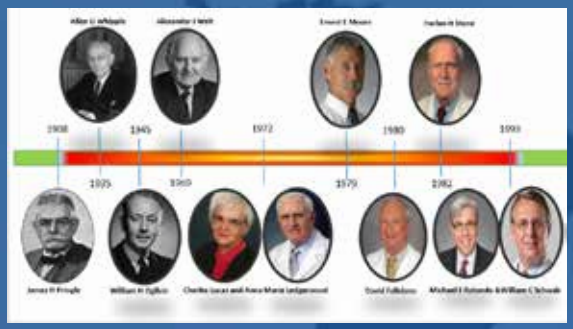
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Milestones and Key Figures in the Development of Damage Control Surgery

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STATE OF THE ART REVIEW

Extracorporeal Membrane Oxygenation (ECMO): A Life-Saving Therapy and Its Challenges of Implementation In Emerging Healthcare Systems

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Abstract:
Extracorporeal membrane oxygenation (ECMO) is an advanced life support technology intended to treat critically ill patients with severe cardiac and/or respiratory failure not responding to standard treatment. By facilitating extra-corporeal gas exchange and circulatory support, ECMO allows recovery from injury and can serve as a transition to transplantation or long-term destination therapy. Since its inception during 1970s, ECMO's applications have expanded from a last-resort intervention to a standard advanced critical care, particularly in the situation of acute respiratory distress syndrome (ARDS), cardiogenic shock, and refractory cardiac arrest. Key studies, underline ECMO's role in improving survival rates in severe ARDS when applied in specialized centers. Despite its effectiveness, ECMO poses significant technical challenges, resource demands, and complications such as bleeding and infection. Moreover, the Covid-19 pandemic demonstrated the ECMO utility for critical care patients but also highlighted implementation difficulties in resource-limited settings. The technical functioning of ECMO involves veno-venous (VV-ECMO) only for respiratory support and veno-arterial (VA-ECMO) which supports both, the cardiac and respiratory needs. Contemporary systems utilize advanced materials and monitoring for improved patient outcomes. Addressing the logistical and financial barriers to ECMO integration into healthcare systems is crucial for its sustainable and safe application globally.

Keywords: ECMO; extracorporeal membrane oxygenation; respiratory failure; cardiac support; ARDS; complications; critical care; healthcare challenges.

Introduction: ECMO Definition and Significance

Extracorporeal membrane oxygenation (ECMO) is an effective temporary lifesaving technique[1], intended to treat severely ill patients[2]. These patients have severe, yet potentially reversible, cardiac and/or respiratory failure and do not respond to conventional treatment[1–3]. ECMO offers gas exchange and hemodynamic support[2], enables cardiac and pulmonary recovery from injury or pathologic process. It also serves as a transitory support to transplantation or long-term mechanical support in the patients with severe cardiac insufficiency[4]. ECMO was developed in the 1970s following pioneering work by Hill et al. and Bartlett et al[5,6]. Since then, considerable advances have been seen in both its technology and clinical applications and expanding indications. Previously considered "last resort therapy," ECMO nowadays is recognized as a therapeutic option for certain patients. Rather than being considered an experimental rescue therapy, ECMO has become a core component of advanced critical care[4,7]. For the past twenty years, there has been increased evidence supporting ECMO usage

in ARDS, cardiogenic shock, refractory cardiac arrest, and septic shock both in adults and children. This evidence has come from large registries and randomized trials[8]. Improved survival in severe ARDS was demonstrated in the CESAR trial when patients were referred to ECMO centers[9]. The EOLIA trial confirmed these findings, showing that death rates in patients with severe ARDS may be reduced through early initiation of ECMO, despite the study's crossover limitations[10]. Similarly, registry-based analyses from the Extracorporeal Life Support Organization (ELSO) registry and multicenter trials have validated the benefit of VA-ECMO in severe cardiogenic shock and extracorporeal cardiopulmonary resuscitation (ECPR)[11–13]. Despite these advances, ECMO remains technically challenging and high resource-consuming. To optimize outcomes, specialized equipment, highly trained multidisciplinary teams, and careful patient selection are required[8]. Furthermore, this therapy carries several adverse events, including hemorrhage, thromboembolism, infection, vascular ischemic problems, neurological injury[14]. The worldwide growth of ECMO programs, particularly during the Covid-19 pandemic, highlights its pivotal role in advanced intensive care[15]. However, implementation remains challenging. This is especially true in resource-limited settings. Examples of these settings include countries currently developing ECMO capacity. The challenges arise due to financial, logistical, and training constraints[16,17]. It is crucial to address these barriers to safely and sustainably integrate ECMO into national healthcare systems[18].

Technical Overview and Modes of ECMO

ECMO systems work by extracting deoxygenated blood through the venous circulation. The blood is subsequently oxygenated and decarboxylated via a membrane oxygenator before being returned to the circulatory system (2). Depending on the type of underlying pathology, there are two types of ECMO configurations: VV-ECMO and VA-ECMO[4].

VV-ECMO provides respiratory support only and is indicated for patients with severe but potentially reversible respiratory failure and preserved cardiac function, such as those with ARDS[19]. The process involves extracting blood out of a major central vein (usually the femoral or internal jugular vein), oxygenating it outside the body (in an oxygenator), and reintroducing it into a central venous site[2] (Figure 1). This configuration facilitates efficient gas exchange while minimizing ventilator-induced lung injury, thereby promoting lung rest and recovery[9]. Multiple meta-analyses and registry data confirmed the beneficial role of ECMO in well-selected ARDS patients managed in experienced centers[20–22].

In the other hand, VA-ECMO provides both cardiac and respiratory support, and is used for severe cardiogenic shock, cardiac arrest (ECPR), or combined cardiorespiratory

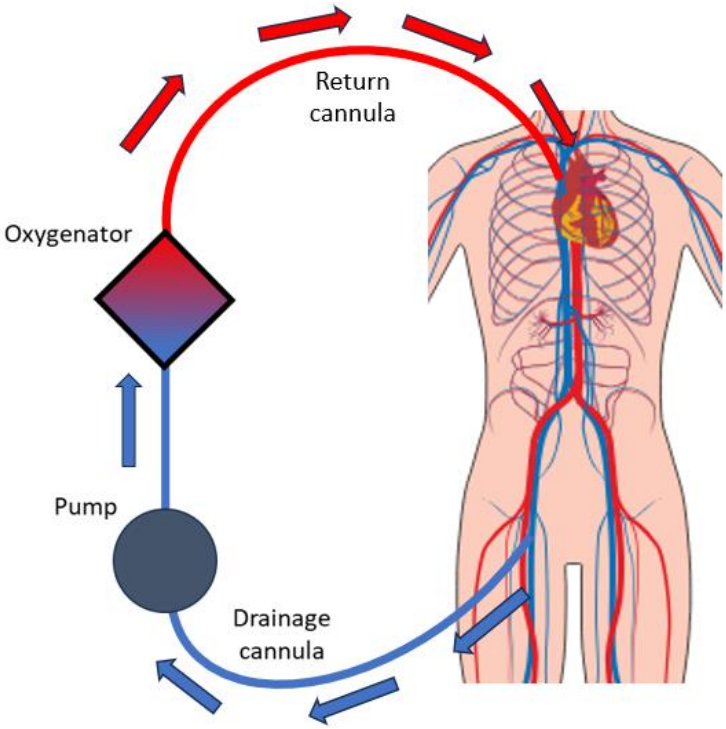


Fig.1: Veno-venous (V-V) ECMO

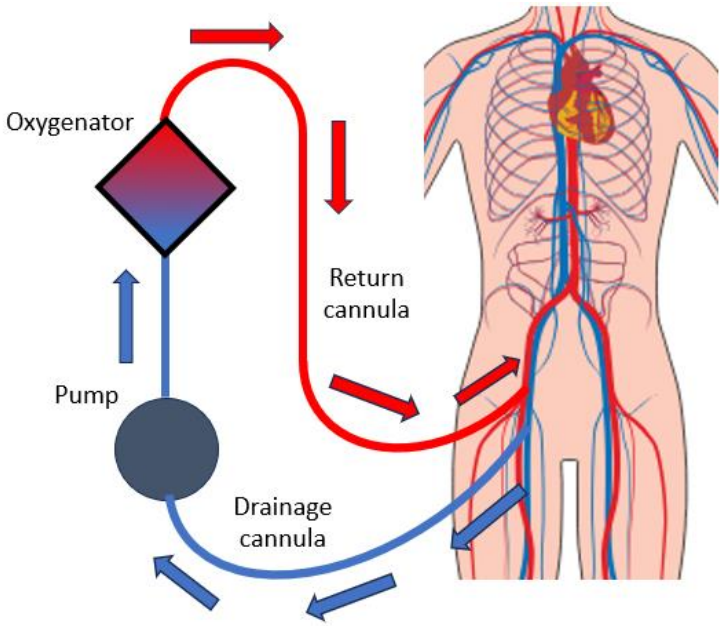


Fig.2: Veno-arterial (V-A) ECMO

failure[11–13,15,23–25]. The extraction of blood is initiated through a central vein access, most often the femoral vein or the right atrium. The extracted blood is then reintroduced into an artery, such as the femoral, subclavian, or carotid artery (Figure 2). This process effectively enables blood to bypass the native heart and lungs[2,4]. Peripheral VA-ECMO via femoral access is the most common approach, primarily due to its rapid bedside deployment, particularly in emergency or intensive care unit settings. The central cannulation procedure, in which direct access is provided to the right atrium and ascending aorta, is a specialized procedure reserved for post-cardiotomy patients or cases where peripheral access is contraindicated[4,11].

Contemporary ECMO systems utilize biocompatible, heparin-coated circuits, centrifugal pumps, polymethylpentene-based oxygenators, and heat exchangers to ensure thermic stability and to limit hemolysis and thrombosis[26]. Portable ECMO devices, such as the CardioHelp™ and Rotaflow™ models, have facilitated secure inter-hospital transfers, thereby enabling the development of regionalized ECMO networks[27]. The necessity of continuous monitoring is imperative for the following parameters: circuit flow, pre- and post-oxygenator pressures, venous and arterial oxygen saturation, coagulation status, lactate levels, and echocardiographic parameters[28]. It is imperative to focus on left ventricular unloading during VA-ECMO, as retrograde arterial flow increases afterload, potentially resulting in ventricular distension and pulmonary congestion. This complication can be managed with inotropes, percutaneous ventricular assist devices (Impella®), or atrial septostomy[29,30].

Indications: Respiratory and Cardiac

The selection of appropriate patients is a fundamental aspect of effective ECMO therapy[15,31–32]. The decision to initiate ECMO is made with careful consideration of the potential for organ recovery in relation to the risks of associated complications[1]. The classification of indications is generally divided into two primary categories: respiratory (VV-ECMO) and cardiac (VA-ECMO)[4]. However, it is important to note that mixed or hybrid configurations may be employed in cases of combined heart-lung failure[4].

VV-ECMO is used primarily for severely ill patients with potentially reversible respiratory failure who are unresponsive to optimal usual care[31,33]. This includes severe ARDS, air leak syndromes (e.g., bronchopleural fistula), near-fatal asthma, and massive pulmonary hemorrhage[34–36]. In addition to its primary function, ECMO can serve as a transition to lung transplantation for patients with end-stage lung disease[37]. During the global coronavirus pandemic, VV-ECMO emerged as a critical therapeutic strategy for patients with refractory hypoxic respiratory failure[21]. A review of the extant literature, including data from the ELSO Registry and multicenter studies, suggests that the procedure is beneficial for carefully selected patients[19,32]. The mortality rate remains substantial, ranging from 37% to over 60%, depending on the presence of comorbidities and the duration of mechanical ventilation prior to ECMO[38–39].

VA-ECMO is primarily employed in patients suffering from profound cardiogenic shock or during cardiac arrest, when myocardial recovery appears feasible, or as a temporary bridge to either heart transplantation or long-term mechanical circulatory support[23–40]. The main clinical situations in which VA-ECMO may be considered include: acute decompensation of chronic heart failure; cardiogenic shock secondary to acute coronary syndromes; fulminant myocarditis; low cardiac output syndrome following cardiac surgery; primary graft dysfunction occurring after heart transplantation; massive pulmonary embolism with circulatory collapse; refractory anaphylaxis or severe hypothermia complicated by cardiac arrest; drug-induced cardiac failure due to overdose of cardiotoxic agents; peripartum cardiomyopathy[41]. Extensive registry data and results from large multicenter cohorts demonstrate that VA-ECMO can offer a meaningful survival benefit in patients with otherwise unsurvivable cardiocirculatory failure[15,32,42].

Extracorporeal cardiopulmonary resuscitation (ECPR) refers to the implementation of ECMO support during, or immediately following, conventional cardiopulmonary resuscitation (CPR) when spontaneous circulation has failed to be restored[43]. This strategy may result in a survival benefit, particularly in cases of witnessed cardiac arrest with minimal no-flow time and a potentially reversible underlying cause[44]. A comprehensive analysis of randomized clinical trials and observational registries has indicated that the efficacy of treatment outcomes is closely associated with the timely implementation of cannulation, the meticulous selection of candidates, and the presence of a highly skilled, multidisciplinary ECMO response team[45].

Contraindications and Ethical Considerations

The complexity of the procedure, the significant demands on resources, and the potential for severe complications necessitate its judicious application to patients with a reasonable probability of recovery[46]. In addition to identifying those who may benefit, it is also crucial to be able to

recognize individuals who are unlikely to have a positive outcome[47]. Contraindications to ECMO are generally categorized as absolute or relative, depending on the extent to which they preclude successful treatment[48]. Absolute contraindications include situations such as irreversible cardiac or pulmonary failure in the absence of a transplant option, disseminated malignancy, or severe permanent neurological damage[49]. ECMO is also contraindicated in patients with uncontrolled type A aortic dissection, severe aortic regurgitation, or those presenting with profound multiorgan failure following a prolonged low-flow state after cardiac arrest[1,49]. In addition, the presence of a valid do-not-resuscitate order or an advance directive declining life-sustaining treatment must be respected[15,31,50]. In contrast, relative contraindications require a case-by-case evaluation and depend on institutional experience and ethical considerations. These may include advanced age (typically above 75 years), morbid obesity (BMI > 40 kg/m^2), significant peripheral vascular disease, active bleeding disorders or an inability to tolerate anticoagulation, and severely reduced functional status prior to the acute illness[42,49]. The ethical considerations associated with ECMO involve a range of complex issues, particularly in the context of end-of-life care and resource allocation[41,47,51]. Prolonged ECMO support in the absence of signs of recovery, particularly in settings with limited ICU capacity, can result in moral and societal dilemmas[41]. The utilization of ECMO should not be regarded exclusively as a technological intervention[53]. Its application requires a patient-centered, ethically justified medical decision[41,46,51]. This approach is founded on the integration of palliative care principles, when recovery is unfeasible[52].

Complications Associated with ECMO

ECMO is associated with a high incidence of serious and potentially fatal complications[14,52]. The causes of such complications include the extracorporeal circuit itself, the process of invasive cannulation, or the systemic effects of prolonged circulation and anticoagulation[19,31,53]. These complications depend on the type of the ECMO configuration (VA vs. VV), the underlying patient's pathology, the comorbidities, and the experience of the treating center[54]. Based on the results of a large multicenter study, 57% of patients reported at least one major ECMO related complication[10]. Vascular complications are among the most frequent and serious problems encountered during ECMO, especially when peripheral cannulation is used. Typical complications include arterial injury (e.g., dissection or perforation), limb ischemia, bleeding events, and, in severe cases, compartment syndrome[53,55]. The femoral route, the most widely used access site, is also associated with the highest incidence of vascular injury. The central cannulation avoids peripheral ischemia but carries its own risks, including perforation of the right atrium and significant mediastinal bleeding[40]. Preventive measures, such as the use of distal perfusion catheters, continuous ultrasound doppler surveillance, and routine evaluation of distal limb perfusion, have significantly reduced ischemic complications[56]. Beyond vascular issues[1], VA-ECMO with femoral access profoundly alters the patient's cardiovascular physiology. The retrograde flow generated by the arterial cannula increases left ventricular afterload, which can lead to distension, pulmonary congestion, and delayed myocardial recovery[57]. These effects are especially harmful in individuals with severely impaired ventricular function. To manage these hemodynamic disturbances, strategies focusing on left-sided heart decompression have been adopted. These strategies include pharmacological unloading through inotropes and vasodilators, mechanical approaches, such as percutaneous ventricular assist systems (e.g., Impella), or the creation of an atrial septostomy to facilitate decompression and prevent thrombus formation[11,25,58].

When blood comes into contact with the synthetic surfaces of the extracorporeal circuit, it triggers a complex inflammatory and hemostatic response[26]. This response includes platelet activation, stimulation of the coagulation cascade, and secondary fibrinolytic disturbances, creating a complex balance between thrombosis and bleeding[59]. Thrombotic complications may develop within the ECMO system itself, such as oxygenator clot formation or circuit obstruction[60]. They may also manifest as systemic embolic events, including ischemic stroke[61,62]. On the other hand, hemorrhagic complications are among the most frequent and serious problems encountered during ECMO, affecting between 40% and 60% of adult recipients in large observational series[60]. Bleeding episodes may occur at cannulation or surgical insertion sites, in the gastrointestinal tract, or intracranially. The latter carries the most severe prognosis[14,59,60]. This dual risk is the result of multiple mechanisms. The continuous need for anticoagulation combined with thrombocytopenia, platelet dysfunction, hemodilution, and acquired von Willebrand factor abnormalities significantly increases the risk to bleeding[60]. Meticulous monitoring of coagulation markers, including activated clotting time, anti-Xa activity, platelet count, and fibrinogen concentration, is essential to reduce the occurrence

of such events[63]. Maintaining a safe therapeutic balance is crucial. Protocols based on the patient's evolving condition and supported by a multidisciplinary team experienced in hemostasis and critical care are essential[64].

Neurological complications are among the most serious and prognostically significant adverse events in patients supported by ECMO[61,62]. A large proportion of morbidity and late disability among survivors is still attributed to cerebral injuries of various natures, including ischemic, hemorrhagic, and hypoxic[65]. According to data from major ECMO registries, acute brain insults, including stroke, seizure activity, prolonged coma, and diffuse hypoxic ischemic damage, are experienced by one in ten patients[61]. These events typically result from a combination of mechanisms, including the migration of thrombotic material, bleeding related to anticoagulation, and unstable cerebral perfusion due to rapid hemodynamic changes[62]. Neurological deterioration can develop insidiously, so continuous surveillance is crucial. The use of multimodal neuro-monitoring tools, particularly near-infrared spectroscopy (NIRS) to assess regional oxygenation, and periodic neuroimaging, when clinically feasible, can help identify early signs of compromise and guide timely intervention[66].

Up to 85% of ECMO patients develop acute kidney injury (AKI), with approximately half requiring renal replacement therapy (RRT)[67]. The pathophysiology is characterized by a complex interaction of multiple mechanisms, involving hemodynamic instability, inflammatory response, hemolysis, and exposure to nephrotoxic substances[67]. AKI is strongly associated with increased mortality. It is also associated with prolonged ECMO duration[14]. Infections are another major source of morbidity, affecting over 50% of ECMO patients[68–70]. The most frequent infections include ventilator-associated pneumonia[14,71], catheter-related bloodstream infections, and cannula-site infections[70]. Prolonged ECMO support, multiple invasive lines, and immunoparesis contribute to increased susceptibility[69,72]. To limit nosocomial infections, it crucial to implement strict aseptic protocols, early source control, and antimicrobial stewardship[68].

Harlequin syndrome, also known as north–south syndrome, is a unique phenomenon[1,73]. It may occur in VA-ECMO when native cardiac output recovers but remains poorly oxygenated. This leads to hypoxia in the upper body and brain[73]. Management involves increasing the FiO_2 on the ventilator, adjusting the ECMO flow rate, or converting to a hybrid configuration (V-AV ECMO), in order to optimize oxygen delivery[1,11].

Even in experienced centers, ECMO complications remain common and can overcome its survival benefits[74]. To minimize adverse events, it is essential to strictly adhere to standardized protocols, continuously train staff, hold multidisciplinary rounds, and implement early detection systems[18,75]. ECMO complications highlight the importance of continuously reviewing the indications and benefits of the therapy[74]. The ECMO collaborative project can improve survival rates, the weaning rates, and reduce complications without increasing costs[76].

ECMO in Specific Clinical Scenarios

In addition to its traditional use in ARDS and cardiogenic shock, ECMO has shown its effectiveness in a variety of specific and serious medical situations[4]. These rare or complex scenarios frequently pose challenges to conventional management algorithms, but they highlight the adaptability and lifesaving potential of ECMO when used in suitable cases[42,49].

Fulminant myocarditis is characterized by the rapid onset of heart failure and cardiogenic shock[77]. It frequently affects previously healthy young adults[78]. In this situation, VA-ECMO provides essential hemodynamic support while allowing the heart muscle to rest and recover[77–79]. Studies have shown survival rates of 60–70%, particularly when ECMO is initiated before the onset of multiorgan failure[80–81]. Early initiation of ECMO was strongly associated with improved outcomes in patients with fulminant myocarditis[78]. Following resolution of the inflammatory process, most patients can be successfully weaned from ECMO without experiencing any long-term complications[77].

Peripartum cardiomyopathy (PPCM) is a rare, but potentially reversible, cause of acute heart failure happening during the last weeks of pregnancy or the first weeks after childbirth[82]. When conventional management fails, VA-ECMO can serve as a temporary circulatory bridge to either myocardial recovery or heart transplantation[83,84]. Recent studies report that 72% of patients were weaned off ECMO, with survival rates above 60% for well-selected patients[85]. Further research is needed to understand the long-term morbidity, functional status of peripartum ECMO survivors, and the potential impact of cardiopulmonary and psychosocial recovery programs[83].

Another setting where ECMO provides a unique benefit is severe accidental hypothermia (core temperature <28°C), where this technology enables controlled rewarming and cardiopulmonary support[86]. Numerous case reports describe full neurological recovery, even after prolonged

cardiac arrest at extremely low core temperatures[87]. Ledoux and Saint-Léger published a case report describing the resuscitation of a 46-year-old patient with a core temperature of 22.4 °C[88]. The patient achieved full neurological recovery following VA-ECMO support. These cases have become the basis of the expression, "No one is dead until they're warm and dead."

In cases of acute, massive pulmonary embolism (PE) accompanied by hemodynamic collapse, VA-ECMO serves as a bridge to reperfusion therapy (89). It restores systemic oxygen delivery and stabilizes the patient for thrombolysis or surgical thrombectomy[89,90]. A multicenter study by Kjaergaard et al. found that 50% of 22 patients treated with ECMO for PE survived at one month, and 45% at one year[34]. Current evidence supports ECMO use in selected patients when prompt reperfusion therapy is expected to reverse the cause of failure[91].

Overdoses with cardiotoxic drugs, such as beta-blockers, calcium channel blockers, and tricyclic antidepressants, can lead to refractory cardiac arrest or shock unresponsive to pharmacologic therapy[92,93]. ECMO can provide temporary circulatory and respiratory support in these cases until the drugs are eliminated from the body[92,93]. ECMO can be used to treat a variety of pharmacological and non-pharmacological exposures in both adults and pediatric patients. Survival rates were high when ECMO was administered prior to cardiac arrest[94].

In cases of severe anaphylactic shock refractory to epinephrine and conventional resuscitation measures, VA-ECMO offers the potential to maintain perfusion while allowing for the resolution of the hypersensitivity response[95]. Despite the paucity of empirical evidence, the available case reports indicate that this application is consistent with the role of ECMO as a bridge to recovery in cases of cardiovascular collapse caused by reversible conditions[95,96].

During the COVID-19 pandemic, VV-ECMO became a pivotal therapeutic intervention for patients with refractory hypoxemia secondary to severe viral ARDS. A comprehensive analysis of data from the ELSO registry and multiple cohort studies has confirmed survival rates of 40–50% in carefully selected patients[21,22,97,98]. The early referral to experienced ECMO centers and strict selection criteria emerged as critical determinants of success[10,55]. These findings further solidify the critical role of ECMO in the management of severe, reversible respiratory failure, even in the context of unprecedented global healthcare challenges.

ECMO may be considered for some cases of septic shock complicated by severe and unresponsive cardiac and/or respiratory failure[99]. In this context, VA-ECMO can provide temporary circulatory support in patients with septic cardiomyopathy and severe myocardial depression that does not respond to maximum medical therapy[100]. However, its use remains controversial because ECMO does not treat the underlying infection and may exacerbate inflammatory and coagulation disturbances[101]. Therefore, careful patient selection is essential, observing the greatest benefit in younger patients with reversible myocardial dysfunction and limited comorbidities[99–101].

These clinical scenarios illustrate the expanding role of ECMO beyond its traditional indications. The success of the intervention is determined by optimal timing of the intervention, the reversibility of the underlying disease, and the coordination of a multidisciplinary team. In carefully selected patients when ECMO is implemented early, survival rates may exceed 40-50% for conditions previously considered fatal[55].

Outcomes and Prognostic Data

The clinical benefits of ECMO extend beyond its immediate capacity to support organ failure. Its true value lies in improving survival, minimizing complications, and optimizing long-term functional recovery. The results obtained vary considerably based on the indication for the procedure, the timing of its initiation, the patient's characteristics, and the experience of the medical center[102]. The ELSO registry constitutes the most extensive and comprehensive global database on the utilization and outcomes of ECMO. As stated in the 2023 ELSO International Report, the survival rate for VV-ECMO used in respiratory failure was approximately 58%, whereas VA-ECMO for cardiac support demonstrated survival rates between 44%[8]. For ECPR, survival remains lower, with an average of 25–30%[8,103]. However, significant variability exists depending on institutional experience and post-resuscitation care. More recent reports show incremental improvements, particularly in centers with high ECMO volumes and structured multidisciplinary teams[104].

In patients with cardiogenic shock, VA-ECMO provides rapid hemodynamic stabilization and improves end-organ perfusion, resulting in better short-term survival (105). However, complication rates remain high, including bleeding, thromboembolism, and limb ischemia[40,105]. Other publications identified a pooled in-hospital mortality rate of 62%. Higher mortality was associated with patient age, infection, and duration of ECMO support[52]. Thirty percent of patients remain alive and free of disability at 12 months

after VA-ECMO initiation, with differences in outcomes associated with the reason for initiation. The majority of disability appears to develop within the first six months after VA-ECMO initiation and continues through the 12-month period[106]. Long-term outcomes are more favorable in reversible causes such as myocarditis or post-cardiotomy shock than in chronic heart failure[107].

Two pivotal randomized trials, CESAR[9] and EOLIA[10], established the contemporary function of ECMO in ARDS. The CESAR trial reported an improved survival rate without severe disability at six months among patients in the ECMO group compared to patients in the conventional ventilation group (63% vs. 47%; p = 0.03)[9]. The EOLIA trial found no statistically significant difference in 60-day mortality (35% in the ECMO group versus 46% in the control group; p = 0.09). However, 28% crossover from the control group to the ECMO group likely diluted the observed benefit[10]. Additional meta-analyses and studies of individual patient data have confirmed a modest survival advantage associated with early VV-ECMO initiation in patients with severe, refractory hypoxemia[20]. In addition, ECMO patients experienced improved lung recovery and reduced ventilator-induced lung injury when treated at experienced centers[27].

The use of ECMO during cardiac arrest, also known as ECPR, has increased in recent years. While survival remains relatively low, typically ranging from 20% to 30% for hospital discharge[24,43], selected patients, particularly those with a witnessed arrest and a short low-flow time, can achieve favorable neurological recovery[42,108]. There is evidence from meta-analyses suggesting that ECPR may offer superior neurologically intact survival compared with conventional CPR in well-selected populations[54]. These outcomes highlight the importance of selecting patients according to a protocol and activating the ECMO team rapidly.

The following prognostic factors influence the patient treated with ECMO: age; severity of illness indicated by SOFA or SAPS II scores; pre-ECMO lactate levels; duration of mechanical ventilation before ECMO; and timing of ECMO initiation[39,54,109]. Higher survival rates correlate with early cannulation and ECMO initiation, a reversible etiology, and a low pre-ECMO lactate level. Conversely, prolonged pre-ECMO mechanical ventilation (>7 days) and severe comorbidities predict poor outcomes[39]. Despite the advances in technology and management, ECMO remains a high-risk, life-saving therapy. When applied early and under strict selection criteria in experienced centers, survival rates can reach 60% for respiratory failure and 40%-45% for cardiogenic shock. Nevertheless, a successful outcome depends on expertise, infrastructure, and post-ECMO rehabilitation. According to long-term follow-up studies, a structured neurologic, pulmonary, and psychological evaluation after ECMO is essential to optimizing quality of life among survivors[110,111].

Long-Term Outcomes

Even though ECMO can be life-saving in cases of refractory cardiac or respiratory failure, functional recovery among survivors varies[38]. Long-term outcomes depend on survival to hospital discharge and the quality of neurological, physical, and psychological recovery[45,106,109]. Approximately 30-50% of ECMO survivors sustain various degrees of neurological impairment, including memory loss, executive dysfunction, attention deficits, and delayed processing speed[61,62,112]. Such complications are often associated with hypoxic-ischemic injury, microemboli, and intracranial hemorrhage, possibly occurring during extracorporeal support[65]. Post-ECMO cognitive impairment is similar to post-intensive care syndrome (PICS), which underlines the importance of early neurorehabilitation and cognitive screening[113].

Prolonged ECMO treatment is often followed by physical decline, muscle weakness, and exercise intolerance, primarily due to immobility, steroid exposure, and critical illness myopathy[114,115]. Different studies have shown that early mobilization protocols and multidisciplinary rehabilitation programs improve functional abilities and quality of life[116,117]. Approximately half of VA ECMO survivors experience excellent long-term functional outcomes[118].

Neuropsychiatric symptoms, neurocognitive and functional impairments have been observed in a considerable number of ECMO patients during long-term follow-up. Survivors are affected by anxiety, depression, and post-traumatic stress disorder (PTSD) in 30–40% of cases[119]. The use of ECMO is associated with substantial psychiatric disorders in patient families[120]. Patients treated with ECMO are significantly associated with a modestly increased risk of a new mental health or social problem diagnosis after discharge compared to non ECMO ICU survived patients[121]. Patients describe memories of the ICU environment that are so intense they resemble nightmares and cause emotional distress. These symptoms resemble those observed in other critically ill populations, but they may be intensified by the invasive and prolonged nature of ECMO therapy[122]. Psychological support and long-term post discharge

follow-up are essential for improving the quality of life of ECMO survivors[38,123].

Prognostic factors strongly correlate with both short and long-term outcomes[31]. Predictors of a favorable outcome include younger age (under 60 years), short pre-ECMO duration of mechanical ventilation, early initiation of ECMO especially in cases of cardiogenic shock, low lactate levels at cannulation, absence of multiorgan failure, and reversible primary pathology[31,54]. On the other hand, delayed ECMO initiation, prolonged CPR, and severe comorbidities have been associated with poor neurological and functional outcomes[45]. Clinical tools such as the RESP, SAVE, and PRESERVE scores can help clinicians estimate prognosis and inform families[54,107].

The survival and long-term outcomes of patients are significantly influenced by institutional expertise and the volume of cases at ECMO centers[124]. High-volume centers have lower mortality rates, fewer complications, and better functional recovery after ECMO treatment[27,125]. This evidence supports centralizing ECMO programs in specialized referral centers to ensure access to multidisciplinary teams skilled in-patient selection, management, and post-ECMO rehabilitation[126]. In conclusion, survival with ECMO treatment is only the first step toward recovery. Survivors often encounter long-term neurological, physical, and psychological challenges[110,127]. Therefore, a structured post-ECMO follow-up that integrates rehabilitation, neuropsychological assessment, and psychosocial support is crucial[123]. As technology and clinical experience evolve, the focus must shift from survival to quality of life.

Cost, Logistics, and Resource Allocation

Treating a patient with ECMO is a highly resource-intensive therapy that requires advanced technology, continuous specialized care, and substantial institutional infrastructure and expertise[32]. Its clinical efficacy is well established[21] but, the economic and logistical burden remains a major limitation, especially in low- and middle-income countries[128–132]. The substantial cost of ECMO comprises initial setup, consumables, ICU care, and ongoing therapy-related interventions[133]. Depending on factors such as the duration of support, complications, and ancillary treatments, the total hospital cost per patient costs varies widely between indications[130,131]. Analyses of cost-effectiveness suggest that ECMO may be justifiable for select populations, such as young patients with severe ARDS or reversible cardiogenic shock[134]. However, it is generally resource-intensive when viewed from a population health perspective[135].

Managing ECMO requires specialized personnel, including critical care physicians, perfusionists, ECMO-trained nurses, and respiratory technicians. These specialists are supported by a multidisciplinary team consisting of cardiologists, infectious disease specialists, nephrologists, surgeons, and physiotherapists[136–138]. There is evidence that centers with dedicated ECMO teams and structured training programs have lower complication rates and have reported better outcomes[125–139]. Maintaining high standards of care requires simulation-based training, standardized protocols, and quality-monitoring programs, especially in new programs or centers that are introducing ECMO for the first time[49,140,141]. Centralized ECMO programs and high-volume centers enable efficient care and resource allocation while ensuring patient safety[125]. Several western countries have successfully implemented mobile ECMO units or coordinated referral systems (UMAC), enabling safe inter-hospital transport, timely initiation of therapy, and equitable access for geographically dispersed populations[126,142,143]. Requirements for infrastructure include ICU beds equipped for ECMO, bedside monitoring systems, backup power supplies, and access to rapid imaging, laboratory, and surgical support. Low- and middle-income countries face challenges in replicating this infrastructure, which underscores the importance of strategic national planning and phased implementation[17].

The high costs and limited availability of ECMO raise ethical questions about the allocation of resources[41,51]. ECMO should be prioritized for patients with a high probability of recovery. Transparent national policies and multidisciplinary decision-making are critical to ensuring equitable use[46,144]. During pandemics, resource scarcity may necessitate triage protocols, further emphasizing the importance of centralized, protocol-driven ECMO programs[145].

The Challenge in Emerging Health Systems: The Case of Kosova

Implementing ECMO in emerging health systems, such as in Kosova, presents a series of clinical, logistical, and economic challenges, but should be considered seriously. Key obstacles include the absence of a dedicated ECMO center, limited numbers of trained personnel, underdeveloped technical infrastructure, an unestablished referral network, the absence of a national reimbursement scheme, limited ICU capacity, and potential supply chain constraints.

Despite these challenges, the cost of ECMO per patient may not be prohibitive if the therapy is restricted to young patients with potentially reversible conditions, and if care

is centralized at one or two specialized centers[49]. The careful use of limited resources makes sure that ECMO is both effective for patients and economically feasible, even when resources are limited[27].

Capacity building and international collaboration are essential to overcome training and infrastructure gaps[146]. These programs can facilitate training abroad for local clinicians or visiting expert teams, as well as equipment sharing or donations. They can also provide tele-mentoring and remote supervision and offer simulation-based education to improve staff performance[17,147]. A phased implementation strategy is recommended, beginning with pilot ECMO programs and robust outcome monitoring. This approach enables local teams to gain experience while ensuring patient safety and optimizing resource allocation.

Multiple contextual factors justify the introduction of ECMO in Kosova: a young population with a high incidence of trauma and reversible cardiac or respiratory failure; specialized personnel abroad including Kosovar clinicians trained in Western Europe; strong diaspora networks; and international partnerships willing to support training and equipment acquisition. Additionally, local ICU teams are highly motivated to develop ECMO expertise. The use of ECMO would be particularly valuable in select high-impact clinical scenarios, including: fulminant myocarditis in young adults; peripartum cardiomyopathy; refractory ARDS in otherwise healthy patients; severe hypothermia or drug intoxication[88,148].

A pragmatic approach for integrating ECMO involves several key steps: designating one or two pilot ECMO centers (ideally in Pristina and at one regional hospital); training core ECMO teams abroad or via international experts; acquiring one or two portable ECMO consoles (e.g., CardioHelp™) and initial consumables; developing national protocols and patient selection criteria; implementing simulation-based training and standard operating procedures; and establishing a national ECMO registry to monitor outcomes and guide policy. Evidence from other emerging nations suggests that low-volume programs can succeed with judicious patient selection and centralized care[149].

Conclusion and Recommendations

ECMO is a transformative, life saving technology that serves as a short term replacement for the cardiac or respiratory functions of patients with severe, yet potentially recoverable failure. Technological advances, evidence-based protocols, and multicenter collaborations over the past few decades have improved overall survival rates, especially for patients with ARDS, cardiogenic shock, fulminant myocarditis, peripartum cardiomyopathy, and refractory hypothermia. Despite its clinical benefits, ECMO is complex and resource-intensive. It is also associated with high complication rates. Effective implementation requires centralized, high-volume centers; skilled, multidisciplinary teams; robust patient selection criteria; continuous monitoring; and adherence to standardized protocols. Ethical considerations, including patient selection, equitable allocation of resources, and end-of-life decision-making, must be integrated into clinical practice. When applied judiciously, ECMO can be a lifesaving option for patients with reversible organ failure, even in settings with limited resources. The success depends on careful planning, international collaboration, local expertise, and continuous evaluation of outcomes. As the global experience with ECMO has shown, low-volume programs can be effective when patient selection is strict, care is centralized, and protocols are standardized. In summary, implementing ECMO in Kosova is feasible, ethically justified, and potentially transformative. This can be achieved through strategic, stepwise planning combined with international support, training, and outcome monitoring. Focusing on high-impact, reversible conditions and leveraging centralized expertise can make ECMO a sustainable, life-saving modality within the Kosovar healthcare system.

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