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Review

Clinical applications of oXiris membranes: Targeting inflammation and renal dysfunction in ICU patients

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ABSTRACT

The oXiris membrane represents a notable advance in continuous renal replacement therapy for critically ill patients with severe infection, sepsis, and other conditions characterized by immune dysregulation. Built on a highly adsorptive poly (ethersulfone)/AN69 platform modified to remove inflammatory mediators, endotoxins, and larger molecules, oXiris combines renal support with targeted immunomodulation. In intensive care settings it has been used for sepsis and septic shock, intra-abdominal infection, cardiogenic shock (including during veno-arterial extracorporeal membrane oxygenation, VA-ECMO), acute kidney injury, and selected autoimmune disorders. Observational studies and small trials suggest improved hemodynamic stability, reduced vasopressor requirements, and decreases in circulating cytokines and endotoxin. Sequential extracorporeal therapy combining oXiris with other devices (e.g., CytoSorb, Seraph-100, Toraymyxin) may further potentiate these effects.
Evidence from large, randomized trials remains limited, and questions persist regarding patient selection, timing, and cost-effectiveness. This narrative review summarizes the membrane's technical features and mechanisms of action, synthesizes available clinical data across major indications, and outlines current limitations and research priorities.

Introduction

Sepsis and septic shock are acknowledged leading causes of mortality in critically ill patients, despite advances in diagnostics, etiologic and supportive therapies.[1,2] The underlying systemic inflammatory response is heterogeneous and dynamic, often limiting the impact of pharmacologic therapy alone.[3] Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection.[4] Its pathophysiology involves a complex imbalance between pro-inflammatory activation and immune suppression, leading to profound metabolic, microcirculatory, and immunologic alterations.[5] Excessive release of cytokines such as IL-6 and TNF-α, endothelial and glycocalyx injury, impaired microvascular perfusion, and mitochondrial dysfunction contribute to hemodynamic instability and organ failure.[6] Endotoxin and damage-associated molecular patterns (DAMPs) further amplify this response, sustaining a self-propagating inflammatory loop.[7]

This dynamic imbalance between exaggerated inflammation and immune suppression is considered a major driver of morbidity and mortality in septic shock.[7] In this context, extracorporeal blood purification strategies have emerged as a potential adjunctive approach to mitigate excessive inflammatory burden and restore immune homeostasis.[8] The oXiris membrane, combining renal support with endotoxin and cytokine adsorption capabilities, may help interrupt the pathological amplification cycle observed in sepsis, particularly in patients with severe hemodynamic instability and high inflammatory load. Given these mechanisms, extracorporeal interventions targeting inflammatory mediators and endotoxin have been proposed as potential adjunctive therapies in sepsis.

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Extracorporeal blood purification has therefore gained attention as an adjunctive strategy to remove endotoxin and inflammatory mediators. oXiris, an evolution of the AN69 platform, integrates adsorption of endotoxins and cytokines with the diffusive and convective clearance of Continuous Renal Replacement Therapy (CRRT).[9] Through this combined function, the device enables simultaneous renal support and extracorporeal immunomodulation, which may be relevant in patients with severe sepsis, septic shock, and multiple organ dysfunction. Observational studies, small interventional trials,[10–14] and registry analyses[15,16] report encouraging physiological effects, such as hemodynamic improvement and reductions in inflammatory biomarker, although high-quality randomized evidence remains limited. This review summarizes the technical principles of the oXiris membrane, evaluates current clinical evidence, and discusses challenges and future directions for its integration within critical care practice.

Membrane Characteristics and Technical Features

The OXiris membrane is an advanced evolution of the AN69 hydrogel structure, designed for use in Continuous Renal Replacement Therapy (CRRT) with additional adsorptive properties. Its core material, AN69, is a copolymer of acrylonitrile and sodium methallyl sulfonate that forms a negatively charged hydrogel matrix.[17] This intrinsic structure allows adsorption of both pro-inflammatory and anti-inflammatory cytokines, in addition to its dialytic properties.

To enhance its functionality, the surface of the membrane is modified with a polyethyleneimine (PEI) cationic polymer, which provides a net positive charge. This modification enables efficient adsorption of negatively charged endotoxins (LPS) through ionic interactions.[18] Furthermore, the PEI layer allows covalent heparin grafting, improving hemocompatibility and reducing thrombogenicity, which is particularly relevant in critically ill patients at high bleeding risk.[19]

From a technical standpoint, the hollow-fiber design ensures a large surface area for solute exchange, combined with high mechanical stability suitable for prolonged CRRT sessions.[15] The pore size and porosity are optimized to allow removal of medium- and high-molecular-weight molecules, including endotoxins and cytokines, while maintaining effective clearance of conventional uremic toxins.[20] The biocompatibility profile of the membrane minimizes inflammatory response and maintains favorable interactions with blood and tissues. Moreover, the chemical and thermal stability of the AN69-based structure ensures consistent performance across different treatment conditions.[21]

Altogether, OXiris integrates diffusion, convection, and adsorption in a single device, providing both renal replacement therapy and immunomodulation through simultaneous removal of toxins, endotoxins, and inflammatory mediators (Figure 1). The main structural and functional characteristics are summarized in Table 1.

Mechanisms of Action

To better distinguish the classical renal replacement mechanisms from the immunomodulatory properties unique to oXiris, this section has been reorganized into two complementary components. The first describes solute removal through convection and diffusion, reflecting standard CRRT physiology. The second focuses on adsorption, which enables binding and removal of endotoxin and pro-inflammatory mediators at the membrane surface and within its porous structure.

The oXiris membrane (Vantive, Lyon, France) is based on a modified acrylonitrile-methallyl sulfonate copolymer (AN69), surface-treated (AN69ST) and further functionalized with a polyethyleneimine (PEI) cationic layer and a stabilized heparin surface functionalization.[17] These features improve biocompatibility and reduce thrombogenicity. The PEI layer confers a positive surface charge, supporting electrostatic binding of negatively charged molecules such as endotoxin, while the stabilized heparin surface functionalization enhances hemocompatibility without requiring systemic anticoagulant loading. In parallel, the sulfonate groups and the porous internal structure of the AN69 matrix facilitate cytokine adsorption through ionic interactions.[2–4]

Convection and diffusion (Classical CRRT clearance)

Convection and diffusion are the primary mechanisms for removing low- and medium-molecular-weight solutes during CRRT. Diffusion relies on concentration gradients across the semipermeable membrane and supports clearance of small solutes such as urea, creatinine, and electrolytes. Convection enhances removal by solvent drag under transmembrane pressure, allowing clearance of larger molecules within the cut-off properties of the membrane.[22]

In this regard, oXiris performs similarly to other high-flux CRRT filters and provides standard renal replacement support.

Adsorption (Immunomodulatory component)

Adsorption represents the distinctive therapeutic component of the oXiris membrane. Two adsorption mechanisms contribute to clearance: (1) Surface adsorption: negatively charged phosphate groups of endotoxin molecules (lipopolysaccharide, LPS) interact with the positively charged PEI layer through electrostatic binding at the membrane–blood interface. (2) Intrapore adsorption: cytokines, DAMPs, and other inflammatory mediators diffuse into the porous matrix of the membrane and bind to internal sulfonate groups, supporting sequestration beyond surface interaction.[14,23]

From a kinetic standpoint, adsorption is most effective during the initial phase of treatment, when membrane binding sites are still unoccupied. Clearance progressively decreases as adsorption capacity becomes saturated, supporting the “peak concentration hypothesis”, whereby transient removal of circulating inflammatory mediators may attenuate early hyperinflammation and facilitate immune homeostasis.[24]

Quantitatively, approximately 60%–70% of cytokine clearance results from adsorption, with 30%–40% derived from convective and diffusive transport.[23] This enables a broad molecular removal range from small solutes (urea, 60 Da) to middle molecules (IL-6 ≈ 21 kDa) and larger fragments such as HMGB1 (25–30 kDa). Experimental and clinical evidence has demonstrated removal of endotoxin and a broad panel of inflammatory mediators including TNF-α, IL-6, IL-8, IFN-γ, complement proteins, chemokines, and DAMPs.[14,23,25,26] Comparative in vitro

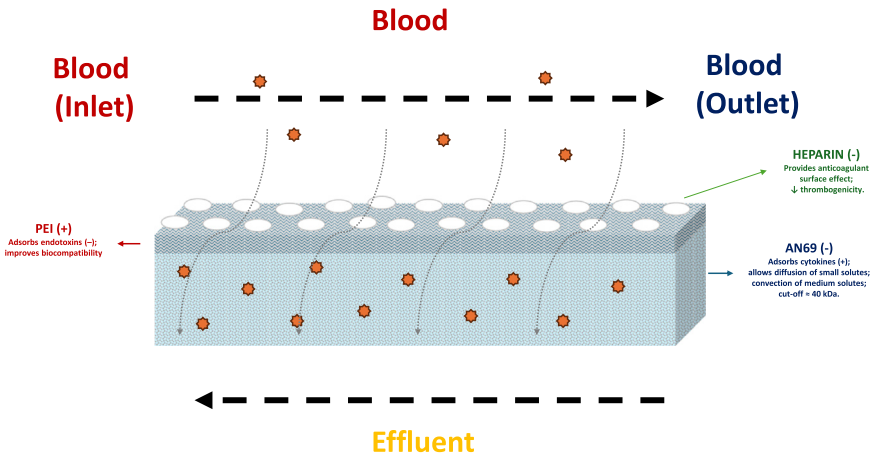

Figure 1. Schematic representation of the OXiris membrane. The three layers —AN69 hydrogel (–), PEI coating (+), and heparin grafting (–)—provide integrated functions of diffusion, convection, and adsorption, with complementary electrostatic properties for cytokines, endotoxins, and anticoagulation.
AN69: Acrylonitrile and sodium methallyl sulfonate copolymer; PEI: Polyethyleneimine.

Table 1
Summary of the structural modifications and associated clearance functions of the oXiris membrane.

Feature	Description/functional role
Base polymer	AN69 hydrogel membrane forming the core filtration structure.
Surface treatment	Modified AN69ST to improve biocompatibility and reduce bradykinin-generation during blood contact.
Cationic functional layer	PEI confers a strong positive surface charge enabling electrostatic adsorption of negatively charged endotoxin (LPS).
Heparin surface functionalization	Stabilized heparin bonded to membrane surface enhances hemocompatibility and reduces thrombogenicity without requiring systemic anticoagulant loading.
Clearance mechanisms	Standard CRRT solute removal through convection and diffusion for low- and middle-molecular-weight solutes (e.g., urea, creatinine, electrolytes).
Adsorption mechanisms	Dual adsorption: (1) surface binding of endotoxin via PEI, and (2) intrapore ionic adsorption of cytokines and other inflammatory mediators (e.g., IL-6, TNF-α, HMGB1).
Target molecular spectrum	Effective clearance from small solutes (~60 Da) to middle molecules (~20–30 kDa), including select immune mediators.
Intended clinical role	Combined renal replacement therapy with adjunctive immunomodulation in sepsis-associated inflammation or hyperinflammatory states.

AN69: Acrylonitrile and sodium methallyl sulfonate copolymer; CRRT: Continuous renal replacement therapy; HMGB1: High-mobility group box-1 protein; LPS: Lipopolysaccharide; PEI: Polyethyleneimine.

data show higher cytokine adsorption with oXiris and CytoSorb, whereas Toraymyxin demonstrates stronger selective endotoxin affinity.[23]

Clinically, reductions in IL-6, Procalcitonin (PCT), lactate, norepinephrine dose, and Sequential Organ Failure Assessment (SOFA) score have been observed in septic shock patients treated with oXiris, together with improved hemodynamic stability.[14,17,25,27,28]

Clinical Applications

A recent meta-analysis pooling 14 randomized controlled trials (RCTs) and observational studies suggested lower short-term mortality and improvements in physiologic parameters, although overall certainty of evidence was graded as low.[28] Although mechanistic and early clinical findings are promising, definitive survival benefit and long-term outcomes remain unproven and require adequately powered randomized trials.

The main clinical applications of oXiris are summarized in Table 2 and detailed in the following paragraphs.

Sepsis and septic shock

Sepsis pathophysiology is characterized by a complex interplay of excessive pro-inflammatory signaling and concurrent immune suppression, leading to endothelial and glycocalyx injury, microvascular dysfunction, mitochondrial impairment, and progressive organ failure.[29] Endotoxin and DAMPs further amplify cytokine release, driving a self-perpetuating inflammatory cascade responsible for vasoplegia, capillary leak, coagulopathy, and hemodynamic instability.[30]

Given this dysregulated host response, extracorporeal strategies targeting cytokines and endotoxin have been proposed as potential adjunctive interventions to stabilize the inflammatory milieu and restore immune homeostasis in septic shock.[8]

To provide a structured overview of the available evidence, we summarized key published clinical studies evaluating the use of the oXiris membrane in septic shock and sepsis-associated acute kidney injury (AKI), including randomized clinical trials, observational cohorts, registry data, and recent systematic reviews and meta-analyses (Table 3).

As shown in Table 3, most available data derive from small, randomized trials, observational cohorts, and registry-based analyses. While several studies consistently report reductions in vasopressor requirements, inflammatory biomarkers, lactate concentration, and early improvements in organ dysfunction scores, the overall certainty of evidence remains low due to methodological heterogeneity, limited statistical power, variability in CRRT settings, and differences in timing of intervention.

These limitations reflect broader challenges inherent to interventional research in sepsis, including biological heterogeneity, dynamic clinical trajectories, and difficulties achieving standardized patient selection and timing criteria. Mul-

Table 2
Main clinical applications of the oXiris membrane in intensive care.

Clinical condition	Predominant mechanism of action	Observed clinical benefits	Challenges/limitations
Severe sepsis and septic shock	Removal of endotoxins and cytokines; modulation of systemic inflammation	Reduced vasopressor requirement, decreased lactate, improved SOFA score, potential mortality reduction [10,14,25,28,46]	Limited high-quality RCTs; heterogeneous study designs; potential removal of beneficial molecules [25,28,46]
Complicated intra-abdominal infections	Removal of endotoxin and inflammatory mediators; hemodynamic stabilization	Reduced endotoxin burden, improved biomarker responses, early hemodynamic stabilization. [33,34]	Evidence mainly retrospective; no RCTs; unclear superiority *vs*. other sepsis sources [33]
Cardiogenic shock & VA-ECMO	Modulation of ECMO-associated inflammatory response	Early cytokine & endotoxin removal; hemodynamic stabilization signals in pilot studies [12]	Mixed or negative RCT outcomes; benefit not confirmed in controlled studies [12,13]
Cardiac surgery–associated AKI	Inflammation reduction + renal protection during extracorporeal circulation	Reduced incidence of CS-AKI in RCT subgroup analyses; benefit in high-risk patients [26]	Evidence limited to cardiac surgery population; unclear applicability to septic AKI broadly [26]
COVID-19 & viral hyperinflammation	Control of cytokine storm and endotoxin translocation in severe viral infection	IL-6 reduction, improved hemodynamics, better oxygenation, lower vasopressor need [27,45]	Mixed RCT signals; benefit may depend heavily on phenotype and CRRT indication [46]
Sequential or combination therapies	Synergistic multimodal extracorporeal clearance (e.g., oXiris + CytoSorb + Toraymyxin)	Faster clinical response and improved biomarker clearance in case series/cohorts [53,62]	No standardized protocol; lack of RCT evidence; high cost & logistic complexity [62,63]

AKI: Acute kidney injury; COVID-19: Coronavirus disease 2019; CRRT: Continuous renal replacement therapy; CS-AKI, cardiac surgery–associated acute kidney injury; DAMPs: Damage-associated molecular patterns; ECMO: Extracorporeal membrane oxygenation; IL-6: Interleukin-6; LPS: Lipopolysaccharide; MODS: Multiple organ dysfunction syndrome; PCT: Procalcitonin; RCT: Randomized controlled trial; SETS: Sequential extracorporeal therapies; SOFA: Sequential organ failure assessment; VA-ECMO: Veno-arterial extracorporeal membrane oxygenation.

Table 3
Summary of key clinical evidence evaluating the oXiris membrane in sepsis and septic shock.

Reference	Study design	Population/setting	Sample size (oXiris/control)	Comparator	Primary outcomes reported	Main findings/interpretation
Turani et al. [64]	Pilot observational study	Septic shock requiring CRRT	20/–	Not applicable (single-arm)	Vasopressor requirement, lactate, IL-6, SOFA score	Demonstrated feasibility and early physiological improvements (↓ vasopressors, lactate, cytokines). No mortality evaluation; hypothesis-generating.
Villa et al. (oXirisNet Registry) [16]	Multicenter registry analysis	Real-world septic shock treated with CRRT	97/–	Not applicable (registry, no comparator)	Feasibility, anticoagulation strategy, filter performance	Feasibility confirmed; registry established for real-world outcome tracking. No comparative outcomes available.
Guan et al. [65]	Controlled observational cohort	Septic shock + AKI on CRRT	70/66	Standard CRRT filter	Mortality, SOFA, PCT, vasopressors	Lower early mortality and faster SOFA and biomarker improvement with oXiris; effect not maintained at 90 days.
Zheng et al. [31]	Retrospective controlled cohort	Sepsis-associated AKI	88/155	Standard CRRT filter	Renal recovery, mortality, lactate, SOFA	No mortality difference; greater improvement in lactate and SOFA in more severely ill subgroups, suggesting phenotype-dependent benefit.
Wang et al. [28]	Systematic review & meta-analysis	Sepsis and septic shock treated with CRRT	14 studies (RCTs + cohorts), 695 total patients	Mixed designs	Mortality, vasopressors, SOFA, ICU LOS	Suggested early mortality and physiological benefit; certainty low due to heterogeneity and predominance of non-randomized studies.
Siew et al. [32]	Systematic review & meta-analysis	Critically ill patients treated with oXiris	10 studies, 481 patients	Mixed designs	Mortality, IL-6, CRP, lactate, organ dysfunction	Reported improvements in organ dysfunction markers and mortality; overall evidence quality graded very low.
Smirnova et al. [10]	Case series	Refractory septic shock (no AKI) treated with hemoperfusion	3/–	Not applicable (single-arm)	Hemodynamics, IL-6, PCT	Rapid IL-6 and vasopressor reduction after short hemoperfusion session; highly exploratory.

AKI: Acute kidney injury; CRP: C-reactive protein; CRRT: Continuous renal replacement therapy; ICU: Intensive care unit; IL-6: Interleukin-6; LOS: Lntensive care unit length of stay; PCT: Procalcitonin; RCTs: Randomized controlled trials; SOFA: Sequential organ failure assessment.

ticenter registries, such as oXirisNet, may facilitate real-world feasibility assessment, phenotype refinement, and hypothesis generation, although their value would be enhanced by the inclusion of comparator sites or quasi-controlled analyses.[16]

Emerging evidence suggests that potential benefit may be greatest in specific clinical phenotypes, such as patients with high inflammatory burden, endotoxin-driven shock, early vasoplegia requiring escalating vasopressors, and sepsis-associated AKI requiring CRRT.[10,31] Future enrichment-based or adaptive randomized trial designs will likely be required to determine attributable treatment benefit and identify true responder populations.[32]

Intra-Abdominal infection

Intra-abdominal infections (IAIs) represent a frequent source of sepsis and septic shock, often associated with severe inflammatory burden and multi-organ dysfunction. However, available clinical studies evaluating oXiris include heterogeneous

sepsis populations, and no published data to date demonstrate a differential response or superior efficacy in IAI-related sepsis compared with other infection sources. Therefore, IAI should not currently be considered a standalone indication or selection criterion for oXiris. At present, treatment decisions appear better guided by physiologic severity (e.g., refractory vasoplegia), inflammatory phenotype (elevated IL-6, PCT, endotoxin), and the presence of sepsis-associated AKI requiring CRRT rather than by infection origin.[33,34] In this context, the ongoing OASES randomized controlled trial[35] will specifically assess the impact of the oXiris membrane on hemodynamic stabilization in critically ill patients with septic shock secondary to IAI. Future studies stratifying outcomes by sepsis source may help determine whether specific etiological subgroups—including IAI—derive preferential benefit from extracorporeal immunomodulation.

Cardiogenic shock and ECMO therapy

Cardiogenic shock has high morbidity and mortality due to impaired tissue perfusion and about 10% of patients with refractory shock require circulatory support like veno-arterial extracorporeal membrane oxygenation (VA-ECMO).[36,37] However, even with VA-ECMO, outcomes remain poor, with mortality rates over 50%.[38] This is due to mechanisms such as tissue hypoperfusion, ischemia-reperfusion injury, and systemic inflammatory response, leading to multiple organ failure (MOF).[39,40]

The digestive tract plays a key role in this process.[41] During ischemia-reperfusion, the intestinal barrier is compromised, allowing bacterial components like lipopolysaccharides (LPS) to enter the bloodstream, triggering inflammation and worsening MOF.[42,43] This creates a vicious cycle of barrier disruption and systemic inflammation.[44] The oXiris filter, with its three-layer structure and specialized membrane, can adsorb cytokines and LPS.[25] Studies have shown it may reduce systemic inflammation and vasoplegia without harming splanchnic perfusion.[23] It appears safe compared to standard hemofiltration membranes and may help control inflammation, reduce bacterial translocation, and prevent MOF. However, the data present in the literature about its use in VA-ECMO-supported cardiogenic shock patients are negative. In the CLEAN ECMO trial[12] the application of an oXiris filter in patients with cardiogenic shock undergoing V-A ECMO did not demonstrate a significant reduction in endotoxin levels at 48 h compared with standard care. The authors observed temporal decreases in IL-6 and GDF-15 levels in oXiris group, even if these changes did not translate into statistically significant improvements in clinical outcomes. OXICARD trial[11] evaluate the oXiris membrane during cardiopulmonary bypass in cardiac surgery patients at high risk of inflammation. Despite the theoretical benefits of the membrane, the study found no significant improvement in microcirculation, major cardio-vascular events, or inflammatory biomarkers compared to standard care. ECMORIX trial[13] showed that, in patients with cardiogenic shock supported by VA-ECMO and requiring renal replacement therapy, patients treated with oXiris filter did not evidence any reduction in LPS blood concentration in comparison to patients treated with ST-150 filter. Therefore, in light of the still controversial data regarding the use of the oXiris filter in patients with cardiogenic shock undergoing V-A ECMO, further randomized clinical trials are necessary to clarify the utility of this filter in this specific patient population.

Cardiac surgery–associated acute kidney injury

Recently, the SIRAKIO2 trial place a role for the oXiris membrane to prevent post-cardiac surgery associated AKI in adult patients, who underwent on-pump elective procedures. In this study, Pérez-Fernández et al.[26] randomized 343 patients to receive oXiris (EBP group) *vs.* standard of care (standard care group) during the cardiopulmonary bypass, and found that the rate of cardiac surgery-associated was 28.4% (95% CI: 21.7% to 35.8%) in the EBP group *vs.* 39.7% (95% CI: 32.3% to 47.3%) in the standard care group (P=0.03), with an adjusted difference of 10.4% (95% CI: 2.3% to 18.5%). Moreover, sensitivity analyses revealed that oXiris was more effective to reduce the occurrence of cardia surgery-associated AKI in those patients who are at increased risk for this condition, as affected by chronic kidney disease, diabetes, hypertension, low left ventricular ejection fraction (<40%), and lower body mass index (<30 kg/m^2). No studies have ever investigated the potential role of oXiris to prevent the occurrence of AKI in sepsis or inflammatory diseases.

COVID-19 and viral infections

In severe viral illness (predominantly COVID-19), oXiris has been investigated mainly in observational cohorts and small controlled studies. Signals are most consistent for biological/physiological improvement (IL-6 reduction, vasopressor down-titration, oxygenation), while effects on clinical outcomes like mortality remain uncertain. In the multicenter retrospective study by Abdelaty et al.[45] including 58 COVID-19 patients requiring CRRT, oXiris significantly reduced IL-6 levels at 24 and 72 h and improved partial pressure of arterial oxygen/fraction of inspired oxygen ratio, suggesting partial reversal of cytokine-driven organ dysfunction, though the survival benefit did not reach statistical significance (adjusted OR 5.97; P=0.117). By contrast, Kang et al.[46] conducted a small randomized study in non-AKI severe COVID-19 and found that oXiris—CRRT did not attenuate cytokine release syndrome, highlighting that benefit may depend on CRRT indication and patient selection. The most rigorous prospective data so far come from Villa et al.,[27] a multicenter observational cohort of 100 COVID-19 intensive care unit (ICU) patients with AKI treated either with oXiris—CRRT (n=50) or standard AN69ST-CRRT (n=50), matched for severity. The oXiris group showed faster IL-6 decline (median reduction −64% *vs.* −36% at 48 h, P=0.02), improved mean arterial pressure and reduced norepinephrine dose within 24 h, better lactate clearance, although there was 28-day mortality difference between study groups (42% *vs.* 46%, P=0.67). Importantly, the authors documented no excess adverse events or loss of CRRT performance, indicating the hemodynamic and immunologic safety of oXiris in viral systemic inflammatory response syndrome (SIRS) contexts. They concluded that oXiris may serve as an adjunctive immunomodulatory tool to stabilize early hyperinflammation, though outcome effects remain unproven. In such mixed sepsis states, Premužić et al. [47] reported that sequential blood purification (often including oXiris) in ICU COVID-19 with confirmed bacterial superinfection was associated with longer survival and improved SOFA trajecto-

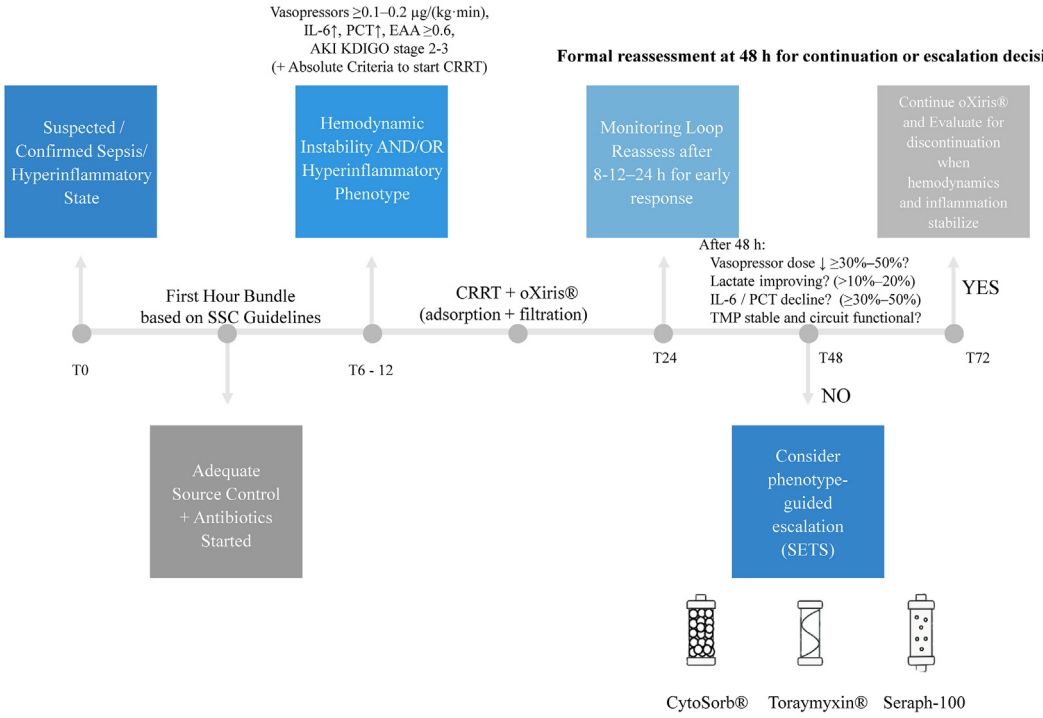

Figure 2. Pragmatic bedside decision flow for oXiris use in critically ill patients (expert-consensus-based model, not intended as a protocol). This framework summarizes a stepwise, response-guided approach to initiation, monitoring, and discontinuation of oXiris during CRRT. Treatment initiation is considered in patients with confirmed or suspected sepsis and hyperinflammatory phenotype after adequate source control and antimicrobial therapy. Early reassessment is recommended within 6–12 h to evaluate hemodynamic response and biomarker trajectories. A formal reassessment at 48 h supports continuation or discontinuation based on predefined clinical response criteria, including reduction in vasopressor requirement (≥30%–50%), improving lactate levels (≥10%–20% reduction), decreasing inflammatory biomarkers (e.g., IL-6, PCT), and stable extracorporeal circuit performance (TMP trends, clotting events, flow stability). In cases of insufficient response and ongoing hemodynamic instability, phenotype-guided escalation to sequential extracorporeal therapies (SETS) may be considered in expert centers and highly selected refractory shock scenarios. This flowchart is not intended as a fixed protocol, but rather as a pragmatic guide to be adapted to patient trajectory, institutional experience, and resource availability.
AKI: Acute kidney injury; CRRT: Continuous renal replacement therapy; EAA: Endotoxin activity assay; IL: Interleukin; KDIGO: Kidney Disease: Improving Global Outcomes; PCT: Procalcitonin; SETS: Sequential extracorporeal therapies; TMP: Transmembrane pressure.

ries. Across studies, oXiris use in viral disease shows consistent physiological improvements—lower cytokines, reduced vasopressors, and better oxygenation—but no definitive mortality advantage. Evidence quality remains moderate-to-low, limited by non-randomized designs and heterogeneity. Future trials should stratify by inflammatory phenotype and timing to confirm whether these physiological signals translate into improved survival.

Practical Guidance For Use of oXiris in Critically Ill Patients

Based on published evidence, expert recommendations, and our institutional experience, the following framework summarizes a pragmatic approach for bedside implementation of oXiris. These recommendations are aligned with the recently published *Asia-Pacific Expert Consensus Statement*[48] (Figure 2).

When and why to start (Initiation criteria and expected response)

The decision to initiate treatment with oXiris should consider both clinical severity and biomarker profile. oXiris may be started in patients with septic shock, especially when vasopressor requirements remain ≥0.1–0.2 μg/(kg·min) norepinephrine despite adequate fluid resuscitation, antibiotics, and source control. Additional criteria supporting initiation include hyperinflammatory phenotype (e.g., IL-6 >500–1000 pg/mL, PCT >5–10 ng/mL, C-reactive protein [CRP] markedly elevated), endotoxemia (Endotoxin Activity Assay ≥0.6), and/or sepsis-associated AKI requiring CRRT.

Evidence from observational cohorts and expert consensus,[48–51] including the 2024 Asia-Pacific statement, suggests that earlier initiation (within the first 6 to12 hours) may provide greater benefit, particularly before irreversible microvascular and immunologic dysfunction fully develops. Once initiated, clinical and biomarker trends should be monitored to assess response.

Indicators of therapeutic effect include a ≥30%–50% reduction in vasopressor dose within 24 to48 hours, improvement or stabilization in SOFA score, decreasing lactate levels and inflammatory markers (IL-6, PCT), and overall improvement in hemodynamic stability. Lack of improvement after an adequate treatment window should prompt reassessment for alternative diagnoses, inadequate source control, or the need for treatment escalation.

Duration and filter exchange strategy

Although the oXiris membrane is approved for continuous use up to 72 h, real-world clinical experience suggests that performance is highly dependent on operational conditions, clotting tendency, and inflammatory burden. Adsorptive capacity is maximal during the first phase of treatment and progressively decreases as binding sites become saturated. In parallel, extracorporeal performance may deteriorate due to transmembrane pressure (TMP) rise, pressure drop across the membrane, or overt filter clotting, particularly in patients with high inflammatory and prothrombotic profiles.[52]

For these reasons, rather than applying a fixed duration, a *dynamic monitoring strategy is recommended*, including: (1) TMP trend and sudden increases (>20–30 mmHg rise from baseline); (2) pressure drop across the filter; (3) blood flow limitations; (4) visible clotting or recurrent alarms; and (5) loss of clearance efficiency (clinical or biochemical).

Filter exchange is therefore best guided by a combination of technical performance (TMP/flow/clotting), clinical response (vasopressor need, lactate, hemodynamics), and Biomarker trajectory (e.g., IL-6, PCT, endotoxin when available).

In most critically ill patients, this approach results in typical replacement intervals of 12 to24 hours during the early high-inflammation phase, with possible extension toward 36 to 48 hours if the circuit remains stable and clearance targets are achieved.

When to stop (stopping criteria)

If no meaningful clinical or biochemical improvement is observed after an adequate trial period (typically 12 to 24 hours), therapy should be reconsidered and discontinued, unless ongoing renal support is still required. In this setting, the oXiris membrane may be replaced with a standard CRRT filter to maintain kidney support while avoiding unnecessary adsorption of antibiotics or beneficial immune mediators.

Finally, discontinuation should also be considered in patients who develop recurrent filter clotting despite appropriate anticoagulation or when rising inlet–outlet pressure gradients suggest mechanical failure. In such cases, persisting with oXiris may increase extracorporeal workload without additional therapeutic gain.

In summary, stopping criteria should integrate clinical status, biomarker trends, membrane functionality, and the evolving patient phenotype rather than rely on fixed duration. A structured reassessment every 8 to12 hours ensure rational continuation, timely discontinuation, and alignment with precision extracorporeal support principles. reconsidered. Ultimately, oXiris should be viewed as a goal- directed, time-limited intervention rather than a continuous default component of CRRT.

Use in the absence of AKI

Although the oXiris membrane is labelled for use during CRRT in patients with AKI, recent expert consensus suggests that in highly selected cases it may be considered *even before AKI develops.*[48] This off-label use should be confined to centers with expertise until regulatory indications are expanded.

Integration or escalation (Including the SETS concept)

In selected critically ill patients, particularly those exhibiting refractory septic shock or persistent hyperinflammation despite oXiris treatment, escalation to sequential extracorporeal therapy (SETS) may be considered.[53] This approach follows the principle that no single extracorporeal device can comprehensively target the heterogeneous and evolving biochemical landscape of sepsis.[53] Rather than representing routine practice, SETS should be reserved for patients in whom oXiris alone provides only partial physiological improvement or when the inflammatory profile suggests specific dominant drivers (e.g., marked endotoxemia or persistent cytokine storm).

Escalation typically follows a reassessment window of 12 to 24 hours, integrating clinical response (vasopressor decline, mean arterial pressure (MAP) stability), biochemical signals (IL-6, endotoxin reduction, lactate trends), and technical performance of the circuit. Device selection should be phenotype-driven, such as Toraymyxin®[49,54] may be added where endotoxemia predominates, CytoSorb®[55] can complement oXiris® when broad cytokine removal remains clinically relevant and Seraph-100® may be used in cases of suspected persistent pathogenemia or device-associated infection.[56]

SETS should remain *individualized rather than protocolized*, as timing and sequencing depend on patient trajectory, biomarker evolution, hemodynamic response, and resource availability. Current evidence supporting escalation to combined extracorporeal therapies remains limited and largely based on case reports, small cohorts, or early feasibility studies. No adequately powered randomized trials have confirmed superiority of multimodal or sequential approaches over single-device therapy. Therefore, escalation beyond oXiris should be considered only in selected patients with refractory shock or persistently elevated inflammatory or endotoxin burden despite adequate source control, antibiotic therapy, and initial extracorporeal support. Due to limited evidence and logistical complexity, escalation beyond oXiris should currently be restricted to experienced centers and carefully selected patients with refractory shock after adequate source control and optimized antimicrobial therapy.

Challenges and Limitations

Non-selective drug removal: impact on antibiotic therapy

Evidence regarding the interaction between the oXiris membrane and antibiotic pharmacokinetics remains scarce. Most available knowledge is extrapolated from studies with AN69ST, which demonstrated significant removal of vancomycin during continuous hemofiltration, accounting for nearly 40% of total clearance.[57] Direct clinical data on oXiris are lacking; however, a prospective pharmacokinetic observational study is currently ongoing (NCT04033029, Hospital Universitari de Bellvitge). This trial is evaluating plasma and effluent concentrations of several antibiotics, including piperacillin, ceftazidime, cefepime, ceftolozane, and daptomycin, in septic patients treated with continuous veno-venous hemodiafiltration (CVVHDF) using oXiris. Its results are expected to provide much-needed evidence on antibiotic clearance and to clarify whether desorption phenomena may further influence drug exposure during treatment.

Hemodynamic instability and extracorporeal risks

Despite encouraging signals from clinical experience, the use of oXiris-based extracorporeal therapies is not without potential risks. Hemodynamic instability may occur due to extracorporeal circulation and changes in intravascular volume status, which can be particularly problematic in already unstable patients with septic shock. Another important limitation is the non-selective nature of adsorption, which may lead to the unintended removal of essential molecules such as antibiotics, albumin, nutrients, or cytokines that play a protective immunoregulatory role.[58] Device-related complications, including circuit clotting, bleeding associated with anticoagulation, and vascular access problems, also remain significant concerns.[59] These issues highlight the importance of close monitoring, careful dose adjustments of concomitant medications, and individualized strategies to maximize benefits while minimizing harm.

Cost-effectiveness and accessibility

The cost-effectiveness of this approach remains debated, particularly given the absence of large randomized controlled trials confirming a survival benefit.[60] Accessibility is also uneven: while tertiary care centers may have the infrastructure and expertise to deliver oXiris therapy, many hospitals, especially in low-resource settings, face substantial barriers to implementation. Current evidence supporting oXiris is largely based on case series, small observational cohorts, and single-center experiences.

Variability in practice and registry data

The oXirisNet Registry[15] represents an important initiative in this context, providing prospective, real-world evidence and creating an interactive platform to improve data collection, bedside feedback, and practice standardization. Importantly, registry analyses have also highlighted a substantial variability among centers in terms of blood purification practices, reflecting differences in expertise, resources, and case-mix. Some centers are highly specialized and experienced in extracorporeal therapies, whereas others lack the same degree of qualification and technical support, which may influence patient outcomes and generalizability of results.

Future research needs

Future research should focus on large, multicenter randomized controlled trials to define optimal timing, patient selection, and integration with other extracorporeal strategies. In parallel, registries will continue to play a pivotal complementary role by providing real-world insights, identifying practice variability, and guiding the standardization of care to reduce disparities across centers. Although these studies provide valuable mechanistic insights and proof-of-concept evidence, they cannot establish causality or inform definitive clinical guidelines. Large, multicenter randomized controlled trials are urgently needed to evaluate efficacy, safety, and cost-effectiveness in broader populations.[61] Future research should also focus on defining the optimal timing of initiation, appropriate patient selection, and integration with other extracorporeal strategies in sequential therapy. The use of biomarker-guided approaches may help identify patients most likely to benefit, while long-term follow-up studies are required to assess sustained outcomes such as renal recovery, immune homeostasis, and overall survival.

Conclusion

The oXiris membrane offers an important advance in intensive care, combining kidney support with the ability to clear endotoxins and cytokines. This dual action not only helps patients with AKI but also addresses the uncontrolled inflammation that often worsens sepsis and septic shock. Current evidence, although limited, shows encouraging signals: improved hemodynamic stability, lower inflammatory markers, and in some cases better survival. However, most data come from small case series and registries, and large randomized clinical trials are still missing. Until stronger evidence is available, oXiris should be reserved for the sickest patients, used in centers with expertise in extracorporeal therapies, and carefully monitored to maximize benefits while minimizing risks. Looking ahead, it is unlikely that one device alone will be sufficient to manage the complexity of sepsis. Future strategies will probably rely on sequential or combined extracorporeal treatments, tailored to each patient's condition. In this scenario, oXiris can play a central role, either alone or in combination with other blood purification systems. More research will be key to defining who benefits most, when treatment should start, and how to integrate it into broader critical care practice.

CRediT Authorship Contribution Statement

Salvatore Lucio Cutuli: Writing – review & editing, Writing – original draft, Conceptualization. **Sergio Lassola:** Writing – review & editing, Writing – original draft, Conceptualization. **Règinald Philippe:** Writing – review & editing, Writing – original draft. **Silvia De Rosa:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization.

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Ethics Statement

Not applicable.

Conflict of Interest

S.L. has given presentations at national and international conferences and has received support from Estor. S.L.C. has received support from Vantive and Estor. S.D.R. has received support from Vantive, Estor, Fresenius Medical, and Toray. R.P. declares no conflicts of interest. The authors declare that they have no other financial or personal relationships that could inappropriately influence (bias) the content or conduct of this study. Given her role as Editorial Board Member, S.D.R. had no involvement in the peer-review of this article and has no access

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References

[1] Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet 2020;395(10219):200–11.
[2] La Via L, Sangiorgio G, Stefani S, Marino A, Nunnari G, Cocuzza S, et al. The global burden of sepsis and septic shock. Epidemiologia 2024;5(3):456–78.
[3] Iskander KN, Osuchowski MF, Stearns-Kurosawa DJ, Kurosawa S, Stepien D, Valentine C, et al. Sepsis: multiple abnormalities, heterogeneous responses, and evolving understanding. Physiological Reviews 2013;93(3):1247–88.
[4] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):801.
[5] Hotchkiss RS, Monneret G, Payen D. Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy. Nat Rev Immunol 2013;13(12):862–74.
[6] Nie J, Zhou L, Tian W, Liu X, Yang L, Yang X, et al. Deep insight into cytokine storm: from pathogenesis to treatment. Sig Transduct Target Ther 2025;10(1):112.
[7] Roh JS, Sohn DH. Damage-associated molecular patterns in inflammatory diseases. Immune Netw 2018;18(4):e27.
[8] Bottari G, Ranieri VM, Ince C, Pesenti A, Aucella F, Scandroglio AM, et al. Use of extracorporeal blood purification therapies in sepsis: the current paradigm, available evidence, and future perspectives. Crit Care 2024;28(1):432.
[9] Cecchi M, Ulsamer A, Villa G. Oxiris membrane in sepsis and multiple organ failure. In: Bellomo R, Ronco C, editors. Contributions to nephrology. S. Karger AG; 2023. p. 55–65. [citato 5 ottobre 2025] Disponibile su: https://karger.com/chapter/doi/10.1159/000527355.
[10] Smirnova D, Serzans R, Klibus M, Liguts V, Lece A, Skesters A, et al. Hemoperfusion using the Oxiris membrane in septic shock patients with preserved kidney function: a case series. J Clin Med 2025;14(6):2113.
[11] Abou-Arab O, Huette P, Ibrahima A, Beyls C, Bayart G, Guilbart M, et al. Cytokine hemoadsorption versus Standard care in Cardiac surgery using the Oxiris membrane: the OXICARD single-center randomized trial. Anesthesiology 2025;142(5):874–84.
[12] Ko RE, Choi KH, Lee K, Jeon J, Jang HR, Chung CR, et al. The effects of extracorporeal blood purification (oXiris®) in patients with cardiogenic shock who require VA-ECMO (CLEAN ECMO): a prospective, open-label, randomized controlled pilot study. Crit Care 2025;29(1):255.
[13] Nguyen M, Alvarez M, Evezard C, Berthoud V, Leleu D, Pais-De-Barros JP, et al. Endotoxin removal by the OXIRIS filter for cardiogenic shock requiring veno-arterial extra-corporeal life support: the ECMORIX randomized controlled trial. Ann Intensive Care 2025;15(1):92.
[14] Ulsamer A, Pomarè Montin D, Bocciero V, Parra Morales TJ, Tofani L, di Girolamo L, et al. Interleukin-6 removal and clinical effects of Oxiris: a systematic review and meta-analysis. Blood Purif 2025:1–10. doi:10.1159/000547587.
[15] Villa G, De Rosa S, Samoni S, Neri M, Cosimo C, Romagnoli S, et al. oXirisNet registry: a prospective, National Registry on the oXiris Membrane. Blood Purif 2019;47(Suppl 3):1–8.
[16] Villa G, Fioccola A, Mari G, Cecchi M, Pomarè Montin D, Scirè-Calabrisotto C, et al. A role of circuit clotting and strategies to prevent it during blood purification therapy with oXiris Membrane: an observational multicenter study. Blood Purif 2022;51(6):503–12. doi:10.1159/000524230.
[17] Li Y, Sun P, Chang K, Yang M, Deng N, Chen S, et al. Effect of continuous renal replacement Therapy with the oXiris Hemofilter on critically ill patients: a narrative review. J Clin Med 2022;11(22):6719.
[18] Wang Q, Wang Y, Huang Y, Wang H, Gao Y, Zhao M, et al. Polyethyleneimine (PEI) based positively charged thin film composite polyamide (TFC-PA) nanofiltration (NF) membranes for effective Mg2+/Li+ separation. Desalination 2023;565:116814.
[19] Zawidlak-Węgrzyńska B, Rydz J, Musioł M, Radziwon-Balicka A. Polymer-drug anti-thrombogenic and hemocompatible coatings as surface modifications. Pharmaceutics 2024;16(3):432.
[20] Liu M, Yu F, Niu L, Chi H. Advances in nanofiltration membrane pore size adjustment techniques: a review. Environmental Functional Materials 2025:S2773058125000109.
[21] Bonomini M, Piscitani L, Di Liberato L, Sirolli V. Biocompatibility of surface-modified membranes for chronic hemodialysis therapy. Biomedicines 2022;10(4):844.
[22] Ronco C, Bellomo R, Kellum JA. Ricci. Critical Care Nephrology. 3rd ed. Philadelphia: Elsevier; 2017.
[23] Malard B, Lambert C, Kellum JA. In vitro comparison of the adsorption of inflammatory mediators by blood purification devices. ICMx 2018;6(1):12.
[24] Ronco C, Tetta C, Mariano F, Wratten ML, Bonello M, Bordoni V, et al. Interpreting the mechanisms of continuous Renal Replacement Therapy in sepsis: the peak concentration hypothesis. Artificial Organs 2003;27(9):792–801.
[25] Broman ME, Hansson F, Vincent JL, Bodelsson M. Endotoxin and cytokine reducing properties of the oXiris membrane in patients with septic shock: a randomized crossover double-blind study. PLoS One 2019;14(8):e0220444.
[26] Pérez-Fernández X, Ulsamer A, Cámara-Rosell M, Sbraga F, Boza-Hernández E, Moret-Ruíz E, et al. Extracorporeal blood purification and acute kidney injury in cardiac surgery: the SIRAKI02 randomized clinical trial. JAMA 2024;332(17):1446.
[27] Villa G, Romagnoli S, De Rosa S, Greco M, Resta M, Pomarè Montin D, et al. Blood purification therapy with a hemodiafilter featuring enhanced adsorptive properties for cytokine removal in patients presenting COVID-19: a pilot study. Crit Care 2020;24(1):605.
[28] Wang G, He Y, Guo Q, Zhao Y, He J, Chen Y, et al. Continuous renal replacement therapy with the adsorptive oXiris filter may be associated with the lower 28-day mortality in sepsis: a systematic review and meta-analysis. Crit Care 2023;27(1):275.
[29] Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent JL. Sepsis and septic shock. Nat Rev Dis Primers 2016;2(1):16045.
[30] Shankar-Hari M, Harrison DA, Rowan KM. Differences in impact of definitional elements on mortality precludes international comparisons of sepsis epidemiology—A cohort study illustrating the need for standardized reporting*. Critical Care Medicine 2016;44(12):2223–30.
[31] Zheng F, Wang YL, Zhou WY, Zhang J, Lu M, Pan NF, et al. Continuous renal replacement therapy with adsorbing filter oXiris in the treatment of sepsis associated acute kidney injury: a single-center retrospective observational study. BMC Nephrol 2024;25(1):456.
[32] Siew LY, Lee ZY, Yunos NM, Atan R, Cove ME, Lumlertgul N, et al. Outcomes of extracorporeal blood purification with oXiris® membrane in critically ill patients: a systematic review and meta-analysis. J Critical Care 2024;83:154844.
[33] Dong Y, Chen J, Zhang X, Wu S, Li Y, Zhang Q. Incorporation of oXiris bioabsorbent filter into CRRT in the treatment of severe abdominal infections and analysis of associated risk factors for early off-machine. Front Public Health, 13; 2025.
[34] Zhou Y, Liu MJ, Lin X, Jiang JH, Zhuo HC. Comparative efficacy of two hemopurification filters for treating intra-abdominal sepsis: a retrospective study. Chinese J Traumatol 2025;28(5):352–60.
[35] Chen J, Zhang Z, Gao J, Liu Y, Zhu B, Gao Y, et al. A multicentre, randomised controlled clinical trial evaluating the effect of the adsorptive filter oXiris on haemodynamics in abdominal septic shock patients requiring continuous renal replacement therapy (Oxiris for Abdominal SEptic Shock study). BMJ Open 2025;15(7):e094792.
[36] Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, et al., Authors/Task Force Members ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal 2011;32(23):2999–3054.
[37] Vahdatpour C, Collins D, Goldberg S. Cardiogenic shock. JAHA 2019;8(8):e011991.
[38] Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, et al. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. JAHA 2014;3(1):e000590.
[39] Millar JE, Fanning JP, McDonald CI, McAuley DF, Fraser JF. The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology. Crit Care 2016;20(1):387.
[40] Al-Fares A, Pettenuzzo T, Del Sorbo L. Extracorporeal life support and systemic inflammation. ICMx 2019;7(S1):46.
[41] De Jong PR, González-Navajas JM, Jansen NJG. The digestive tract as the origin of systemic inflammation. Crit Care 2016;20(1):279.
[42] Brunkhorst FM, Clark AL, Forycki ZF, Anker SD. Pyrexia, procalcitonin, immune activation and survival in cardiogenic shock: the potential importance of bacterial translocation. Int J Cardiol 1999;72(1):3–10.
[43] McILwain RB, Timpa JG, Kurundkar AR, Holt DW, Kelly DR, Hartman YE, et al. Plasma concentrations of inflammatory cytokines rise rapidly during ECMO-related SIRS due to the release of preformed stores in the intestine. Lab Invest 2010;90(1):128–39.
[44] MohanKumar K, Killingsworth CR, Britt McILwain R, Timpa JG, Jagadeeswaran R, Namachivayam K, et al. Intestinal epithelial apoptosis initiates gut mucosal injury during extracorporeal membrane oxygenation in the newborn piglet. Laboratory Investigation 2014;94(2):150–60.
[45] Abdelaty M, Mohamed A, Saad MO, Mitwally H, Alkadi MM, Hashim A, et al. Extracorporeal blood purification with Oxiris® filter in critically ill patients with COVID-19 requiring continuous renal replacement therapy. Int J Artif Organs 2023;46(12):629–35.
[46] Kang K, Luo Y, Gao Y, Zhang J, Wang C, Fei D, et al. Continuous renal replacement therapy with oXiris filter may not be an effective resolution to alleviate cytokine release syndrome in Non-AKI patients with severe and critical COVID-19. Front Pharmacol 2022;13:817793.
[47] Premužić V, Babel J, Gardijan D, Lapić I, Gabelica R, Ostojić Z, et al. Extracorporeal blood purification is associated with improvement in biochemical and clinical variables in the critically-ill COVID -19 patients. Ther Apher Dial 2022;26(2):316–29.
[48] Zhang L, Srisawat N, Lee CC, Lee DH, Lee K, Liu Z, et al. Extracorporeal blood purification with the oXiris® filter for patients with sepsis and hyperinflammatory conditions: the Asia-Pacific oXiris expert meeting 2024 consensus statements. Blood Purif 2025;54(11):621–38. doi:10.1159/000548214.
[49] De Rosa S, Marengo M, Fiorentino M, Fanelli V, Brienza N, Fiaccadori E, et al. Extracorporeal blood purification therapies for sepsis-associated acute kidney injury in critically ill patients: expert opinion from the SIAARTI-SIN joint commission. J Nephrol 2023;63:1731–42.
[50] Chawla LS, Bellomo R, Bihorac A, Goldstein SL, Siew ED, et al., on behalf of the Acute Disease Quality Initiative Workgroup 16 Acute kidney disease and renal recovery: consensus report of the acute disease quality initiative (ADQI) 16 workgroup. Nat Rev Nephrol 2017;13(4):241–57.
[51] Girardis M, Coloretti I, Antonelli M, Berlot G, Busani S, Cortegiani A, et al. Adjunctive immunotherapeutic agents in patients with sepsis and septic shock: a multidisciplinary consensus of 23. J Anesth Analg Crit Care 2024;4(1):28.
[52] Jiang S, Zhang Y, Zhao F, Yu Z, Zhou X, Chu H. Impact of transmembrane pressure (TMP) on membrane fouling in microalgae harvesting with a uniform shearing vibration membrane system. Algal Research 2018;35:613–23.

[53] Ronco C, Chawla L, Husain-Syed F, Kellum JA. Rationale for sequential extracorporeal therapy (SET) in sepsis. Crit Care 2023;27(1):50.
[54] De Rosa S, Villa G. Endotoxin induced-shock: a multidisciplinary approach in Critical care. Springer International Publishing; 2023. [citato 19 luglio 2023]. Disponibile su https://link.springer.com/10.1007/978-3-031-18591-5 .
[55] Taccone FS, Brunkhorst FM, Bottari G, Hidalgo J, Kribben A, Teboul JL, et al. The COSMOS Registry of CytoSorb hemoadsorption therapy in critically ill patients: protocol for an international, prospective registry. JMIR Res Protoc 2024;13:e55880.
[56] Chitty SA, Mobbs S, Rifkin BS, Stogner SW, Lewis MS, Betancourt J, et al. A multicenter evaluation of the Seraph 100 Microbind Affinity blood filter for the treatment of severe COVID-19. Crit Care Explor 2022;4(4):e0662.
[57] Tsuruyama M, Yamashina T, Tsuruta M, Tsukada H, Fujimoto A, Nagano M, et al. Vancomycin pharmacokinetics in critically ill patients receiving continuous haemodiafiltration with a polyethyleneimine-coated polyacrylonitrile membrane. J Clin Pharm Ther 2020;45(5):1143–8.
[58] Gao W, Chen Y, Li B, Liu SP, Liu X, Jiang Q. Determining the adsorption energies of small molecules with the intrinsic properties of adsorbates and substrates. Nat Commun 2020;11(1):1196.
[59] Guha C, Gallego D, Grandinetti A, Warren M, Jaure A. Patient perspectives on clotting in the extracorporeal circuit and decision-making regarding anticoagulation therapy. Semin Nephrol 2023;43(6):151475.
[60] Dianaty S, Khodadadi S, Alimoghaddam R, Mirzaei A. Comparison of outcomes and costs of extracorporeal blood purification therapies in critically ill COVID-19 patients. Ther Apher Dial 2023;27(3):505–16.
[61] Justice J, Miller JD, Newman JC, Hashmi SK, Halter J, Austad SN, et al. Frameworks for proof-of-concept clinical trials of interventions that target fundamental aging processes. J Gerontol A Biol Sci Med Sci 2016;71(11):1415–23.
[62] De Rosa S, Cutuli SL, Lorenzin A, Zanella M. Sequential extracorporeal therapy in sepsis. In: Bellomo R, Ronco C, editors. Contributions to nephrology. S. Karger AG; 2023. p. 149–59. [citato 5 ottobre 2025]. Disponibile su: https://karger.com/chapter/doi/10.1159/000527573.
[63] Monard C, Rimmelé T, Ronco C. Extracorporeal blood purification therapies for sepsis. Blood Purif 2019;47(Suppl 3):1–14.
[64] Turani F, Barchetta R, Falco M, Busatti S, Weltert L. Continuous renal replacement therapy with the adsorbing filter oXiris in septic patients: a case series. Blood Purif 2019;47(Suppl. 3):54–8.
[65] Guan M, Wang H, Tang X, Zhao Y, Wang F, Zhang L, et al. Continuous renal replacement therapy with adsorbing filter oXiris in acute kidney injury with Septic shock: a retrospective observational study. Front Med 2022;9:789623.