East African Medical Journal Vol. 95 No. 5 May 2018

INTRODUCING ECMO/ECLS IN SUB-SAHARAN AFRICA – PROSPECTS AND PERSPECTIVES Justyna Swol, Department of Respiratory Medicine, Allergology and Sleep Medicine, Intensive Care Medicine, Paracelsus Medical University Nuremberg, General Hospital Nuremberg, Prof.-Ernst-Nathan-Street., Nuremberg, Germany; Raj Jutley, Africa Heart Foundation (PANAHF), Nairobi, Kenya; Gerry Capatos, Parkview Mediclinic Hospital Dubai, United Arab Emirates; Farai Nyabadza, Department of Mathematics and Applied Mathematics, University of Johannesburg, Auckland Park Campus, Johannesburg, South Africa; Joseph Lelo, Medical Director, AMREF Flying Doctors, Wilson Airport, P.O. Box 18617 – 00500 Nairobi, Kenya.

Corresponding author, Justyna Swol, MD PhD, Department of Respiratory Medicine, Allergology and Sleep Medicine, Intensive Care Medicine; Paracelsus Medical University Nuremberg, General Hospital Nuremberg. Email: jswol@icloud.com

INTRODUCING ECMO/ECLS IN SUB-SAHARAN AFRICA – PROSPECTS AND PERSPECTIVES

J. Swol, R. Jutley, G. Capatos, F. Nyabadza and J. Lelo

ABSTRACT

Background: The introduction of modern medical technologies reduced mortality in adults and increased survival in infants less than five years old. Cardiac and respiratory failure can be managed through mechanical circulatory support devices such as ECMO/ECLS (Extracorporeal Membrane Oxygenation/ Extracorporeal Life Support).

Main Findings: We evaluate the importance and potential impact of using ECMO/ECLS in improving health care in sub-Saharan Africa. The intention of this recommendation is to introduce this concept as a feasible rescue method for clinicians in the region. The potential use of ECMO/ECLS will be discussed with focus on infrastructure for the retrieval services from the referring hospitals to designated ECMO centres.

Conclusion: ECLS resources and time that should be committed to training of staff and on-going education should not be underestimated. ECLS should only be commenced, maintained and weaned in the hands of trained, experienced and knowledgeable medical personnel cognisant that the results will be benchmarked by ELSO (Extracorporeal Life Support Organization) and available for consumption in the public domain. Partnership models are key to the ECLS success with well-defined roles and responsibilities for each party. The possible way for ECMO/ECLS in Africa should be combining with a two-pronged education programme: Improving critical care services in themselves, and once they get to an acceptable level in this department then is to manage ECLS patients for a few hours. To upgrade critical care services, this is vital for Africa, and only then to introduce ECMO/ECLS.

INTRODUCTION

Infectious and chronic diseases present a disproportionate double burden to the African continent. While many illnesses in East Africa are transmitted by insects and animals, and by the use of contaminated water for washing and drinking, infectious respiratory diseases account for the majority of illnesses and deaths. For instance, in Kenva, AIDS, diarrheal diseases and pneumonia remain the three leading causes of deaths between 2005 and 2015 (1). Despite the fact that infectious diseases still account for at least 69% of deaths on the continent, cerebrovascular disease and ischemic heart disease deaths increased over the last decade (2). Fortunately, over the last three decades, substantial progress has been made globally in reducing child deaths since 1990. The number of deaths for children under five declined from 12.7 million in 1990 to 5.9 million in 2015. Despite these gains, progress remains insufficient some regions, especially sub-Saharan Africa (3). The most common neonatal complications include metabolic disorders, respiratory distress and cardiac disorders (4).

The continent is projected to experience the largest increase in death rates from cardiovascular disease, cancer, respiratory disease and diabetes (5). Unhealthy lifestyles, often marked by unhealthy diets and lack of physical activity, have resulted in a rapid increase in diseases such as hypertension, arthritis, diabetes, depression, heart disease and cancer. This tendency again leads to that immense burden to over stretched health care systems (6). African health care systems are very fragile and weak, and currently, their national budgets focus more on infectious and parasitic diseases. Despite the fact that estimating mortality in Sub-Saharan Africa poses a major epidemiological challenge, an increase in the deaths due to non-communicable diseases (NCDs) has been observed (7).

In response to the rising disease burden from both infectious and NCDs, that has impacted the populations globally, the introduction of quality, modern medical technologies have led to reduced mortality in adults and survival in infants less than five years old. In the case of cardiac disease and any respiratory failure, complications be managed through mechanical can circulatory support devices such as ECMO/ECLS (Extracorporeal Membrane Oxygenation/ Extracorporeal Life Support) which is the focus of this paper. The impact of technology to modern society has been more apparent in the field of medicine and healthcare and cannot be underestimated. Technological advances are changing the dynamics of health care delivery by impacting the structures and organization of the medical arena. The advances of these technologies in bio-medical engineering, are at improving patient survival, aimed outcomes, support and recovery (8).

Purpose

In this article we evaluate the importance and potential impact of using ECMO/ECLS in improving health care in sub-Saharan intention The of Africa. this recommendation is to introduce this concept as a feasible rescue method for clinicians in the region. The potential use of ECMO/ECLS will be discussed with focus on infrastructure for the retrieval services from the referring hospitals to designated ECMO centres.

History

The history of the idea of the extracorporeal circulation and gas exchange began in 1931 when, as a young registrar, John Gibbon monitored a patient with a massive pulmonary embolism. Gibbon developed a device that could oxygenate his nonoxygenated blood outside the body and bring it into the arterial system via a pump. This vision greatly influenced the research goals of Gibbon. After 20 years of Gibbon's research, in 1954, the first heart-lung device was used as a cardiopulmonary bypass. This was the single biggest milestone for the cardiac surgery and lay the foundation for the further development of ECMO (9).

ECMO was introduced for the treatment of ARDS in the 1970s. The first survivor, a trauma patient, was reported by Hill et al. (10). Thereafter, Theodore Kolobow pioneered the research on membrane oxygenators together with Robert Bartlett, who established the use of ECLS in respiratory failure of new-borns and adults in subsequent years [Fig. 1]. In 1989, the body ELSO (Extracorporeal Life Support Organisation) was founded in Ann Arbor (Michigan State, US) to facilitate exchange of ideas between clinicians for the optimal use of ECLS and promote multidisciplinary collaboration of physicians, nurses, perfusionists and other medical professions involved in development of ECMO.

History

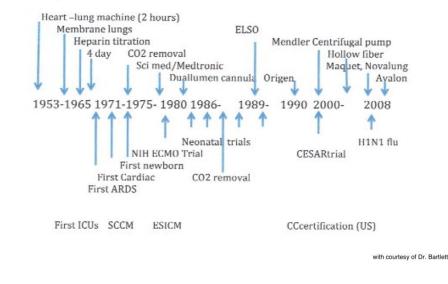
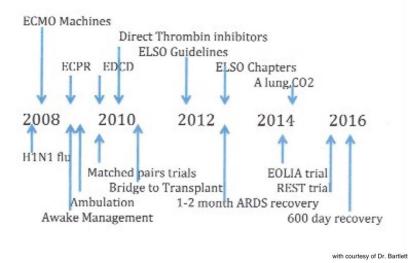


Figure 1. Part I of a brief history of ECMO with courtesy of Dr. Bartlett

ECMO was initially considered as a cost intensive, last resort therapy, potentially lifesaving but very complex, requiring ECMO specialists to be available 24/7. As ECMO technology evolved over the last three decades combined with the good survival rates during the outbreak of the H1N1 influenza pandemic in 2009, the new era of ECMO began. ECMO development was on an accelerated trajectory [Fig. 2]. Patient management also changed radically. Sedated, intubated and paralysed patients with rest ventilator setting, controlled ventilation and lung recruitment belonged to the past. The new approach of "watch and wait" now enabled awake, spontaneous breathing patients who are sometimes even extubated, on CPAP or with a tracheostomy in situ. Bedside management was task shifted to nursing staff who managed both the device and patients. Bleeding complications were also increasingly less common. Cannulation techniques also made advances with heparin coated cannulas inserted percutaneously. From 2008 the advent of the revolutionary membrane lung with low resistance and low priming volume meant a reduction in hemodilution.

Other advances such as centrifugal pumps resulting in less hemolysis along with the extended use of double lumen cannula have simplified ECLS settings (11).



ECMO II: History

Figure 2. Milestones in the history of ECMO support after 2008 with courtesy of Dr. Bartlett

Extracorporeal Life Support Organisation (ELSO), founded 1989 in Ann Arbor, Michigan, US, has become an international consortium of ECMO centres and individuals who are dedicated to the development, evaluation and improvement of extracorporeal devices. The references and guidelines addressed to the technology and patient management during ECLS can be also found on the website elso.org and in "The Red Book" - "ECMO; Extracorporeal Cardiopulmonary Support in the Intensive Care" published by ELSO (12). Global chapters of ELSO provide education and expertise in ECMO delivery around the world. While ECMO has developed globally, there remains a gap in the service provision in sub-Saharan Africa which should be filled.

Definition of ECMO/ECLS

The term Extracorporeal Life Support (ECLS) describes temporary support of heart

or lung function (partially or totally) using extracorporeal devices during cardiopulmonary failure leading to organ recovery or replacement. Extracorporeal Membrane Oxygenation (ECMO) has become a general description for devices that are in use for extracorporeal blood oxygenation and carbon dioxide removal. The acronym ECMO was previously used for modalities providing pulmonary support, and ECLS for pulmonary and cardiac support. The term ECLS is preferable used in the current literature as the more comprehensive term encompassing either cardiac and, or pulmonary support.

The principal application modes of delivering ECLS are veno-venous (VV) and veno-arterial (VA) [Figures 3, 4]. VV ECLS targets primarily respiratory support in which cardiovascular function is not severely compromised. In combination with selective extracorporeal carbon dioxide removal (ECCO₂R) it has increasingly shown

promise to avoid the pitfalls with cardiac or combined cardiopulmonary mechanical ventilation. VA ECLS supports failure.

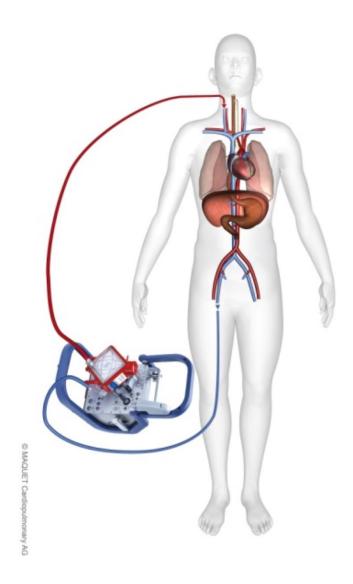


Figure 3. For VV ECLS two single lumen cannulas are placed into the internal jugular and femoral vein. Blood is drained from the inferior vena cava via a femoral venous cannula. The return of oxygenated blood into the venous system is pump driven following the passage through the artificial membrane lung back into the internal jugular vein.

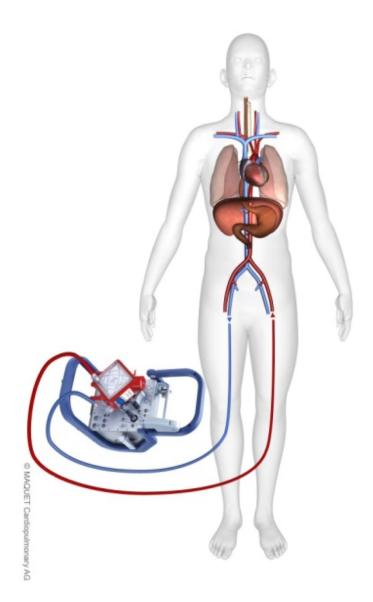


Figure 4. During VA ECLS blood is drained from the right atrium via a femoral venous cannula. Blood is pumped through a membrane oxygenator to add oxygen and remove carbon dioxide. The circuit provides the temperature control at the same time. Oxygenated blood is returned to the arterial system via the cannula placed in the femoral artery by percutaneous access. Drainage via jugular vein and surgical access to the carotid or subclavian artery for return are also an option.

ECMO/ECLS physiology

ECLS devices have the capacity to oxygenate and to rewarm blood, provide circulatory support, correct hypercarbia, infuse fluid volumes offering an advanced technology of life support and resuscitation. ECLS improves tissue oxygen delivery and for this reason can prevent organ damage resulting from insufficient oxygen supply to the vital organs. It allows normal physiologic metabolism on tissue level. The system restores and stabilizes the patient's vital cardiopulmonary functions, providing lung rest and/or cardiac offloading.

Indications for ECMO/ECLS

ECLS should be considered for potentially reversible conditions as summarized in

Tables 1-3. It is important to note that extracorporeal devices do not provide the treatment of the underlying disease. Current ELSO guidelines suggest that ECLS should be *considered* when the patient has a 50% mortality risk - PaO2/FiO2 < 150 mmHg on

FiO2 > 90% and/or Murray score 2-3; and *indicated* at 80% mortality risk - PaO2/FiO2 < 100 mmHg on FiO2> 90% and/or Murray score 3-4 despite optimal care for 6 hours or more (13).

Table 1

| | Pathological conditions suitable for respiratory support with VV ECLS |
|--------|---|
| Condi | itions suitable for veno-venous respiratory extracorporeal support with ECLS |
| - | Severe ARDS according to the Berlin Definition 2012 |
| - | Hypoxemic lung failure due to pneumonia (e.g. N1H1), fungal or viral pneumonia |
| - | Lung injuries (blunt chest trauma with pulmonary contusions, blast injury, |
| | penetrating injuries with intraalveolar bleeding, smoke inhalation) |
| - | Bronchopleural fistula or severe pulmonary air leaks |
| - | Foreign body obstruction |
| - | Aspiration syndromes |
| - | Status asthmaticus |
| - | Bridge to lung transplant |
| - | Acute lung (graft) failure following transplant |
| - | Rare conditions as diffuse alveolar hemorrage attributed to vasculitis, collagen |
| | vascular disease, autoimmune lung disease, bronchiolitis, obliterans, Goodpasture |
| | syndrome |
| Patier | nts selection's criteria for Extracorporeal Carbon Dioxide Removal (ECCO2R) |
| - | Chronic obstructive lung disease (COPD) or primary hypercapnic respiratory |
| | failure |
| - | Permissive hypercapnia during lung protective ventilation |
| - | Uncompensated hypercarbia, pH lower than 7.2 despite conventional management |
| - | Inability to maintain safe inflation pressure (Pplat < 30 mmHg) |
| - | Concominant severe metabolic acidosis |
| - | High intracranial pressure to ensure targeted CO2 between 32-36 mmHg |

Table 2

Pathological conditions suitable for cardiac or cardiac and respiratory support with VA ECLS

- Cardiogenic shock, heart failure
- Low cardiac output syndrome
- Acute myocardial infarction (AMI) with myocardial failure
- Complications of AMI (wall rupture, papillary muscle rupture, VT/VF refractory to conventional therapy including IABP)
- Myocarditis
- Cardiac trauma
- Bleeding in trauma with need for circulatory support, major vessel trauma
- Pulmonary embolism refractory to thrombolysis or as bridge to surgical or persutaneous thrombectomy (also fat embolism, air embolism, amniotic fluid embolism)

- Septic shock, septic cardiomyopathy
- Hypothermia
- Drug overdose with profound cardiac depression (poisoning) as beta/blocker, Ca²⁺ antagonist, hyperkalemia
- Acute anaphylaxis
- Peri-partum cardiomyopahy
- Post- cardiotomy failure
- Failure to wean from the cardiopulmonary bypass in OR
- Cardiopulmonary resuscitation [ECPR] (witnessed, ongoing cardiac arrest, minimal interruptions in CPR, presumed cardiac cause, hypothermia or poisoning arrhythmias)

Table 3

- Early graft failure post heart or heart-lung transplant

| Infants and paediatrics indications | | | |
|-------------------------------------|---------------------------------------|--|--|
| - | Congenital diaphragmatic hernia (CDH) | | |
| - | Birth defects of the heart | | |
| - | Meconium aspiration syndrome | | |
| - | Severe pneumonia | | |
| - | Severe air leak problems | | |
| - | Pulmonary hypertension (PPHN) | | |
| - | During recovery after surgery | | |

Generally, the indications for respiratory support are severe hypoxemic and, or hypercapnia resulting in temporary respiratory failure, or as a bridge to transplant. From present published evidence it is imperative that patient should be considered for ECLS before the terminal ventilator induced lung injury occurs, coupled with the failure of conventional treatment, usually after 7-9 days.

Cardiac, or cardiac and respiratory support is indicated as bridge to recovery, bridge to or bridge to transplant in decision cardiogenic shock with inadequate tissue perfusion manifested as hypotension and low cardiac despite output adequate intravascular volume volume, administration, inotropes and vasoconstrictors, and intra-aortic balloon counter pulsation if appropriate. Typical causes of acute myocardial failure include acute myocardial infarction, myocarditis, peri-partum cardiomyopathy, decompensated chronic heart failure and post cardiotomy shock.

Contraindications

There are no absolute contraindications to ECLS but irreversible cases, unless being considered as a bridge to transplant, should generally be avoided given the grim prognosis for recovery [Table 4]. Several conditions have been identified as relative contraindications such as balancing the risks of the procedure versus the potential benefits and the triaging of valuable resources in a resource limited setting. Although advanced aged is often stated as a relative contraindication, the decision about the cannulation should be considered on a case by case basis taking into account the physiological state of the patient rather the actual chronological age.

| Relative contraindications for ECLS and controversial conditions | | | | | |
|---|--|--|--|--|--|
| Relative contraindication | | | | | |
| - Severe, irreversible brain injury (pre-existing hypoxic brain injury) | | | | | |
| - End stage organ failure with no possibility for transplant | | | | | |
| - Metastatic end stage malignancies with severely limits of life expectancy | | | | | |
| - If the situation is futile and incompatible with life | | | | | |
| Controversial but not contraindicated are: | | | | | |
| - Trauma with intracranial bleeding | | | | | |
| - Pregnancy and delivery | | | | | |
| - Severe sepsis with indication for cardiac support | | | | | |
| - Recipients of bone marrow transplant | | | | | |
| Other immuneuppression status (HIV) | | | | | |

Table 4

Other immunsuppression status (HIV)

The ECLS circuit and components

Adult ECLS circuits are usually primed with crystalloid and blood for smaller children. The key ECLS components include control monitoring, hollow panel the fiber polymethylpentene (PMP) oxygenator (artificial lung with internal heat exchanger), a centrifugal blood pump and cannulas for blood drainage and return connected to polyvinylchloride (PVC) 3/8-inch diameter tubing. Additional devices such as haemodialysis continuous or renal replacement devices can be attached in parallel to the circuit and used for the fluid balance.

Cannulation and circuit management

Percutaneous cannulation of femoral or jugular vessels for extracorporeal support can be performed by intensivists, emergency physicians or surgeons bed side in the ICU (Intensive Care Unit), ER (Emergency Room), OR (Operating Room) or the cardiac catheterisation lab. The established Seldinger guide wire technique and vessel dilatation for vessel insertion for VV or VA access are standard for cannulation [Figs. 3, 4]. In children weighing less than 15 kg, or if percutaneous access has failed, surgical cut down is indicated. In all cases a heparin bolus of 100 IU per kg should be administered before the tubing is connected to the cannulas.

VV ECLS provides partial to full extrapulmonary support with blood flow up to 6 L/min [Fig. 3]. VA ECLS can provide partial or full cardiopulmonary support with the maximum blood flow of 10 L/min [Fig. 4] Femoral cannulation remains the most popular method of cannulation. However, arterial cannulation can result in distal limb ischemia, which may require secondary cannulation at more distal site. In exceptional cases, such as septic shock where high flows may be required, VA cannulation may be necessary via the right atrium and aorta through open-chest cannulation.

The double lumen cannula for use as a single catheter for both venous drainage and the reinfusion of blood via the internal jugular vein during VV ECLS is also being deployed as an alternative technique [Fig. 5]. This single access permits a reduced circuit length and lowers the contact activation of the blood. Patients are able to ambulate and exercise. The technique requires image guidance with with fluoroscopy and ultrasound. Transthoracic echo or transoesophageal echo are also used as supporting tools but may have limitation depending upon resource availability.

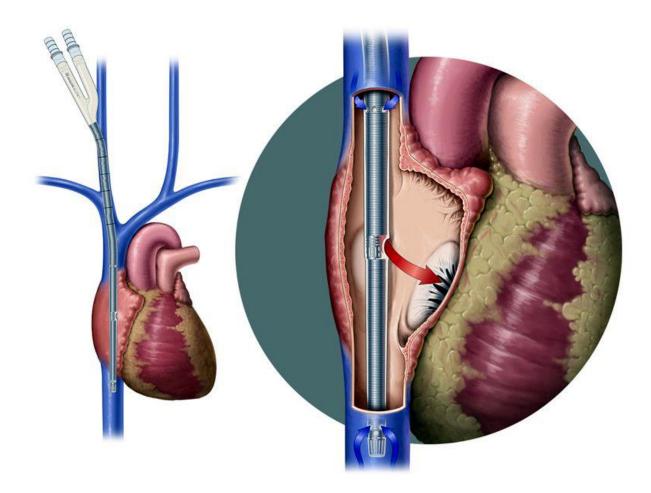


Figure 5. Double lumen cannula enables venous drainage and the reinfusion of blood via the internal jugular vein during VV ECLS. Recommended placement for drainage inlet tip is in the inferior and superior vena cava and for return outlet in right atrium.

Management of the circuit following initiation of support includes the adjustment of the blood flow (50-80 ml/dry kg/min) to maintain the oxygen delivery and the adjustment of the oxygenator sweep gas flow to maintain CO₂ removal. The invasiveness of the ventilator settings can reduced to minimal levels, then be monitored by arterial blood gas analysis. Suggested thresholds are $SaO_2 > 80-85\%$, pO₂ > 60-65 mmHg, pCO₂ < 80-100 mmHg provided that pH > 7.2.

Initial management of VA ECLS requires weaning from the inotropes. Transthoracic echo or trans-oesophageal echo are recommended for the monitoring of the cardiac output and adjustment of vasopressors. Monitoring of tissue perfusion with mixed venous saturation (SvO₂) with a target of 70% and serum lactate are recommended.

Anticoagulation

Management of the circuit includes the maintenance of anticoagulation - a major concern in patients with either excessive clotting or hemorrhagic complications. Heparin is the default anticoagulant for ECLS. Monitoring of anticoagulation can be done using activated clotting time (ACT) and activated partial thromboplastin time (aPTT). Continuously infusion of heparin is recommended at 125 IU/kg/hour to maintain ACT at 160-220 or aPTT 50-80 sec (14). For

patients at risk of bleeding the anticoagulation can be reduced or avoided for a few days at all times balancing the risk of clotting of the circuit's components with the potential risk of bleeding. Large cannula diameters allow not only higher blood flows but also reduce the risk of clotting. Novel centrifugal pumps, PMP oxygenators and heparin coated circuits also ensure lessclotting challenges.

Complications of ECLS

The use of ECLS can be associated with a high risk of complications including

bleeding, clotting, infection and limb ischemia in case of arterial cannulation, especially if performed by inexperienced operators. The hazards can be classified into patient size and circuit site and are detailed in Table 5. A complication particular to VV ECLS relating to cannula position is recirculation. It occurs where oxygenated blood returned from the ECLS circuit is immediately aspirated by the drainage cannula instead of entering the systemic circulation.

| List of primary and s | econdary complications potentially occurring during the cannulation or ECLS run |
|-----------------------|---|
| Primary complication | ons potentially occurring during the cannulation |
| Cannula site | - Failure to cannulate |
| | - Vessel perforation |
| | - Aortic / Vena cava inf. dissection |
| | - Retroperitoneal hemorrhage |
| | - Cannula malposition (wron vessel, misinterpretation) |
| | - Accidental decannulation |
| | - Shifting of the thrombus in deep vein thrombosis |
| Circuit site | - Circuit obstruction |
| | - Low volume state |
| | - Pump malfunction, failure |
| | - Oxygenator malfunction, failure |
| Hemorrhagic | - Bleeding at cannula site |
| Secondary complica | tions in response to the pathophysiology of extracorporeal |
| circulation | |
| Cannula site | - Distal limb ischemia (in VA ECLS) |
| | - Pseudo aneurysm |
| | - Accidental decannulation |
| Circuit site | - Circuit obstruction |
| | - Low volume state |
| | - Pump malfunction, failure |
| | - Oxygenator malfunction, failure |
| Hemorrhagic | - Pulmonary hemorrhage |
| | - Gastrointestinal h. |
| | - Cerebrovascular h. |
| | - Systemic coagulopathy |
| Thromboembolic | - Cerebrovascular |
| | - Pulmonary embolus |

 Table 5

| | - Limł | b ischemia (in case of arterial cannulation) |
|-----------------------|--------|---|
| Insufficient | - Ano | xic brain injury |
| perfusion | - Rena | l failure |
| - | - Hepa | atic failure |
| | - Mult | i-organ failure |
| Cardiac site (in case | - LV d | istension with need for venting (in case of cannulation |
| of arterial | of fe | moral artery) |
| cannulation) | - Puln | nonary edema, Systemic embolizations |

Transport on ECLS

During patient transport the same level of critical care support should always be maintained. Over the last several years, ECLS systems have been minimized and simplified such that safe transfers to referral hospitals are feasible. Retrieval services provided by an ECLS team with around the clock coordination are now established with referral networks that facilitate early recognition and transfer of the patients.

Early communication between referring and receiving hospitals and the transferring ECMO team is essential and ideally should take place in anticipation before the patient deteriorates irreversibly. An agreement on the indications for ECMO support and on the subsequent management pathway prior to transfer must always be in place within the network. Early communication also provides a window of opportunity to safely transfer less ill (non-ECMO) patients using conventional methods for ECMO support in the referral hospital.

While the delay in cannulation may be tolerated or bridged by ventilator in case of respiratory failure this may not be the case in patients with acute severe cardiogenic shock who require VA Support. This delay can be reduced if the patient is in specialist tertiary referral cardiac centre that can initiate VA ECLS support. Other advantages are that the referral centre can establish ECLS without the need to provide on-going management, which requires medical, perfusion and nursing staff with specialised training.

Transport of critically ill patients in sub-Saharan Africa remains a great challenge owing to the distances between health facilities well underdeveloped as as infrastructure. In many low-income countries, critical care remains in its infancy (15). Development of an ECMO retrieval service will require an in-depth understanding of the limitations of the area as well as locally based specialised teams to perform the transfers.

ECMO transport

Currently there are no ECMO centres in sub-Saharan Africa except in South Africa. Transportation of patients on ECMO is high risk and deaths have occurred as eligible patients are, in general, in an unstable condition supported by maximal ventilator support and other intensive care salvage therapies (16).

ECMO transfers from sub-Saharan Africa in the initial phases will adopt a hub-andspoke model, with patients being referred from remote primary care centres in other countries to highly specialized centres in South Africa. Transport of critically ill patients on ECMO can be challenging; however, this has been demonstrated to be if undertaken safe and feasible by adequately trained teams, with appropriate equipment and a platform that can accommodate the team and allows full access to the patient (17).

Owing to the relative lack of ICU facilities and specialists in sub-Saharan Africa, it is anticipated that multidisciplinary specialised ECMO retrieval team will mobilise, cannulate and initiate ECMO at the remote primary care hospital and proceed to transfer the patient to the tertiary ECMO centre. Initiation of ECMO on critically ill patients in the primary care hospital with subsequent transport to a tertiary care centre yields excellent results (18).

Due to the vast inter-facility distances involved, air transport using a fixed wing aircraft will be the ideal mode of transport. This will mean that the transfer will be multi-modal, with a ground ambulance service on both ends of the transfer.

AMREF Flying Doctors based in Nairobi, Kenya conducted 570 medical flights in the year 2016 with approximately 15% of these patients on ventilators suffering from sepsis and respiratory failure. It is possible that outcomes for these patients may improve if ECMO is started early if indicated. There is little data from the intensive care units in sub-Saharan Africa on the number of patients in whom ECMO is indicated.

The ELSO guidelines recommend ground transport for distances up to 400 km (250–300 miles) and helicopter transport for distances up to 650 km (300–400 miles) (19). With poor road infrastructure and traffic congestion in most parts of sub-Saharan Africa, air transport would be the ideal means to move these critical patients rapidly and safely.

ECMO Team

Safe and effective ECLS requires specialized medical expertise and highly specialized staff. An ECLS team typically includes a combination of physician and nurses specialized on ECLS. The part of optimal support involves the education of clinicians in the referring hospitals.

Outcomes and ELSO Registry

Because of the past selection criteria for ECLS considered as a rescue option numerous cohort studies exist but only a single randomized study on outcome. The CESAR trial published in 2009 randomized 180 adult patients with severe respiratory failure to conventional management versus ECMO referral to for consideration of ECLS (20). A 16% absolute reduction in the primary endpoint of death or severe disability in the ECMO group was described with overall 55% survival. In adult trauma cohorts survival rates of 65% to hospital discharge have been noted (21, 22). In infective cases such as H1N1 associated ARDS, 75% survival rates have been achieved by the Australian and New Zealand ECMO network (23). Since 1989, ELSO has maintained a registry of data on all patients receiving ECMO. As of July 2016, 78,397 ECLS patients were treated with ECLS of which 70% were weaned off support and 58% survived to discharge or were transferred [Fig. 6]. ELSO registry also supports clinical research, individual ELSO centre quality assessment and regulatory needs for ECMO. Extracorporeal life support use and centres providing ECLS have increased worldwide. Extracorporeal life support use in the support of adults with respiratory and cardiac failure represented the largest growth in the recent time period. Extracorporeal life support indications are expanding, and it is increasingly being used to support cardiopulmonary resuscitation in children and adults (24).

ECLS Registry Report

International Summary July, 2016



Overall Outcomes

Extracorporeal Life Support Organization 2800 Plymouth Road Building 300, Room 303 Ann Arbor, MI 48109

| | Total Patients | tients Survived ECLS | | Survived to DC or Transfer | | | |
|-------------|----------------|----------------------|-----|----------------------------|-----|--|--|
| Neonatal | | | | | | | |
| Respiratory | 29,153 | 24,488 | 84% | 21,545 | 74% | | |
| Cardiac | 6,475 | 4,028 | 62% | 2,695 | 42% | | |
| ECPR | 1,336 | 859 | 64% | 547 | 41% | | |
| Pediatric | | | | | | | |
| Respiratory | 7,552 | 5,036 | 67% | 4,371 | 58% | | |
| Cardiac | 8,374 | 5,594 | 67% | 4,265 | 51% | | |
| ECPR | 2,996 | 1,645 | 55% | 1,232 | 41% | | |
| Adult | | | | | | | |
| Respiratory | 10,601 | 6,997 | 66% | 6,121 | 58% | | |
| Cardiac | 9,025 | 5,082 | 56% | 3,721 | 41% | | |
| ECPR | 2,885 | 1,137 | 39% | 848 | 29% | | |
| Total | 78,397 | 54,866 | 70% | 45,345 | 58% | | |

Figure 6. Overall outcomes of ECLS treatment due to the International Summary of the ELSO

Registry

DISCUSSION AND CONCLUSION

The randomised CESAR trial reported its findings in 2008 with a relative risk in favour of ECMO of almost 0.70. This translated to one extra survivor for every 6 patients treated by conventional ventilation. Since then ECLS has progressed remarkably and in the last decade it has become the standard of care in many centres where conventional methods for respiratory and cardiorespiratory support have failed. In recent years the indication has extended to cardiac Extracorporeal arrests using Cardiopulmonary Resuscitation (ECPR) with a recent meta-analysis in 260 patients suggesting superior outcomes with ECPR to conventional cardiopulmonary resuscitation (25).

The ELSO registry has demonstrated that overall 70% of patients receiving ECLS are eventually weaned off support with certain subgroups, notably paediatric respiratory conditions, reporting better outcomes of 84%. On the face of it ECLS may seem like the panacea for many critical clinical conditions offering improved outcomes. However, the immediate relevance to the sub-Saharan region of this complex intervention must be closely evaluated.

At present there are seven ELSO registered centres in Africa, six in South Africa and one in Egypt. Considering that in 2015 there were 310 centres registered worldwide, Africa represented only 1.9% of these – a humbling statistic considering the continent contains over 16% of the world's population. What remains more humbling is that the sub-Saharan region, with a population of over 1 billion has no access to ECLS services and with the region's population set to quadruple in this century, unless drastic measures are taken, the prospects will remain grim.

A key limitation of ECMO remains the investment in training and education and the steady supply of patients that would potentially benefit from it along with means of payment. In an already struggling healthcare space the introduction of ELCS may cripple the infrastructure instead of supporting it. Unless of course certain steps are taken to phase the service in and with key partnership models. Firstly, the successful provision of ECLS in sub-Saharan Africa should involve the amalgamation of 3 core services - a transport partner, a clinical partner and an industry partner. This ménage à trois requires dedicated roles from all parties with vested interests around commercial gains side lined until а sustainable ECLS service is established. The transport partner, especially one providing a 24/7 response switchboard service is in an excellent position to also piggyback the ECLS provision whenever calls for expatriation are made, or advice sought for specific cases. In addition, the existing critical care capability is a strong backbone in supporting incoming or outgoing patients on ECLS. The clinical partner is in a position to develop guidelines for local hospitals as well as provide cannulation for cases. The partner would also provide a destination for incoming patients in due course. The industry partner would provide the hardware and training support for the ECLS service on terms kind to the start-up of the service. In return a commercial arrangement for the supply of consumables can be reached by mutual consensus.

The phasing of ECLS is crucial to the longterm success of the service. It is our belief that in the initial stages the service should focus on repatriation of patients to existing centres of excellence that have the capability to receive such cases, in this case South Africa which is an estimated 4 to 5-hour flight. These can be VV and VA ECMO cases. As local capability increases the hub in sub-Saharan Africa can be positioned to initially receive incoming VV ECMO cases with a transition to VA ECMO as experience increases.

There is no doubt that ECLS use is increasing and as techniques are refined will lead to improved outcomes with time. However, the resources and time that should be committed to training of staff and on-going education should not be ECLS should only underestimated. be commenced, maintained and weaned in the hands of trained, experienced and knowledgeable medical personnel cognisant that the results will be benchmarked by ELSO and available for consumption in the public domain. Partnership models are key to the ECLS success with well-defined roles and responsibilities for each party.

REFERENCES

1. Institute for Health Metrics and Evaluation. Kenya statistics. Available at: http://www.healthdata.org/kenya.

2. Dalal, S., Beunza, J.J., Volmink, J., Adebamowo, C., Bajunirwe, F., Njelekela, M., *et al.* Non-communicable diseases in sub-Saharan Africa: what we know now. *Int. J. Epidemiol.* 2011; **40**:885-901. doi: 10.1093/ije/dyr050.

3. Levels & Trends in Child Mortality. UNICEF report, 2015. Available at: http://www.childmortality.org/files_v20/downlo ad/IGME%20report%202015%20child%20mortali ty%20final.pdf.

4. Mitanchez, D., Yzydorczyk, C. and Simeoni, U. What neonatal complications should the pediatrician be aware of in case of maternal gestational diabetes? *World J. Diabetes* 2015; **6**:734–743. doi: 10.4239/wjd.v6.i5.734.

5. de-Graft, A.A., Unwin, N., Agyemang, C., Allotey, P., Campbell, C. and Arhinful, D. Tackling Africa's chronic disease burden: from the local to the global. *Globalization Health* 2010; **6**:5 doi: 10.1186/1744-8603-6-5.

6. Steyn, K. and Damasceno, A. Lifestyle and related risk factors for chronic diseases. In: Jamison, D.T., Feachem, R.G., Makgoba, M.W., et al., editors. Disease and mortality in sub-Saharan Africa, 2nd ed. Washington, DC: The International Bank for Reconstruction and Development / World Bank, 2006. Available at: https://www.ncbi.nlm.nih.gov/books/NBK2290/.

7. Rao, C., Lopez, A.D. and Hemed, Y. Causes of death. In: Jamison, D.T., Feachem, R.G., Makgoba, M.W., et al., editors. Disease and mortality in sub-Saharan Africa, 2nd ed. Washington (DC): The International Bank for Reconstruction and Development / The World

Bank, 2006. Available at:

https://www.ncbi.nlm.nih.gov/books/NBK2298/. 8. Hessels, A., Flynn, L., Cimiotti, J.P., Bakken, S. and Gershon, R. Impact of Heath information technology on the quality of patient care. *On-line Journal of Nursing Informatics* 2015;19 9. Gibbon, J.H. Jr. Application of a mechanical heart and lung apparatus to cardiac surgery. *Minn. Med.* 1954; **37**:171–185.

10. Hill, J.D., O'Brien, T.G., Murray, J.J., Dontigny, L., Bramson, M.L., Osborn, J.J., *et al.* Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. *N. Engl. J. Med.* 1972; **286**:629-634.

11. Conrad, S.A., Grier, L.R., Scott, L.K., Green, R. and Jordan, M. Percutaneous cannulation for extracorporeal membrane oxygenation by intensivists: a retrospective single-institution case series. *Crit. Care Med.* 2015; **43**:1010-5. doi: 10.1097/CCM.00000000000883.

12. Extracorporeal Life Support Organization (ELSO). Available at: http://www.elso.org.

13. Extracorporeal Life Support Organization (ELSO). Guidelines for adult respiratory failure, supplement to the ELSO general guidelines, 2013. Available at: http://www.elso.org/Portals/0/IGD/Archive/File Manager/989d4d4d14cusersshyerdocumentselso guidelinesforadultrespiratoryfailure1.3.pdf.

14.ExtracorporealLifeSupportOrganization (ELSO). Anticoagulation guideline,2014.Availableat:http://www.elso.org/Portals/0/Files/elsoanticoagulationguideline8-2014-table-contents.pdf.

15. McCormick, B. Intensive care medicine in resource-limited settings: a general overview. *Update In Anaesthesia Journal* 2012: 7-10,

16. Broman, L.M. and Frenckner, B. Transportation of critically ill patients on extracorporeal membrane oxygenation. *Front. Pediatr.* 2016; **4**:63. doi: 10.3389/fped.2016.00063.

17. Bryner, B., Cooley, E., Copenhaver, W., Brierley, K., Teman, N., Landis, D., *et al.* Two decades' experience with interfacility transport on extracorporeal membrane oxygenation. *Ann. Thorac. Surg.* 2014; **98**:1363–1370.

18. Rupprecht, L., Philipp, A., Camboni, D., Müller, T., Bein, T., Luchner, A., Lunz, D., Hilker, M. and Schmid, C. ECMO transport of critically ill patients. *Thorac. Cardiovasc. Surg.* 2013;**61**(S 01): OP68. doi: 10.1055/s-0032-1332307

19. ELSO. Guidelines for ECMO transport. Ann Arbor, MI: ELSO, 2015. Available at: http://www.elso.org.

20. Peek, G.J., Mugford, M., Tiruvoipati, R., Wilson, A., Allen, E., Thalanany, M.M., et al. economic Efficacy and assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (Cesar): a multicentre controlled trial. randomised Lancet 2009; **374**:1351-1363. doi:10.1016/S0140-6736(09)61069-2 21. Guirand, D.M., Okoye, O.T., Schmidt, B.S., Mansfield, N.J., Aden, J.K., Martin, R.S., et al. Venovenous extracorporeal life support improves survival in adult trauma patients with acute hypoxemic respiratory failure: а multicenter retrospective cohort study. J. Trauma Care Surg. 2014; 76:1275-1281. doi: Acute 10.1097/TA.000000000000213.

22. Ull, C., Schildhauer, T.A., Strauch, J.T. and Swol, J. Outcome measures of extracorporeal life support (ECLS) in trauma patients versus patients without trauma: a 7-year single-center retrospective cohort study. *J. Artif. Organs* 2016.

23. Bailey, M., Beca, J., Bellomo, R., Blackwell, N., Forrest, P., Gattas, D., *et al.* Extracorporeal membrane oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. *JAMA* 2009; **302**:1888-1895. doi: 10.1001/jama.2009.1535.

24. Thiagarajan, R.R., Barbaro, R.P., Rycus, P.T., McMullan, D.M., Conrad, S.A., Fortenberry, J.D., *et al.* Extracorporeal Life Support Organization Registry International Report 2016. *ASAIO J.* 2017; **63**:60-67. doi: 10.1097/MAT.00000000000475.

25. Wang, G.N., Chen, X.F., Qiao, L., Mei, Y., Lv, J.R., Huang, X.H., *et al.* Comparison of extracorporeal and conventional cardiopulmonary resuscitation: A meta-analysis of 2 260 patients with cardiac arrest. *World J. Emerg. Med.* 2017; 8:5-11.