Is polypharmacy necessary when continuous NMBA is used to control work of breathing and avoid pSILI?
	Can pSILI be prevented by managing ECMO settings (changes in extracorporeal blood flow and sweep gas to modify Pao_2 or $Paco_2$) instead of over-sedating patients?
	Is there a more accurate way to assess paralysis and reduce NMBA dosing? Could quantitative vs. qualitative train-of-four monitoring or titration of NMBA based on patient-ventilator dyssynchrony respiratory rate control and work of breathing measurements (e.g., occlusion pressure, esophageal pressure, or diaphragmatic function) offer better guidance?
	Is it feasible to use lower NMBA doses if work of breathing measurements are used (partial paralysis)?
Optimization of anticoagulation	Which ECMO-supported patients require anticoagulation?
	What are the safest and most effective agents and dosing?
	Which is the best monitoring practice? Is it a combination of monitoring assays?
	How does advanced circuit materials impact patient outcomes, such as bleeding and thrombotic complications?

ECMO = extracorporeal membrane oxygenation, NMBA = neuromuscular blocking agent, PK/PD = pharmacokinetic/pharmacodynamic, pSILI = patient self-inflicted lung injury, RRT = renal replacement therapy.

establishing a consistent set of parameters to be reported is essential (**Supplemental Table 2**, https://links.lww.com/CCM/H772). This ensures that data generated across studies are comparable and can be effectively used to optimize pharmacotherapy (26–29). Although comprehensive reporting of all elements in Supplemental Table 2 (https://links.lww.com/CCM/H772) is ideal, we acknowledge that some may be difficult to achieve in small case series or resource-limited settings. A tiered approach that prioritizes core components—such as drug regimen, ECMO configuration, and sampling strategy—may facilitate broader implementation while still supporting reproducible, clinically translatable research.

Interactions With Renal Replacement Therapy

Acute kidney injury frequently occurs in ECMO-supported patients (30–32). For these patients, renal replacement therapy (RRT) indications align with

those for the non-ECMO population, with no definitive evidence supporting either early or late initiation (33, 34). The use of RRT during ECMO varies widely and is often influenced by the treating center's experience and practices, including the preferred modality (e.g., continuous RRT or sustained low-efficiency dialysis) (31). Whether RRT is integrated directly with the ECMO circuit or performed separately, its necessity is consistently associated with increased mortality (33–37).

There is a lack of pharmacokinetics/pharmacodynamics studies including detailed data on patients supported with ECMO and RRT (38). The few available studies seldom provide crucial information regarding the specific RRT modality used, dialysis duration, and settings (38). This gap is concerning, as concurrent use of RRT has been shown to increase pharmacokinetics variability (38). In the largest study on antimicrobials in ECMO-supported patients, 45% of patients received RRT, with up to a 200-fold variation in antimicrobial blood concentrations (39). Despite these variations, target attainment rates were not significantly different between patients receiving RRT vs. those who did not, although both groups exhibited alarmingly low rates of target attainment (39). Multicenter studies are needed to evaluate ECMO-RRT interactions for key drug classes, define therapeutic targets, and establish pharmacokinetics models that account for RRT modality and intensity.

Antimicrobial Dosing

Critically ill patients receiving ECMO face a higher risk of nosocomial infections, with studies reporting up to a 50% increase compared with the general critically ill population (40–42). Several factors likely contribute to this elevated risk, including the severity of critical illness, invasiveness of the ECMO procedure, prolonged ICU stay, use of multiple intravascular catheters, and the need for mechanical ventilation, along with other invasive interventions (40–42). Furthermore, some centers maintain pre-primed ECMO circuits readily available for urgent cannulation or circuit changes. While the Extracorporeal Life Support Organization (ELSO) endorses pre-primed circuits for up to 30 days, there have been reports of bacterial contamination, which may represent an additional infection source (43, 44). Despite the association of these infectious complications with longer hospital stays and increased mortality, scientific evidence on the prevention, diagnosis, and treatment of these infections remains limited (42, 45, 46).

Optimal antimicrobial dosing regimens aligned with pharmacokinetics/pharmacodynamics principles are crucial for minimizing resistance emergence and prolonging the lifespan of existing antimicrobials (13, 47, 48). The largest multicenter prospective study to date found that antimicrobial concentrations in ECMO-supported patients were generally comparable to those in critically ill patients without ECMO (39). Other studies suggest that pharmacokinetics/pharmacodynamics alterations are more likely attributable to pathophysiological changes inherent to critical illness rather than the ECMO support itself (49–64). However, a significant proportion of critically ill patients fail to reach predefined pharmacodynamics targets, which may compromise treatment effectiveness and could contribute to the development of antimicrobial resistance (50, 63, 65–67).

Antimicrobial therapeutic drug monitoring (TDM) for severe infections and critical illness has already been advocated to optimize antimicrobial dosing (47). Guidelines such as The Surviving Sepsis Campaign recommend TDM-guided dosing when feasible (48). However, evidence on TDM-guided antimicrobial dosing on ECMO-supported patients is scarce, and TDM practices differ widely between institutions (39, 64). When considering studies that analyzed ECMO-pharmacodynamics responses, TDM-guided dose adjustments are recommended for several antimicrobials (38, 39, 68). However, despite the potential benefits, several limitations hinder the widespread adoption and efficacy of TDM. Prolonged TDM turnaround times can delay necessary dose adjustments, validated assays for newer antimicrobials are often lacking, and the absence of predefined pharmacodynamics targets for many antimicrobials complicates the interpretation and clinical application of the results. Finally, TDM is not widely available in all healthcare centers, particularly in resource-limited settings, with cost as an important barrier (6, 15, 39, 69). To ensure effective and safe antimicrobial exposure in ECMO-supported patients, clinical studies are necessary to define the role of TDM-guided antimicrobial dosing, identify suitable therapeutic targets, and assess their impact on patient outcomes.

Analgesia and Sedation for Pain and Agitation

Achieving and maintaining optimal sedation and analgesia in critically ill patients is challenging (70, 71). Current guidelines stress prioritizing pain management, avoiding benzodiazepine use, and encouraging early awakening to improve patient-centered outcomes (72, 73). However, these strategies may not be suitable for some ECMO-supported patients (e.g., severe acute respiratory distress syndrome [ARDS], delayed chest closure), who often require deep sedation (74–76).

Various sedation scales, including the Richmond Agitation-Sedation Scale (77, 78), Sedation Agitation Scale (79), and Ramsay score (80) have been used to monitor sedation in ECMO-supported patients. Nevertheless, international surveys found that only 49% of ECMO centers employ a sedation score, with few centers using daily sedation breaks and 75% of patients managed with deep sedation (80, 81). The use of objective sedation monitoring tools (e.g., processed electroencephalography) has proven effective for critically ill patients (82, 83), but remains understudied on ECMO-supported patients. A recent study validating the use of processed electroencephalography to monitor sedation levels in venovenous ECMO patients revealed that these patients were frequently over-sedated (84).

Several ex vivo studies have shown decreased concentrations of sedatives with ECMO (18, 85–89). Similarly, single-center cohort studies have reported higher opioid and sedative requirements during ECMO (79, 90–92). To date, only three pharmacokinetics studies have been published for ECMO patients, although pharmacodynamics targets were analyzed in only one of these studies (84, 93, 94). This study revealed that increased sedative clearance was limited to the initial hours of support, likely due to venovenous ECMO circuit saturation (84, 95). Additionally, three retrospective studies have compared fentanyl vs. hydromorphone analgesia in ECMO patients. While two showed no differences in sedative requirements or agitation-sedation scores (96, 97), the other demonstrated a significant reduction in daily narcotic doses and an increase in ECMO days alive without delirium or coma in the hydromorphone group (98).

Whether increased sedative requirements are driven by ECMO-induced pharmacokinetics changes, clinical practices of maintaining deep sedation, or the development of tolerance over time, IV sedatives are associated with well-known side effects, including increased prevalence of agitation and delirium, risk of ICU-acquired weakness, drug accumulation, and tachyphylaxis (69, 70, 90).

Recently, attention has increasingly focused on the use of volatile anesthetics as an alternative to IV sedation (99). A meta-analysis on mechanically ventilated patients demonstrated a reduction in time to extubation and an absence of short-term side effects with volatile-based sedation (99). Similarly, a retrospective study including patients with ARDS undergoing venovenous ECMO found that isoflurane provided sedation with a more profound effect than IV agents (70). When volatile anesthetics are used on venovenous ECMO patients, including those with COVID-19, they have opioid-sparing effects while preserving hemodynamics (70, 100, 101). Nevertheless, concerns have been raised with very low tidal volumes (< 100–150 mL), as some reports suggest failure to suppress agitation in these patients (102). Furthermore, recent publications found higher mortality rates with prolonged use of sevoflurane (103). Finally, the environmental impact of using volatile anesthetics should be cautiously considered (70, 101, 104).

Standardized management strategies for pain and agitation are paramount, particularly to facilitate the weaning of these therapies (105–107). Protocolized sedation, shown to improve outcomes and decrease mortality in critically ill patients (108), remains understudied in ECMO-supported patients. The safety of targeting light sedation and conducting spontaneous awakening trials for all patients receiving ECMO remains uncertain. However, strategies proven effective in non-ECMO patients, like opioid rotation (109) and transitioning from IV to enteral therapy (110, 111), may facilitate sedation weaning. The emerging "awake ECMO" approach, used to facilitate early mobilization and improve outcomes, should be implemented only in specialized ECMO centers and after carefully evaluating contraindications (112–114). Future research must focus on the safety and effectiveness of standardized sedation practices and weaning strategies.

Sedation and Neuromuscular Blocking Agents for Increased Work of Breathing

The use of sedatives and NMBA to reduce the work of breathing and prevent patient-ventilator dyssynchronies or patient self-inflicted lung injury (pSILI) during

venovenous ECMO has gained attention recently (115, 116). Notably, it appears that the depth of sedation does not always correlate with reduced work of breathing and may not effectively prevent pSILI (117). Consistent with studies in critically ill patients showing little to no effect of sedatives on respiratory effort (117–120), a recent pharmacokinetics/pharmacodynamics study showed that respiratory effort—measured via inspiratory effort against an occluded airway and occlusion pressure during first 0.1 seconds (121)—could not be adequately explained by propofol or fentanyl concentrations (84).

While NMBA can effectively control the work of breathing and may be the only reliable method to prevent pSILI, adequate sedation is required to prevent awareness during NMBA use. Prolonged deep sedation and continuous paralysis expose patients to the long-term risks of immobility, contributing to increased ICU-related morbidity and mortality (79, 114). Further research is required regarding appropriate monitoring techniques for respiratory effort and therapeutic strategies to modulate such effort and achieve lung and diaphragm protective ventilation.

Anticoagulation

The optimal anticoagulation strategy for adult ECMO patients remains a subject of ongoing debate. Unfractionated heparin remains the most used anticoagulant, given that it can be easily titrated due to its short half-life and has a specific antidote (122–124). Direct thrombin inhibitors (DTIs) such as bivalirudin and argatroban may also be safely used for ECMO-supported patients, especially in patients with a history of heparin-induced thrombocytopenia (122, 123, 125). Bivalirudin has shown comparable thromboembolism and bleeding rates, with perhaps superior coagulation profiles than heparin, quicker achievement of therapeutic targets, and reduced bleeding and transfusion requirements (123, 126–129). Less is known regarding argatroban, but retrospective reviews suggest comparable bleeding risk with heparin (125, 130). Low-molecular-weight heparin may be used as an alternative in selected patients (131). Finally, emerging evidence supports the safety of "low-dose" anticoagulation strategies, particularly in patients receiving venovenous ECMO (132–134). Small studies have reported using ECMO without systemic anticoagulation, with a similar prevalence of circuit and patient thrombosis (133, 135). Special populations, such as patients with COVID-19 requiring ECMO, present additional complexities due to increased risk of thrombosis and bleeding (136).

One of the key challenges in optimizing anticoagulation during ECMO is the lack of a single, universally accepted, reliable laboratory test for monitoring anticoagulation (137). ELSO guidelines recommend using anti-Xa levels for heparin monitoring (137). In addition, anti-Xa levels and exogenous antithrombin administration may be helpful in the setting of heparin resistance (138–141). Activated clotting time is widely available, but it is affected by factors unrelated to anticoagulant levels, limiting its specificity (137). For DTIs, activated partial thromboplastin time is considered the gold standard, but its reliability diminishes at higher drug concentrations and in critically ill patients (140). Viscoelastic hemostatic assays like thromboelastometry and thromboelastography have also been used for anticoagulation monitoring (142–144).

Large randomized clinical trials are urgently needed to accurately determine the necessity of anticoagulation, appropriate therapeutic dosing, and optimal target levels in ECMO-supported patients.

Limitations

This study had several limitations. First, the panel's relatively small sample size with experts from certain continents may limit the generalizability of the findings to other regions. Additionally, using a Delphi process could have introduced selection bias. However, efforts were made to minimize this bias by selecting experts from multiple geographic regions with diverse resource settings, including all the ELSO Chapters. The methodology was also prone to response bias, as the research priorities list was drafted by the organizing committee after consolidating the expert responses and suggestions. Although the position paper provided a literature review of the current evidence, a more individualized approach might be required for specific patients. In addition, while the consensus threshold was predefined at 70%, other priorities hovered near the cutoff. Given the panel size, a single vote could influence inclusion. These near-threshold topics, however, remain highly relevant to clinical practice and warrant continued attention in future research agendas. Nevertheless, this study had notable strengths. It is the first of its kind to establish consensus on ECMO

pharmacology research priorities, with expert statements that have strong potential to shape future studies. Second, the Delphi process used was rigorous and anonymous, ensuring unbiased input by preventing dominance and peer pressure. Last, the experts were selected based on predefined criteria, and four Delphi rounds were conducted with a diverse panel of 25 experts, maintaining a 0% attrition rate.

CONCLUSIONS

This position paper identifies six key research priorities—ranging from pharmacokinetics/pharmacodynamics reporting to antimicrobial dosing, sedation, neuromuscular blockade, anticoagulation, and interactions with RRT. These priorities provide a roadmap to advance pharmacological care for ECMO-supported patients, aiming to guide future research, inform funding strategies, and promote evidence generation that can be translated to improved bedside decision-making and improved clinical outcomes.

1 *Interdepartmental Division of Critical Care Medicine, Toronto General Hospital, University of Toronto, Toronto, ON, Canada.*

2 *Department of Anesthesia, Critical Care Medicine and Pain Medicine, Kuwait Extracorporeal Life Support Program, Al-Amiri Hospital, Kuwait City, Kuwait.*

3 *Department of Health Science Anesthesia and ICU School of Medicine, University of Basilicata San Carlo Hospital, Potenza, Italy.*

4 *Cardiothoracic Transplantation and Mechanical Circulatory Support, Royal Brompton and Harefield Hospitals, Guy and St Thomas NHS Foundation, London, United Kingdom.*

5 *Department of Pharmacy, Cleveland Clinic, Cleveland, OH.*

6 *Cardiothoracic and Transplant Intensive Care Unit, Hospital Calderon Guardia, San José, Costa Rica.*

7 *Center for Clinical Research, University of Queensland Centre for Clinical Research, Herston, QLD, Australia.*

8 *Surgical Critical Care, Medical University of South Carolina, Charleston, SC.*

9 *Anesthesia Department, Charite University Hospital, Berlin, Germany.*

10 *Critical Care Patient Center, Coordinator Critical Care Patient Center, Clínica Las Condes, Universidad Finis Terrae, Faculty of Medicine, Santiago, Chile.*

11 *Pharmacology Department, Pontificia Universidad Católica de Chile, Santiago, Chile.*

12 *Pharmaceutical Biology, University of Basilicata, Potenza, Italy.*

13 *Division of Clinical Pharmacology, University of Utah, Salt Lake City, UT.*

14 *Department of Pharmacy Practice, College of Pharmacy, Kuwait University, Kuwait City, Kuwait.*

15 *Intensive Care Unit, Hospital Italiano, Buenos Aires, Argentina.*

16 *Center for Clinical Research, University of Queensland Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, QLD, Australia.*

17 *Herston Infectious Diseases Institute (HeIDI), Metro North Health, Brisbane, QLD, Australia.*

18 *Departments of Pharmacy and Intensive Care Medicine, Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia.*

19 *Division of Anaesthesiology Critical Care Emergency and Pain Medicine, Nîmes University Hospital, University of Montpellier, Nîmes, France.*

20 *Intensive Care Department, SODIR Research Group, Vall d'Hebron Hospital Universitari, Vall d'Hebron Institut de Recerca, Barcelona, Spain.*

21 *Biomedical Research Networking Center, CIBERES, ISCIII, Madrid, Spain.*

22 *Pharmacy Department, Vall d'Hebron University Hospital, Barcelona, Spain.*

23 *Critical Care Division, Cleveland Clinic Abu Dhabi, Al Maryah Island, Abu Dhabi, United Arab Emirates.*

24 *Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, OH.*

25 *Sorbonne University, Clinical Research Group in Anesthesia, Resuscitation, and Perioperative Medicine, Public Hospitals of Paris, Department of Anesthesiology and Critical Care, Cardiology Institute, Pitié-Salpêtrière Hospital, Paris, France.*

26 *Department of Pharmacy, McGill University Health Centre, Montreal, QC, Canada.*

27 *Faculté de Pharmacie, Université de Montréal, Montreal, QC, Canada.*

28 *Department of Perfusion Services, Toronto General Hospital, Toronto, ON, Canada.*

29 *Department of Anaesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.*

30 *Adult Intensive Care Services, The Prince Charles Hospital and the University of Queensland, Brisbane, QLD, Australia.*

31 *Adult Critical Care Unit, New York Presbyterian Hospital, Columbia University, Irving Medical Center, New York, NY.*

Board members of the Extracorporeal Membrane Oxygenation Pharmacology Network (ECMOPharm Net) are: Diana Morales Castro, Kiran Shekar, and Amy L. Dzierba.

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Drs. Shekar and Dzierba are joint senior authors.

For information regarding this article, E-mail: diana.moralescastro@uhn.ca

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