A Comprehensive Review of ECMO: Mechanisms, Indications, Benefits, and Complications

Asmi S[1], Mageshwari S[2], Logeshwaran R[3], Vishnumayaa P[4], Moulishwaran M[5], Sreelekhaa T[6], Vivek Reddy Murthannagari[7*], Divya Baskaran[8]

[1,2,3,4,5,7,8]Department of Regulatory Affairs, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, India

[6]Student, Department of Pharmaceutical Regulatory Affairs, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Udhagamandalam, India

[7*]Corresponding Author: Vivek Reddy Murthannagari, PhD, Assistant Professor, Department of Regulatory Affairs, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, India

Department(s) and institution(s): Department of Regulatory Affairs and JSS College of Pharmacy, JSS Academy of Higher Education & Research.

Acknowledgement: *The Department of Science and Technology – Fund for Improvement of Science and Technology (DST-FIST), New Delhi, provided infrastructural support to the department. No specific funding was received for the conduct or publication of this article.*

Conflicting Interest: *All authors declare that there is no conflict of interest.*

ABSTRACT

Background: Extracorporeal membrane oxygenation (ECMO) is a form of advanced life support in critically ill patients with severe cardiac and/or respiratory failure refractory to conventional therapy. This is when the blood flows through an external circuit where gas exchange takes place and delivery of oxygen and removal of carbon dioxide occurs. ECMO temporarily takes over the function of the lung and/or heart so that these organs can rest and recover. Technological advances over the years have made it safer, more efficient and clinically applicable in intensive care settings.

Objective: To provide a comprehensive overview of ECMO including classification, mechanism, clinical indications, therapeutic benefits and risks.

Methodology: This narrative review is based on published literature, clinical evidence and key trials assessing the efficacy and safety profile of ECMO in patients with severe respiratory and cardiac failure.

Results: ECMO is categorized as veno-venous (VV) ECMO, which provides respiratory support, and veno-arterial (VA) ECMO, which provides both cardiac and respiratory support. It is used extensively in such conditions as acute respiratory distress syndrome, acute respiratory failure, cardiogenic shock and severe COVID-19. ECMO supports lung-protective ventilation and improves survival in selected patients, but complications such as bleeding, thrombosis, infections, and neurological injury can occur.

Conclusion: ECMO remains a complex but life-saving intervention for carefully selected patients. Further developments in technology, patient selection and clinical management are expected to enhance its safety, broaden its applications and improve patient outcomes.

Keywords: ECMO, Extracorporeal Membrane Oxygenation, VV ECMO, VA ECMO, Respiratory Failure, Cardiac Failure, Life Support, Critical Care

How to cite this article: Asmi S, Mageshwari S, Logeshwaran R, Vishnumayaa P, Moulishwaran M, Sreelekhaa T, Murthannagari VR, Baskaran D. A Comprehensive Review of ECMO: Mechanisms, Indications, Benefits, and Complications. Int J Drug Deliv Technol. 2026;16(49s): 70-79. DOI: 10.25258/ijddt.16.49s.8
Source of support: Nil (DST-FIST provided infrastructural support only).
Conflict of interest: None

ABSTRACT
Background:
Extracorporeal membrane oxygenation (ECMO) is a form of advanced life support in critically ill patients with

severe cardiac and/or respiratory failure refractory to conventional therapy. This is when the blood flows through an external circuit where gas exchange takes place and delivery of oxygen and removal of carbon dioxide occurs. ECMO temporarily takes over the function of the lung and/or heart so that these organs can rest and recover. Technological advances over the years have made it safer, more efficient and clinically applicable in intensive care settings. Objective: To provide a comprehensive overview of ECMO including classification, mechanism, clinical indications, therapeutic benefits and risks. **Methodology:** This narrative review is based on published literature, clinical evidence and key trials assessing the efficacy and safety profile of ECMO in patients with severe respiratory and cardiac failure. Results: ECMO is categorized as veno-venous (VV) ECMO, which provides respiratory support, and veno-arterial (VA) ECMO, which provides both cardiac and respiratory support. It is used extensively in such conditions as acute respiratory distress syndrome, acute respiratory failure, cardiogenic shock and severe COVID-19. ECMO supports lung-protective ventilation and improves survival in selected patients, but complications such as bleeding, thrombosis, infections, and neurological injury can occur. **Conclusion:** ECMO remains a complex but life-saving intervention for carefully selected patients. Further developments in technology, patient selection and clinical management are expected to enhance its safety, broaden its applications and improve patient outcomes.

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is an advanced form of life support that provides temporary cardiac and respiratory assistance to patients with life-threatening conditions that are unresponsive to conventional therapy [1]. ECMO functions by circulating blood through an artificial membrane, where oxygen is supplied, and carbon dioxide is removed, before returning the blood to the patient's circulation. The first successful clinical application of ECMO was reported in the 1970s, and since then, the technology has evolved significantly [2]. These advancements include improvements in circuit design, the development of biocompatible membranes, the use of centrifugal pumps, and enhanced safety monitoring systems, all of which have contributed to improved patient outcomes and wider clinical application.

Veno-venous (VV) extracorporeal membrane oxygenation is a form of advanced life support used in patients with severe but potentially reversible respiratory failure in whom cardiac function remains adequate [3]. In this technique, deoxygenated blood is drained from large central veins, most commonly the femoral or internal jugular vein, and circulated through an extracorporeal circuit consisting of a pump and a membrane oxygenator. Within the oxygenator, gas exchange takes place as oxygen is added and carbon dioxide is removed from the blood [4]. The oxygenated blood is then returned to the venous circulation, typically near the right atrium, from where it is pumped by the patient's own heart into the systemic circulation. Since the circuit does not directly support cardiac output, VV ECMO relies entirely on an intact and functioning heart to maintain adequate perfusion. It is therefore indicated in conditions such as acute respiratory distress syndrome, severe pneumonia, and other causes of refractory hypoxemia or hypercapnia [5]. While VV ECMO effectively supports gas exchange and allows the lungs to rest and recover, it does not provide circulatory support and is not suitable for patients with cardiac failure.

Veno-arterial (VA) extracorporeal membrane oxygenation, in contrast, is employed in patients with severe cardiac dysfunction with or without associated respiratory failure, as it provides both hemodynamic and respiratory support. Similar to VV ECMO, blood is initially drained from a central vein and passed through an extracorporeal circuit where oxygenation and carbon dioxide removal occur [6]. However, in VA ECMO, the oxygenated blood is returned to the arterial system, typically via the femoral artery or directly into the aorta, thereby bypassing both the heart and lungs. This configuration allows the ECMO circuit to assume the function of the failing heart by maintaining systemic circulation and ensuring adequate oxygen delivery to vital organs. VA ECMO is therefore indicated in conditions such as cardiogenic shock, cardiac arrest, myocarditis, and post-cardiac surgery failure, and is often used as a bridge to recovery, transplantation, or mechanical circulatory support devices. Despite its life-saving potential, VA ECMO is more invasive and associated with higher risks, including bleeding, thrombosis, and limb ischemia, due to arterial cannulation and altered hemodynamic [7].

Table 1: **Comparison Between Veno-Venous (VV) and Veno-Arterial (VA) Extracorporeal Membrane Oxygenation**

FEATURE	**Veno-Venous ECMO**	**Veno – Arterial ECMO**
Primary Support	Lung / Respiratory	Heart & Lung (Circulatory)

Drainage Site	Large Vein Eg : Femoral	Large Vein
Return Site	Large Vein Eg : Internal Jugular	Large Vein Eg : Femoral Artery
Cardiac Output	Provided by the Patient's heart	Provided by the ECMO machine
Common Use Case	ARDS, Severe Pneumonia	Cardiogenic Shock, Cardiac arrest

This table compares Veno-venous and Veno-arterial ECMO based on support type, circulation mechanism, and clinical applications [8,9].

Device Description of ECMO System

The extracorporeal membrane oxygenation (ECMO) system consists of several essential components that work together to provide effective cardiopulmonary support. A central element of the ECMO circuit is the blood pump, which is responsible for propelling blood through the extracorporeal system [10]. Two main types of pumps are used in clinical practice: centrifugal pumps, which are commonly preferred in adult patients due to their lower risk of haemolysis and better flow control, and roller pumps, which are typically used for short-term support .

Another critical component is the membrane oxygenator, often referred to as the artificial lung. It facilitates gas exchange by delivering oxygen to the blood and removing carbon dioxide. Modern oxygenators are constructed using hydrophobic polymer membranes, which enhance gas transfer efficiency while minimizing plasma leakage and improving biocompatibility [11].

The ECMO circuit also includes a heat exchanger, which plays a vital role in maintaining the patient's blood temperature within a physiological range. This helps prevent hypothermia or hyperthermia during prolonged extracorporeal circulation, thereby ensuring metabolic stability [10]. In addition, cannulas are used to access the patient's vascular system. These flexible tubes are inserted into large blood vessels to enable the drainage and return of blood, and their proper selection and placement are crucial for minimizing complications such as bleeding or vascular injury [12].

Finally, the system is interconnected by tubing, which allows continuous blood flow between all components, including the pump, oxygenator, heat exchanger, and cannulas, thereby ensuring efficient and uninterrupted extracorporeal circulation [13].

Table 2: **Components of the ECMO Circuit with Their Biological Equivalents and Primary Functions**

COMPONENT	BIOLOGICAL EQUIVALENT	PRIMARY FUNCTION
Cannula	Access point for blood to enter / exit the body	The pipes / plumping
Blood Pump	Moves blood through the circuit	The Heart
Oxygenator	Exchange O_2 & CO_2	The Lung
Sweep Gas Blender	Controls the gas mixture sent to the oxygenator	The ventilation controls

Heat Exchanger	Regulates blood temperature	The thermostat

This table outlines ECMO components with their biological equivalents and corresponding physiological functions [14,15].

MECHANISM OF ECMO

The extracorporeal membrane oxygenation (ECMO) system functions by continuously circulating blood outside the body through a specialized circuit to provide cardiopulmonary support [16]. The process begins with the insertion of a cannula into a large vein, through which deoxygenated blood is drained from the patient and directed into the ECMO circuit. The blood then passes through a centrifugal pump, which propels it forward at a controlled and consistent flow rate. Following this, the blood enters a membrane oxygenator, where gas exchange occurs across a semipermeable membrane, allowing oxygen to diffuse into the blood while carbon dioxide is simultaneously removed [17]. To ensure physiological stability, the blood subsequently passes through a heat exchanger, which maintains it at an appropriate temperature before returning it to the patient. The oxygenated blood is then reinfused into the circulation, either into a vein in veno-venous (VV) ECMO or into an artery in veno-arterial (VA) ECMO, depending on the type of support required. Through this continuous cycle of drainage, pumping, gas exchange, temperature regulation, and reinfusion, ECMO effectively supports or replaces the function of the lungs and/or heart in critically ill patients [18].

Acute Respiratory Distress Syndrome (ARDS)

Acute respiratory distress syndrome (ARDS) is a severe inflammatory condition characterized by diffuse injury to the alveolar–capillary membrane, leading to impaired gas exchange and respiratory failure. It may result from direct lung injury, such as pneumonia or aspiration, or indirect causes, including sepsis, trauma, and systemic inflammation. ARDS is associated with high morbidity and mortality and requires prompt and effective management [19].

Pathophysiology

The pathophysiology of ARDS occurs in overlapping phases beginning with the exudative phase, which is characterized by damage to alveolar epithelial and endothelial cells, leading to increased permeability of the alveolar–capillary barrier. This results in leakage of protein-rich fluid into the alveoli, causing pulmonary edema and formation of hyaline membranes [20]. The accumulation of fluid reduces lung compliance and impairs oxygen diffusion, leading to severe hypoxemia. This is followed by an inflammatory phase in which activated neutrophils, macrophages, and inflammatory mediators further damage lung tissue, resulting in alveolar collapse, ventilation–perfusion mismatch, and worsening gas exchange. Subsequently, the fibroproliferative phase occurs, characterized by proliferation of fibroblasts and deposition of collagen in the lung interstitium, leading to fibrosis, reduced lung elasticity, and persistent respiratory dysfunction. These pathological changes collectively result in severe hypoxemia, decreased lung compliance, and impaired ventilation [21].

ECMO in ARDS

Extracorporeal membrane oxygenation (ECMO), particularly veno-venous (VV) ECMO, provides extracorporeal gas exchange in patients with severe ARDS who are unresponsive to optimal conventional therapy. It facilitates oxygenation and carbon dioxide removal while allowing lung-protective ventilation strategies, thereby minimizing ventilator-induced lung injury. Clinical trials such as the CESAR trial demonstrated improved survival in patients referred to ECMO centers compared to conventional management (63% vs 47%), while the EOLIA trial (2018) evaluated early initiation of VV ECMO in severe ARDS and suggested potential mortality benefits, although statistical significance was not definitive [22]. Evidence from systematic reviews further supports the use of ECMO in reducing mortality and the need for adjunctive therapies such as renal replacement therapy. Despite its benefits, ECMO is associated with complications including bleeding, thrombosis, infection, and neurological injury, and therefore requires careful patient selection and management. Overall, ECMO remains a life-saving intervention for patients with severe ARDS refractory to standard treatment [23].

Acute Respiratory Failure

Acute respiratory failure is a life-threatening condition that occurs when the respiratory system fails in one or both of its primary gas exchange functions, namely oxygenation and carbon dioxide elimination. It is broadly classified into two types: Type I (hypoxemic) respiratory failure, characterized by reduced arterial oxygen levels ($PaO_2 < 60$ mmHg), and Type II (hypercapnic) respiratory failure, defined by elevated carbon dioxide levels ($PaCO_2 > 50$ mmHg) often accompanied by respiratory acidosis. Acute respiratory failure can result from a variety of pulmonary and extrapulmonary conditions, with severe lung injury, including acute respiratory distress syndrome (ARDS), being one of the leading causes worldwide [24].

Pathophysiology

Efficient respiration depends on several critical factors, including adequate alveolar ventilation, proper matching of ventilation and perfusion (V/Q ratio), an intact alveolar–capillary membrane, functional respiratory muscles, and an effective central nervous system respiratory drive. Disruption at any of these levels can lead to acute respiratory failure. In normal physiology, the alveolar–capillary membrane is thin, allowing efficient diffusion of oxygen into the bloodstream and removal of carbon dioxide. However, in conditions such as ARDS or severe pneumonia, this membrane becomes thickened and damaged due to inflammation, edema, and cellular injury, impairing gas exchange. Additionally, ventilation–perfusion mismatch, reduced lung compliance, and respiratory muscle fatigue further exacerbate hypoxemia and/or hypercapnia, ultimately leading to respiratory failure [25].

ECMO in Acute Respiratory Failure

Extracorporeal membrane oxygenation (ECMO) is used in patients with severe acute respiratory failure when conventional therapies fail to maintain adequate oxygenation and carbon dioxide removal. Standard management typically includes lung-protective mechanical ventilation, prone positioning, and optimized medical therapy. In such cases, veno-venous (VV) ECMO is the preferred modality, as it provides extracorporeal gas exchange without direct cardiac support [26]. In VV ECMO, deoxygenated blood is drained from the venous circulation, passed through a membrane oxygenator where oxygen is added and carbon dioxide is removed, and then returned to the venous system. This process ensures adequate systemic oxygen delivery while facilitating carbon dioxide clearance. ECMO also enables the use of lung-protective or “lung rest” ventilation strategies, thereby reducing ventilator-induced lung injury. Clinical trials such as the CESAR (Conventional Ventilation or ECMO for Severe Adult Respiratory Failure) and EOLIA studies have demonstrated improved survival outcomes in selected patients. The CESAR trial showed increased survival without disability at six months in patients referred for ECMO, while also highlighting factors such as prolonged mechanical ventilation and intensive care unit stay as important considerations in overall patient outcomes [27].

Harlequin Syndrome (Differential Hypoxia / North–South Syndrome)

Harlequin syndrome, also known as differential hypoxia or North–South syndrome, is a clinical condition characterized by unequal oxygenation between the upper and lower parts of the body. It is most commonly observed in patients receiving peripheral veno-arterial extracorporeal membrane oxygenation (VA ECMO). Under normal physiological conditions, oxygenated blood from the lungs is uniformly distributed throughout the systemic circulation [28]. However, during peripheral VA ECMO, oxygenated blood is delivered retrogradely through the femoral artery into the descending aorta. When cardiac function begins to recover while pulmonary function remains severely impaired, the left ventricle ejects poorly oxygenated blood into the ascending aorta. As a result, the upper body, including the brain and coronary arteries, receives inadequately oxygenated blood, whereas the lower body continues to receive well-oxygenated blood from the ECMO circuit. This condition reflects a complex interaction between native cardiac output and extracorporeal circulation [29].

Pathophysiology

In peripheral VA ECMO, typically using a femoro-femoral configuration, oxygenated blood is infused into the descending aorta in a retrograde manner. As native cardiac output increases in the presence of ongoing pulmonary dysfunction, a mixing zone develops within the aorta where oxygenated ECMO blood and deoxygenated blood from the left ventricle meet. When cardiac output becomes dominant, poorly oxygenated blood preferentially perfuses the proximal aorta, supplying the upper body with desaturated blood, while the distal aorta continues to receive oxygen-rich blood from the ECMO circuit. This differential distribution of oxygenated blood leads to hypoxia in vital organs despite apparently adequate systemic circulation, making early recognition clinically important [30].

ECMO in Harlequin Syndrome

Harlequin syndrome represents a serious complication of VA ECMO that requires prompt recognition and management to prevent neurological and cardiac injury. Continuous monitoring of upper body oxygenation, particularly using right radial arterial blood gas analysis, is essential for early detection. Management strategies focus on improving oxygen delivery to the upper body and may include optimizing ventilator settings to enhance native lung oxygenation, increasing ECMO flow, or adjusting cannulation strategies. In some cases, conversion to alternative configurations such as veno-arterial-venous (VAV) ECMO or central cannulation may be necessary to ensure adequate oxygenation of both upper and lower body regions. Early intervention is critical to minimize complications and improve patient outcomes [31].

COVID-19

Coronavirus disease 2019 (COVID-19) is a highly infectious respiratory illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first identified in 2019. The disease spread rapidly across the globe and was declared a pandemic due to its high transmissibility and significant impact on public health. COVID-19 primarily affects the respiratory system; however, in severe cases, it can involve multiple organ systems, including the cardiovascular, renal, and nervous systems. Clinical manifestations range from mild

respiratory symptoms to severe pneumonia, acute respiratory failure, and multi-organ dysfunction. In critically ill patients, extracorporeal membrane oxygenation (ECMO) is used as an advanced supportive therapy when conventional treatment approaches fail [32].

Pathophysiology

The pathophysiology of COVID-19 begins when SARS-CoV-2 enters the body through the respiratory tract and binds to angiotensin-converting enzyme 2 (ACE2) receptors on alveolar epithelial cells. Following viral entry, replication within host cells triggers an inflammatory response that damages the alveolar epithelium and capillary endothelium, leading to increased vascular permeability and leakage of fluid into the alveolar spaces. This results in pulmonary edema, diffuse alveolar damage, and impaired gas exchange, ultimately causing severe hypoxemia and respiratory failure [33]. In advanced stages, an exaggerated immune response, known as a cytokine storm, leads to excessive release of inflammatory mediators, further worsening lung injury and contributing to multi-organ dysfunction. Additionally, COVID-19 is associated with endothelial injury and a hypercoagulable state, increasing the risk of microvascular thrombosis and impairing oxygen delivery. These combined effects contribute to the development of acute respiratory distress syndrome (ARDS) in critically ill patients [34].

ECMO in COVID-19

During the COVID-19 pandemic, ECMO emerged as a rescue therapy for patients with severe respiratory failure who did not respond to conventional management, including lung-protective mechanical ventilation, prone positioning, and optimized medical treatment. In such cases, veno-venous (VV) ECMO is most commonly used, as it provides extracorporeal oxygenation and carbon dioxide removal while preserving cardiac function. In VV ECMO, deoxygenated blood is drained from the venous circulation, passed through a membrane oxygenator where gas exchange occurs, and then returned to the venous system. This process ensures adequate systemic oxygen delivery and facilitates carbon dioxide clearance, allowing clinicians to reduce ventilator settings and adopt lung-protective or "lung rest" strategies, thereby minimizing ventilator-induced lung injury [35]. Clinical data from international ECMO registries during the pandemic demonstrated that survival outcomes in selected COVID-19 patients were comparable to those observed in patients with severe ARDS treated with ECMO. However, management of ECMO in COVID-19 is particularly challenging due to the associated hypercoagulable state, which increases the risk of thrombosis within the ECMO circuit and necessitates careful anticoagulation monitoring. Overall, ECMO played a crucial role in the management of severe COVID-19 cases, particularly in specialized centers with expertise in extracorporeal support [36].

Anticoagulation Practices in ECMO

Although extracorporeal membrane oxygenation (ECMO) plays a life-saving role in critically ill patients, it is associated with complex haemostatic challenges. The exposure of blood to the artificial surfaces of the ECMO circuit activates the intrinsic coagulation pathway, platelets, and inflammatory cascades. This process promotes thrombin generation and fibrin deposition, thereby increasing the risk of circuit thrombosis and systemic thromboembolism. At the same time, systemic anticoagulation increases the risk of bleeding complications, making the balance between thrombosis prevention and bleeding control one of the most critical aspects of ECMO management [37].

Pathophysiology

The haemostatic alterations observed during ECMO are multifactorial and begin with the activation of coagulation pathways upon contact of blood with non-endothelial surfaces of the extracorporeal circuit. This interaction triggers the intrinsic (contact) pathway through activation of factor XII, followed by sequential activation of downstream coagulation factors, ultimately leading to thrombin generation and conversion of fibrinogen to fibrin, resulting in clot formation within the circuit if not adequately anticoagulated. In parallel, inflammatory cytokines stimulate tissue factor expression, activating the extrinsic pathway via factor VII and factor X, further amplifying thrombin production and contributing to a prothrombotic state [38]. Additionally, platelet function is significantly altered due to shear stress and mechanical trauma within the circuit, leading to platelet activation, consumption, thrombocytopenia, and acquired von Willebrand factor deficiency. Complement activation and endothelial injury further exacerbate the imbalance between procoagulant and anticoagulant mechanisms. These combined effects create a complex haemostatic environment in which patients are at simultaneous risk of thrombosis and bleeding during ECMO therapy [39].

Discussion

Clinical Effectiveness of ECMO

Extracorporeal membrane oxygenation (ECMO) has emerged as a crucial life-saving intervention in patients with severe cardiac and respiratory failure who are unresponsive to conventional therapies. Evidence from major clinical trials such as CESAR and EOLIA demonstrates improved survival in carefully selected patients, particularly those with severe respiratory failure managed in specialized centers. ECMO also enables lung-protective ventilation strategies, thereby reducing ventilator-

induced lung injury and improving recovery outcomes [40].

Impact of ECMO Type and Indication on Outcomes

The type of ECMO and underlying clinical indication significantly influence patient outcomes. Veno-venous (VV) ECMO, primarily used for respiratory failure, is associated with better survival rates compared to veno-arterial (VA) ECMO, which is used in cardiac failure. This difference is largely due to the severity of illness and the presence of multi-organ dysfunction in patients requiring VA ECMO. Conditions such as cardiogenic shock and cardiac arrest are associated with higher mortality rates, often exceeding 50%, whereas respiratory indications demonstrate comparatively improved outcomes [41].

Age-Related Differences in Survival

Age is an important determinant of ECMO outcomes. Pediatric patients, particularly neonates, generally show higher survival rates compared to adults, which may be attributed to fewer comorbidities and greater physiological adaptability. In contrast, adult patients often present with chronic conditions and complex disease states that adversely affect prognosis. These differences highlight the importance of patient-specific factors in determining ECMO success [42].

Anticoagulation Challenges and Hemostatic Complications

Anticoagulation management remains one of the most critical and challenging aspects of ECMO therapy. The exposure of blood to artificial circuit surfaces activates coagulation pathways, increasing the risk of thrombosis, while systemic anticoagulation increases the risk of bleeding complications. Achieving an optimal balance between these opposing risks is complex and requires continuous monitoring. Complications such as intracranial hemorrhage, circuit thrombosis, and oxygenator failure significantly impact patient outcomes and require careful clinical management [43].

Complications and Risk Factors

Despite its life-saving potential, ECMO is associated with several complications that influence morbidity and mortality. These include bleeding, thrombosis, infections, neurological injury, and limb ischemia, particularly in VA ECMO. Additional complications such as hemolysis, acute kidney injury requiring renal replacement therapy, and multi-organ dysfunction further complicate patient management. Early recognition and prompt intervention are essential to minimize these risks [44].

Technological Advancements in ECMO

Recent advancements in ECMO technology have significantly improved its safety and efficiency. The development of biocompatible circuits, polymethylpentene membrane oxygenators, and centrifugal pumps has reduced complications such as hemolysis and plasma leakage. Portable ECMO systems and integrated monitoring technologies have enabled inter-hospital transport and expanded clinical applicability. Emerging innovations, including extracorporeal carbon dioxide removal ($ECCO_2R$) and wearable artificial lungs, offer promising future directions in extracorporeal support [45].

Factors Influencing Outcomes

Multiple factors influence ECMO outcomes, including the severity of the underlying disease, timing of initiation, type of ECMO support, duration of therapy, and presence of complications. Early initiation of ECMO in appropriate candidates has been associated with improved survival, whereas delayed initiation and prolonged support duration may worsen outcomes. Additionally, institutional experience and availability of specialized ECMO centers play a significant role in determining patient prognosis [46].

CONCLUSION

Extracorporeal Membrane Oxygenation (ECMO) has emerged as vital life support in modern critical care, especially for patients with severe respiratory or cardiac failure in which the patient does not respond to the conventional therapy. It is essential to provide oxygenation and removal of carbon dioxide from the body that allows the lungs and heart to rest and recover. Over the past decades, advancements in ECMO, which have better oxygenators, safer pumps and better monitoring systems, have significantly improved capacity, efficacy and clinical applicability. The ECMO has plays a important role in acute respiratory distress syndrome (ARDS), acute respiratory failure and severe COVID-19. Clinical trials and observational studies are demonstrated which show improved survival rates by using ECMO in specialised centres. By enabling lung-protective ventilation strategies. ECMO reduces ventilator-induced lung injury, which supports better long-term outcomes in selected patients. Despite its benefits, ECMO is associated with risks and challenges. Complications include blood bleeding, thrombosis, infection, neurological injury and device-related injuries and infections. Anticoagulation plays an important role, but the balance between clot prevention and avoiding bleeding is complex. Patient outcomes on ECMO vary upon multiple factors, including the underlying patient disease, timing of initiation, patient age, comorbidities, etc. Paediatric patients show better survival rates than adults. Whereas the adult outcomes are improving with advancements in care and technology. Early detection in appropriately selected patients has shown increased survival rates and reduces risk and complications. In conclusion, ECMO shows powerful but complex therapeutic intervention in critical care medicine. It offers life-saving potency in severe conditions. Its success,

then, depends on careful patient selection, skilled multidisciplinary management and continuous technical innovation. As research and clinical experience grow, ECMO is expected to play a role in improving survival and quality of life in critically ill patients.

LIST OF ABBREVIATIONS

ECMO – Extracorporeal Membrane Oxygenation
VV ECMO – Veno-Venous Extracorporeal Membrane Oxygenation
VA ECMO – Veno-Arterial Extracorporeal Membrane Oxygenation
VAV ECMO – Veno-Arterial-Venous Extracorporeal Membrane Oxygenation
ARDS – Acute respiratory distress syndrome
ARF – Acute Respiratory Failure
COVID-19 – Coronavirus Disease 2019
SARS-CoV-2– Severe Acute Respiratory Syndrome Coronavirus 2
ACE2 – Angiotensin-Converting Enzyme 2
PaO_2 – Partial Pressure of Oxygen in Arterial Blood
$PaCO_2$ – Partial Pressure of Carbon Dioxide in Arterial Blood
V/Q Ratio – Ventilation–Perfusion Ratio
ACT – Activated Clotting Time
aPTT – Activated Partial Thromboplastin Time
TEG – Thromboelastography
Anti-Xa – Anti-Factor Xa Assay
HIT – Heparin-Induced Thrombocytopenia
PMP – Polymethylpentene
$ECCO_2R$ – Extracorporeal Carbon Dioxide Removal
RRT – Renal Replacement Therapy
ICU – Intensive Care Unit
ABG – Arterial Blood Gas
FiO_2 – Fraction of Inspired Oxygen

REFERENCES:

1. Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med*. 2018;378(21):1965–75.
2. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*. 2009;374(9698):1351–63.
3. Makdisi G, Wang IW. Extra corporeal membrane oxygenation (ECMO) review of a lifesaving technology. *J Thorac Dis*. 2015;7(7):E166–76.
4. Abrams D, Combes A, Brodie D. Extracorporeal membrane oxygenation in cardiopulmonary disease in adults. *J Am Coll Cardiol*. 2014;63(25 Pt A):2769–78.
5. Schmidt M, Bailey M, Sheldrake J, Hodgson C, Aubron C, Rycus PT, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure: the RESP score. *Am J Respir Crit Care Med*. 2014;189(11):1374–82.
6. Marasco SF, Lukas G, McDonald M, McMillan J, Ihle B. Review of ECMO (extra corporeal membrane oxygenation) support in critically ill adult patients. *Heart Lung Circ*. 2008;17 Suppl 4:S41–7.
7. Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med*. 2012;38(10):1573–82.
8. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. Extracorporeal life support organization registry international report 2021: patient characteristics and outcomes. ASAIO J. 2022;68(7):831–40.
9. Ramanathan K, Tan CS, Maclaren G, Morozova SV, Brodie D. Extracorporeal membrane oxygenation for adult respiratory and cardiac failure: indications and outcomes. *Crit Care*. 2011;15(2):R63.
10. Lequier L, Annich G, Al-Ibrahim O, Bembea M, Brodie D, Brogan TV, et al. ELSO anticoagulation guideline. *ASAIO J*. 2014;60(4):379–83.
11. Bartlett RH, Ogino MT, Brodie D, McMullan DM, Lorusso R, MacLaren G, et al. Initial ELSO guidance document: ECMO for COVID-19 patients with severe cardiopulmonary failure. *ASAIO J*. 2020;66(5):472–4.
12. MacLaren G, Combes A, Bartlett RH. Contemporary extracorporeal membrane oxygenation for adult respiratory failure: life support in the new era. *Intensive Care Med*. 2012;38(2):210–20.
13. Combes A, Brodie D, Bartlett R, Brochard L, Brower R, Conrad S, et al. Position paper for the organization of ECMO programs for acute respiratory failure in adult patients. *Intensive Care Med*. 2014;40(3):388–91.
14. Sidebotham D, McGeorge A, McGuinness S, Edwards M, Willcox T, Beca J. Extracorporeal membrane oxygenation for treating severe cardiac and respiratory disease in adults: Part 1—overview of ECMO. *J Cardiothorac Vasc Anesth*. 2009;23(6):886–92.

15. Lorusso R, Gelsomino S, Parise O, Mendiratta P, Prodhan P, Rycus PT, et al. Venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock in adults: an overview of contemporary practice. *Intensive Care Med*. 2016;42(5):706–16.
16. Zwischenberger JB, Lynch JE. Will CESAR answer the adult ECMO debate? *Lancet*. 2009;374(9698):1307–9.
17. Diddle JW, Almodovar MC, Rajagopal SK, Rycus PT, Thiagarajan RR. Extracorporeal membrane oxygenation for respiratory failure in adults: state of the art. *Semin Respir Crit Care Med*. 2014;35(1):87–98.
18. Conrad SA, Rycus PT, Dalton H. Extracorporeal life support registry report 2017. *ASAIO J*. 2017;63(1):60–7.
19. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526–33.
20. Thompson BT, Chambers RC, Liu KD. Acute respiratory distress syndrome. *N Engl J Med*. 2017;377(6):562–72.
21. Matthay MA, Ware LB, Zimmerman GA. The acute respiratory distress syndrome. *J Clin Invest*. 2012;122(8):2731–40.
22. Grasselli G, Pesenti A, Cecconi M. Cardiopulmonary support with extracorporeal membrane oxygenation in COVID-19 and ARDS: a review of current evidence. Lancet Respir Med. 2020;8(12):1269–78.
23. Munshi L, Walkey A, Goligher E, Pham T, Uleryk EM, Fan E. Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. *Lancet Respir Med*. 2019;7(2):163–72.
24. Scala R, Heunks L. Highlights in acute respiratory failure. *Eur Respir Rev*. 2018;27(147):180008.
25. Tobin MJ. Principles and practice of mechanical ventilation. 3rd ed. New York: McGraw-Hill; 2013.
26. Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med*. 2011;365(20):1905–14.
27. Bein T, Weber-Carstens S, Goldmann A, Muller T, Staudinger T, Brederlau J, et al. Lower tidal volume strategy (EOLIA background analysis and ventilation strategy discussion). *Crit Care*. 2015;19:163.
28. Hou X, Yang X, Du Z, Xing J, Li H. Differential hypoxia during venoarterial ECMO: a review of mechanisms and management. *J Card Surg*. 2020;35(9):2155–61.
29. Lorusso R, Raffa GM, Heuts S, Lo Coco V, Meani P, Natour E, et al. Venoarterial extracorporeal membrane oxygenation and differential hypoxia. *Crit Care*. 2017;21(1):1–9.
30. Napp LC, Kühn C, Bauersachs J. ECMO in cardiac arrest and cardiogenic shock. *Cardiovasc Res*. 2017;113(10):1181–90.
31. Biscotti M, Lee A, Basner RC, Agerstrand CL, Abrams D, Brodie D, et al. Hybrid configurations via VAV ECMO. *Ann Thorac Surg*. 2014;97(6):2136–43.
32. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of COVID-19 patients in Wuhan. *Lancet*. 2020;395(10223):497–506.
33. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2. *Cell*. 2020;181(2):271–80.
34. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, et al. Endothelial cell infection in COVID-19. *Lancet*. 2020;395(10234):1417–8.
35. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. ECMO support in COVID-19 patients. *Lancet*. 2020;396(10257):1071–8.
36. Schmidt M, Hajage D, Lebreton G, Monsel A, Voiriot G, Levy D, et al. ECMO for severe COVID-19. *Lancet Respir Med*. 2020;8(11):1121–31.
37. Olson SR, Murphree CR, Zonies D, Meyer AD, McCarty OJ, Deloughery TG, et al. Thrombosis and bleeding in ECMO. *J Thromb Haemost*. 2020;18(9):2204–13.
38. Esper SA, Levy JH, Waters JH, Welsby IJ. Extracorporeal membrane oxygenation in adult patients. *Anesth Analg*. 2014;118(4):731–43.
39. Doyle AJ, Hunt BJ. Current understanding of how extracorporeal membrane oxygenators activate haemostasis. *Br J Haematol*. 2018;182(2):192–201.
40. Combes A, Brodie D, Bartlett R, Brochard L, Brower R, Conrad S, et al. Position paper for the organization of ECMO programs for acute respiratory failure in adult patients. *Intensive Care Med*. 2014;40(3):388–91.
41. Lorusso R, Combes A, Lo Coco V, De Piero ME, Belohlavek J, Delnoij T, et al. ECMO for cardiogenic shock: current practice and outcomes. *Eur Heart J Acute Cardiovasc Care*. 2019;8(2):109–17.
42. Barbaro RP, Paden ML, Guner YS, Raman L, Ryerson LM, Alexander P, et al.

Pediatric extracorporeal life support: outcomes and trends. *Lancet Respir Med*. 2017;5(2):163–72.
43. Murphy DA, Hockings LE, Andrews RK, Aubron C, Gardiner EE, Pellegrino VA, et al. Extracorporeal membrane oxygenation-hemostatic complications. *Semin Thromb Hemost*. 2015;41(1):90–101.
44. Aubron C, Cheng AC, Pilcher D, Leong T, Magrin G, Cooper DJ, et al. Factors associated with outcomes of ECMO in ICU patients. *Intensive Care Med*. 2013;39(3):505–12.
45. Biscotti M, Gannon WD, Abrams D, Agerstrand CL, Brodie D, Bacchetta M. Extracorporeal membrane oxygenation use in adult patients: evolving indications and outcomes. *Expert Rev Med Devices*. 2015;12(5):581–92.
46. Schmidt M, Zogheib E, Rozé H, Repesse X, Lebreton G, Luyt CE, et al. The PRESERVE mortality risk score for ECMO. *Intensive Care Med*. 2013;39(10):1704–13.