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THE REVIVAL

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Society Reg.No.: EKM/TC/186/2013, **Society secretariat:** Address 36/117, 2nd Floor, Lisie Hospital Road, Kottecanal Junction, Kochi 682018. Ph.: 025750048, **Email:** infoshft@gmail.com, www.sfhft.org

EDITOR'S NOTE

Dr Manoj Durairaj

Heart Transplant Surgeon, MS, MCh. (AIIMS, New Delhi), FACC.

Director, Marian Cardiac Centre and Research Foundation.

Program Director, Department of Heart and Lung Transplantation, Sahyadri Hospitals, Pune.

Dear Colleagues,

Greetings from the Editor's desk. The August 2022 issue features an Overview on ECMO in Children by Dr Debasis Das and Dr Shubhadeep Das. ECMO is a valid alternative and improves the survival rates in patients with severe respiratory and cardiorespiratory failure. This article provides a ready reckoner for clinicians in decision making for initiating ECMO in neonatal and paediatric patients. It throws light on management of these patients in terms of priming, initiation of support, gas flow rates and anticoagulation, hematologic management and weaning strategies. The authors have to be congratulated on writing this brief review and I am sure our readers will benefit from their effort.

Wishing our dear readers a Happy Reading!

Dr Manoj Durairaj
Editor "The Revival"

SUB EDITOR

Dr Talha Meeran

MBBS, MD, FACC, Consultant Cardiologist, Dept of Advanced Cardiac Sciences and Cardiac Transplant, Sir HN Reliance Foundation Hospital, Mumbai.

Dear Colleagues,

The August edition of The Revival focuses again on ECMO however this time with a particular focus on pediatric and neonates. The basic concept of ECMO circuit along with the basics of management of the circuit along with the resuscitation end goal points have been summarized succinctly. The pediatric specific indications for VA ECMO and VV ECMO are descriptive yet simple to follow. Of particular note are the encouraging outcomes that were reviewed in the discussion section towards the end. The editorial team sincerely thanks Dr Das for this valuable contribution."

Sincerely,
Dr Talha Meeran
Sub Editor "The Revival"

PRESIDENTIAL MESSAGE

Prof. (Dr) V. Nandakumar

Director & Chief, Division of Cardio Vascular/Thoracic Surgery & Cardiac Transplantation, Metromed International Cardiac Centre, Calicut, Kerala.

Dear Colleagues,

Greetings from the Society for Heart Failure and Transplantation

August issue of 'The Revival' presents an overview on Extracorporeal Membrane oxygenation in Children. Dr Debasis Das has covered the topic well to include all aspects of it.

This article will provide an insight into the less commonly used life saving intervention especially in children.

Best wishes,
Prof. (Dr) V. Nandakumar
President

Please call or write to us:
Call: 9822322072, 9167048815,
manojdurairaj@hotmail.com,
talha.meeran@gmail.com

Link for membership,
http://www.sfhft.org/application.html

Special thanks to Dr Debasis Das and Dr Shubhadeep Das for authoring this month's article.

Designed by Maithili Kulkarni

EXTRA-CORPOREAL MEMBRANE OXYGENATION IN CHILDREN: AN OVERVIEW

DR DEBASIS DAS

MBBS, MS, MRCS (Edin), MCh, DNB (CTVS), FIACS, Senior Consultant Cardiac Surgeon, Narayana Superspecialty Hospital, Howrah, Kolkata.

Dr Debasis Das is a Sr. Consultant Cardiac & Heart Transplant Surgeon working in Kolkata since 2009 with the Narayana Health group.

Dr Debasis Das has more than 15 years of experience and has over 4000 adult and paediatric surgeries to his credit.

Dr Debasis Das is currently associated with Narayana Superspeciality Hospital, Howrah as Senior Consultant Cardiac Surgeon, where he started the department in 2013. Prior to joining Narayana Superspeciality Hospital, he was associated with Rabindranath Tagore International Institute of Cardiac Sciences as Consultant Cardiac Surgeon from 2009.

Dr Debasis Das did his MBBS from Maulana Azad Medical College, New Delhi. After graduation he completed his MS (General Surgery) from MAMC, New Delhi.

Dr Debasis Das completed MCh in Cardiovascular & Thoracic Surgery from Post Graduate institute of Medical Education and Research, Chandigarh. He also acquired DNB (CTVS) after that. Dr Das went to Australia for advanced training and completed two years of Adult Fellowship in Austin Hospital, Melbourne and one year of Paediatric Cardiac Fellowship from The Children's Hospital at Westmead, Sydney, Australia.

His main area of interests are Heart Transplant, Congenital Heart Surgery, Assist Devices and MCS, Aortic surgery and and valve repairs.

He has many publications in reputed national and international journals and has active interest in clinical research. He is on the review panel and editorial board of many international journals. He has many awards to his credit. He is a member of many professional associations of cardiac surgeons.

DR SHUBHADEEP DAS

MBBS (Hons), MD (Pediatrics), Fellowship in Pediatric Critical and Cardiac Critical Care (University of Toronto, Sick Kids, Canada) RCPCH Fellowship, Pediatric Critical and Cardiac Critical Care (UK), European Board Certified in Pediatric Intensive Care (EPIC)

Dr. Shubhadeep is a Consultant Pediatric Cardiac intensivist at NH Narayana Superspeciality Hospital, Howrah. He has extensive experience of working in cardiac PICUs/general medical and surgical and ICUs across Canada, United Kingdom and India. He is very experienced at managing kids on ECMO, CRRT, HFOV, iNO. Led the ICU care of eastern India's first pediatric heart transplant patient at NSH, Howrah.

Dr. Das is passionate about teaching and research activities and has multiple publications in international journals.
He is certified in Pediatric Intensive Care by ESPNIC (European Society of Pediatric and Neonatal Intensive Care) and is an 'IAP-Pediatric Intensive Care Chapter-College of Pediatric Critical Care' accredited teacher of pediatric critical care.

His areas of interests include Extra Corporeal Life Support, Post operative management and follow up of heart transplant patients, Non Invasive ventilation and infection control in ICU.

Introduction

ECMO or Extra Corporeal Membrane Oxygenation is a modification of conventional cardiopulmonary bypass used to support heart and lungs for extended period of time till the underlying disease process is treated.

The fundamental principle of this form of extracorporeal life support consists of desaturated blood being drained via a venous cannula, removal of CO_2 and addition of O_2 through an "extracorporeal" device which functions as artificial lungs and then blood being returned to systemic circulation via another vein (VV ECMO) or artery (VA ECMO) [1]. The basic components of ECMO circuit include a blood pump, membrane oxygenator & heat exchanger controller, cannulas and tubings (Figure 1). Venous-venous cannulation is used for isolated respiratory failure (hypoxemia), whereas venous-arterial cannulation is used for cardiac failure (tissue hypoxia secondary to hypoperfusion) with or without respiratory failure.

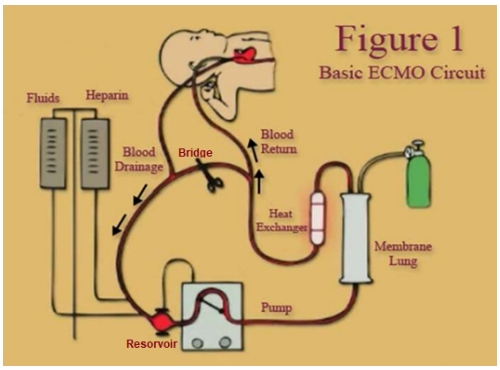

Figure 1: Demonstrates basic components of ECMO circuit.

Deoxygenated blood from the patient flows in the tubing through a pump and on to an oxygenator and heat exchange unit, before being returned to the patient. If a roller pump is used, a reservoir is incorporated before the pump. Reservoir is not necessary for a centrifugal pump

History and evolution of ECMO

The history of ECMO goes back to 1937 when Dr. John Gibbon started working on developing the heart-lung machine resulting in first successful cardiac surgery using a heart-lung machine in 1953, on an 18 yr old girl with Atrial Septal Defect[2]. Though ECMO provided a great opportunity of directly operating on the heart by diverting the venous return and returning directly to systemic circulation, but it was self-limited by causing a lot of damage to blood and was not used for more than 2-3 hrs due to its fatal complications. Subsequently, from 1960s-70s there was a lot of development in the ECMO technology enabling its long term use by using a gas exchange membrane between blood phase and gas phase, thereby reducing hemolytic complications. Prolonged ECMO as support for severe respiratory failure was first successfully used in 1971 in an adult patient with post-traumatic ARDS by Dr. J.D..Hill and associates [3]. In 1972, Bartlett et al. reported the first successful use of ECMO in a newborn "Esperanza" with severe respiratory distress suffering from meconium aspiration syndrome with PPHN [4, 5].

After the initial few successful a lot of prospective and retrospective clinical trial were presented. Most of them showed favorable results with ECMO while few were against the use of ECMO with limitations present in almost all of these studies.

The usage of ECMO received a boost after the publication of the CESAR trial in 2009 [6], clearly showing an improvement death rate and severe disability 6 months after randomization of patients with severe respiratory failure treated with extracorporeal support in an expert high-case-volume center compared with no specialized hospital care. Since then the ECMO support applications exploded and continue to progress. Currently, ECMO is considered a valid alternative in refractory cases of reversible cardiopulmonary failure.

Modes of ECMO

ECMO can be categorized according to the circuit used into Veno-arterial (VA) and Veno-venous (VV) configurations

Veno-arterial - VA ECMO provides both gas exchange and circulatory support (Heart & Lung failure). Cannulas are placed in a major artery and one or more major veins. Venous blood is oxygenated and pumped back directly into the arterial circulation, bypassing both the heart and lungs.

Veno-venous - VV-ECMO allows gas exchange only (Isolated Lung failure). A double lumen cannula is commonly placed in a major vein. Deoxygenated blood flows from the venae cavae and oxygenated blood is returned to the right atrium. Alternatively, separate inflow and outflow cannulas may be used.

Indications for initiation of ECMO

Cardiac ECMO indications

Indications for pediatric cardiac ECLS generally fall into four broad categories, those related and those unrelated to cardiac surgery and catheterization [7]

1. Cardiac Surgery and Catheterization

a) Pre-operative stabilization – in cases where physiological stability is likely to be achieved over time or early operative repair is likely to have a successful outcome.

b) Failure to wean from cardiopulmonary bypass.

c) Elective support during high-risk catheter procedures.

d) Low cardiac output in the post-operative period.

2. Cardio-circulatory failure due to various etiologies

a) Cardiogenic: Myocardial failure due to myocarditis and cardiomyopathy, intractable arrhythmia.

b) Distributive: Sepsis, Anaphylaxis.

c) Obstructive: Pulmonary hypertension, pulmonary embolus.

3. As a bridge to heart transplantation

4. In-hospital cardiac arrest not responsive to conventional CPR, with rapid availability of specialist ECMO team[8]

Difference Between VA-ECMO and VV-ECMO	
VA-ECMO	VV-ECMO
Requires arterial and venous cannulation	Requires only venous cannulation
Provides cardiac support to assist systemic circulation	Does not provide cardiac support to assist systemic circulation
Bypasses pulmonary circulation /decreases pulmonary aerial pressures	Maintains pulmonary blood flow
Can be used in RV failure	Cannot be used in RV failure
Lower perfusion rate is needed	Higher perfusion rates are needed
Higher PaO2 is achieved	Lower PaO2 is achieved
ECMO circuit connected in parallel to the heart and lungs	ECMO circuit connected in series to the heart and lungs

Strict criteria for selection of pediatric patients for cardiac ECMO are not available. Presence of any two criteria from following, for more than 4-6hrs after maximum conventional management might be helpful in selecting pediatric patients for cardiac ECMO support.

- Cardiogenic shock with Inotropic score > 20
- Lactate levels >50 mg/dl or 5mmol/L or rising levels
- Refractory arrhythmia
- pH less than 7.15 with oliguria (<1 ml/kg/hr)in spite of inotropic support and IABP(intra-aortic balloon pulsation) in selective group of patients
- Central venous oxygen level(ScvO2)<60%
- Cardiac index < 2 L/min

Respiratory ECMO indications [9]

Neonate:

- Meconium aspiration syndrome
- Persistent pulmonary hypertension of newborn/persistent fetal circulation
- Respiratory distress syndrome
- Congenital diaphragmatic hernia
- Pneumonia (viral/bacterial/aspiration)
- Sepsis

Pediatric:

- Pneumonia (viral/bacterial/aspiration)
- Acute respiratory distress syndrome (ARDS)
- Non ARDS respiratory failure

Presence of any two of the criteria from the following observed over a period of 4 to 6 hours after maximum medical resuscitation:

- PaO2/FiO2 <75%
- Oxygen index (OI)>40 for 4-6 hrs
- Murrays Score of >3
- A-a gradient >600
- Hypercapnia with PH of <7.2 observed over more than 3 hours.
- Lung compliance <0.5 cc/cmH2O/kg

Exclusion Criteria:

Irreversible disease- eg: malignancy, end-stage hepatic or renal failure

- Patient on the ventilator for >15 days
- Intracranial bleed or recent neurosurgical procedure
- Active bleeding from a noncompressive site
- Irreversible neurological status or severe CNS injury like persistent vegetative state with poor neurological outcomes
- Unwitnessed arrest or arrest >30minutes
- Gross multi-organ failure (relative)

Circuit components

The components of an ECLS circuit, although based on the traditional cardiopulmonary bypass circuit, have been developed or adapted for long-term support (Figure 1). Vascular cannulas are placed for blood drainage and reinfusion. A centrifugal pump provides blood flow through the circuit (Figure 2). An artificial lung (oxygenator) provides gas exchange. Previously, silicon membrane oxygenators were used which are being replaced by hollow fibre PMP (polymethyl pentene) membrane

Figure 2: A centrifugal pump now used on modern ECMO machines

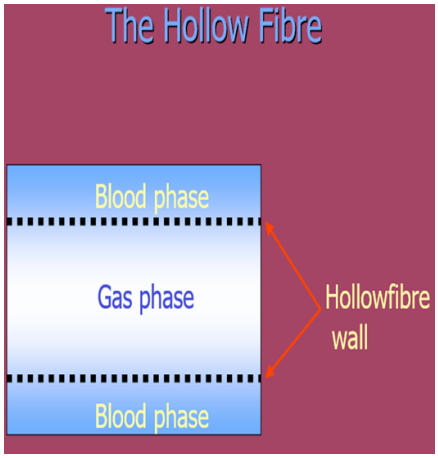

Figure 3: Hollow fibre PMP (polymethyl pentene) membrane oxygenators

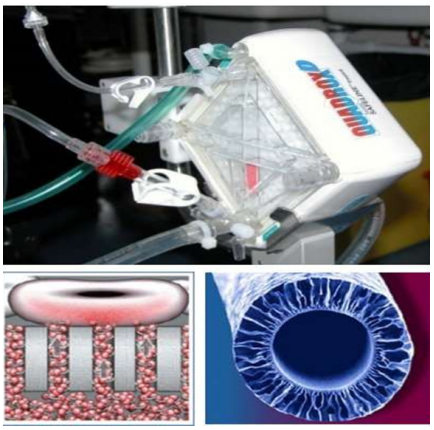

Figure 4: Hollow fiber membrane oxygenator. Fresh gas called 'Sweep' runs through the center of the membrane while RBCs flow over it

oxygenators (Figure 3). These are extremely efficient at gas exchange and demonstrate minimal plasma leakage, low resistance to blood flow. A heater-cooler provides precise temperature control. Other circuit components allow for infusion of medications, incorporation of a hemofilter or other adjunctive techniques such as plasmapheresis and monitoring systems for blood gas, flow, and pressure.

ECMO Management

Priming

The extracorporeal circuit volume is substantial relative to patient blood volume, requiring circuit prime consisting of a solution that has normal electrolyte concentrations. In smaller children, especially neonates necessitate using a blood prime. Priming begins with a balanced electrolyte solution (such as Normosol or Plasmalyte). Albumin, packed red blood cells, or fresh frozen plasma may be added later.

Initiation of Support

Preparation of the patient prior to cannulation includes adequate sedation and analgesia and neuromuscular blockade. Activated clotting time (ACT) is measured as a baseline prior to heparin administration. An initial bolus of heparin (50-100 U/kg) is administered just prior to cannulation. After vascular access is achieved, the circuit is connected and flow is initiated at a low-flow rate, increased incrementally to the target rate over a short duration. Minimum blood flow for cardiac support i.e. VA ECMO are as follows Neonate- 100ml/kg/min, Pediatric-80ml/kg/min, Adult-60ml/kg/min. The blood flows are adjusted according to hemodynamic status of the child. VV-ECMO blood flow rates of 120ml/kg/min in neonates, 80-100ml/kg/min in children and 60-80ml/kg/min in adults [10].

Gas flow rates

It should be set in relation with blood flow, the ratio of sweep gas flow: blood flow is 0.5: 1 & can go maximum up to 1.5: 1. It is adjusted according to the carbon dioxide level.

Anticoagulation and Hematologic Management

The ECLS circuit is pro-coagulant, requiring continuous administration of a systemic anticoagulant. Inadequate anticoagulation leads to clot formation in the circuit. At present, heparin remains the anticoagulant of choice. Maintaining the ACT between 180 and 200 seconds is a usual target that may balance the risk of bleeding complications and circuit clotting, but will vary according to institutional preference, clinical situation, type of ECLS circuit, and type of ACT machine being used (kaolin or celite). Platelet dysfunction is very common during ECLS support. and daily transfusions are not uncommon during the early

phase of support. A platelet count of 80,000-100,000 is maintained during the initial phase of support and during management of bleeding complications. Red blood cell transfusions are often required. The target hemoglobin is generally 10-12 g/dL, fresh blood is preferred[11].

Ventilator Management

Although the goal for ventilator management is to provide a protective ventilation strategy. The goal is to maintain alveolar recruitment, avoid overdistension and atelectasis, and reduce exposure to elevated concentrations of O2. Use of pressure-limited ventilation, elevated levels of positive end-expiratory pressure (PEEP) (10–12 cm H2O), low ventilator rates (6–10/min), and small tidal volumes (<6 mL/kg) will meet these goals.

Hemodynamic Management

The requirement for vasoactive agents is almost universal in patients about to undergo extracorporeal support. Inotropic and vasopressor agents are weaned after initiation of support. After the initial period of support, vasoactive agents can often be weaned off completely. In patients on VA ECLS with severe cardiac dysfunction, it is common practice to enhance contractility with low-dose inotropes (e.g., ≤0.05 mcg/kg/min epinephrine or ≤5 mcg/kg/min dobutamine) in order to facilitate aortic valve opening and prevent stasis of blood in the systemic ventricle and aortic root [12].

Sedation and Analgesia

Routine ICU sedation is used in ECLS and is often unit specific. It usually consists of a benzodiazepine (midazolam or lorazepam) or dexmedetomidine and an opioid analgesic (morphine or fentanyl). Dosing requirements may be elevated, as drugs may be adsorbed by the circuit, tolerance can develop, and hemofiltration can remove administered drugs.

Fluids and Renal Replacement Therapy

Maintenance of normal intravascular volume is important during ECLS, as an adequate venous return is necessary to maintain pump flow. Volume can be replaced with crystalloid, colloid, or blood products

Excess interstitial edema leads to organ dysfunction, contributing to worsening pulmonary, cardiac, gastrointestinal, and renal function. Diuretics (intermittent or continuous infusion) are the first choice in reducing interstitial edema, but if response to diuretics is inadequate, hemofiltration can be incorporated into the ECLS circuit.

Hemofiltration

Hemofiltration can be performed by inserting a hemofilter between high-pressure and low-pressure points in the circuit, such as pre-oxygenator and into the bladder, respectively. Another approach is to siphon post-oxygenator blood into a dedicated pediatric continuous renal replacement therapy (CRRT) circuit and return the blood pre-oxygenator, where air or debris from the CRRT circuit can be trapped by the oxygenator.

Nutritional Support

It is well established that enteral nutrition has substantial benefits over IV nutrition in critically ill patients and is the preferred route of administration. Initiation of enteral nutritional support should begin after resuscitation is complete and perfusion is restored, usually within 12–24 hours. IV nutritional support is used when the enteral route is contraindicated or to supplement it when full support cannot be achieved by the enteral route alone.

Monitoring On ECMO

- Monitor vitals
- Monitor ACTs
- Daily Na, K, Ca, KFT, Chest X - ray
- Pre and Post ECMO gases
- Patient ABG, SPO2
- Strict Intake /Output
- Urine Output
- Monitor for Blocks /Clots in circuit
- CO2 control by sweep gas flow
- ScvO2 monitoring

Complications of ECMO

Bleeding (7-34%) and thrombosis (8-17%) are the most common serious complications. Because of blood-surface interaction, clots can form in the circuit and embolize. Systemic infusion of unfractionated heparin helps to reduce thrombus formation but bleeding risk is then increased. Monitoring and appropriate treatment for disseminated intravascular coagulation (2-5%), hemolysis (7-12%), and fibrinolysis is also needed. Cannulation (7-20%) and surgical site bleeding (6-34%) are common. Intracranial bleeding (1-11%), especially in neonates; gastrointestinal hemorrhage (1-4%); and pulmonary hemorrhage (4-8%), seizures (2-10%) and infarction (1-8%) are common complications. Despite these problems, extracorporeal life support is becoming ever safer, especially when appropriately selected patients are managed in specialized units with well trained and experienced staff supported by multidisciplinary teams[13].

Weaning ECMO flows and Decannulation

The criteria for weaning depend on the indication of ECMO, in general when the underlying disease process improves and native organ recovers with their increased contribution in maintaining vital parameter, then weaning is attempted. Patient is weaned to low ECMO flows(30-50ml/kg/min) and optimal ventilator settings, decannulation is done after the patient maintains adequate oxygenation and perfusion in these settings for 2-4 hrs. Weaning of flows can be achieved in slow reduction of flow rate by 10-20 ml/kg/min every 1-2 hrs, upto flow of 30-50 ml/kg/min. During the process of weaning, blood gases and mixed venous saturations should be frequently monitored. If deterioration is seen, high flow is re-established for 24hrs before a repeat trial is performed.

Outcome on ECMO

Early success with ECMO was mainly reported from the neonatal population[13, 14]. Extracorporeal Life Support Organization (ELSO) is 'an international non-profit consortium of health care centers and individuals who are dedicated to the development, evaluation and improvement of ECMO … in the neonate, child and adult'. Till July 2022, ELSO registry recorded 81306 neonatal and pediatric ECMO runs across all indications, of which around 60% survived till hospital discharge[15]. This number has remained fairly constant over the number of years18. Advances in ECMO has led to growing interest of its utility in Cardiopulmonary Resuscitation (E-CPR). However, there is paucity of data regarding the exact timing or indications of initiating E-CPR and practices are often institution and experience driven. E-CPR and cardiac indications now account for almost 50% of the ECMO cannulations[16]. Neonatal respiratory ECMO cannulations have shown survival rate between 67% to 91% in single center studies[17, 18]. Similar data has been shown in a Cochrane review of 2008 of 3 RCTs and a non-randomized study which demonstrated significant mortality benefit in neonatal ECMO due to reversible respiratory indications[19]. All studies demonstrated that ECMO support increased survival to hospital discharge when compared to conventional therapeutic strategies. Of the total 244 infants, 77% survived in the ECMO group compared with 44% in the conventionally managed group ($p < 0.00001$). Data of the ELSO registry also shows that outcome is best in neonatal pulmonary ECMO runs with a 73% survival rate. In contrast, the evidence for ECMO in pediatric respiratory indications is less robust. Most of the pediatric evidence is based on case series or retrospective cohort analysis. Despite this, the fact is ECMO is a widely utilized in children beyond neonatal period for both refractory respiratory and cardiac failures. Latest ELSO data has shown survival of around 60% in respiratory ECMO and 50% in cardiac ECMO. The increasing use of this form of therapy has led to inclusion of VV ECMO in the Pediatric Acute Lung Injury Consensus Conference as a strongly agreed upon recommendation for severe pediatric ARDS[20]. The effect of ECMO on long term neurodevelopment is even more limited. Hanekamp et al in Netherlands evaluated national wide newborns treated with ECMO at 5 years of age and assesses impact on cognitive, neuromotor, and neuropsychological aspects. Only a small percentage (6%) suffered major neurodevelopmental disability, but overall mean cognitive development was similar compared to the control group[21]. Needless to say, more research is needed to evaluate effect of ECMO on long term neurodevelopment of children.

CONCLUSION:

ECMO is one of the most advanced forms of life support therapy in the Intensive Care Unit. The goal of ECMO is to provide a physiologic milieu for recovery in refractory cardiac/respiratory failure. The technology is not a definitive treatment for a disease, but provides valuable time for the body to recover. In that way it can be compared to a bridge, where patients are initiated on ECMO as a bridge to recovery, bridge to decision making, bridge to transplant or bridge to diagnosis. The use of this modality in children is not backed by a lot of randomized controlled trials, but the use has increased dramatically everywhere in last 10years.
When judiciously used, ECMO support in children is an important tool which can salvage many lives under challenging circumstances.

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PRESIDENT

DR V NANDAKUMAR
Mob: 9843015888
Email: drvnandakumar@gmail.com

PRESIDENT ELECT

DR RONY MATHEW
Mob: 9846097812
Email: drronymathew@yahoo.com

VICE PRESIDENTS

DR JULIUS PUNNEN
Mob: 9980072785
Email: jpunnen@hotmail.com

DR AJITKUMAR V K
Mob: 9895153684
Email: ajitkumarvk@yahoo.com

SECRETARY

DR JABIR ABDULLAKUTTY
Mob: 9447011773
Email: drjabi@yahoo.co.in

JOINT SECRETARY

DR RAJAGOPAL S
Mob: 9747606600
Email: srajagovindam@gmail.com

TREASURER

DR PRAVEEN G PAI
Mob: 9847334434
Email: praveen.pai.g@gmail.com

PAST PRESIDENTS

DR GEEVAR ZACHARIAH
(2013-2014 and 2014-2015)
Mob: 9846066816
Email: geevarzachariah@gmail.com

DR SHIV K NAIR (2015-2016)
Email: shivnairmd@ gmail.com

DR K VENUGOPAL (2016-2017)
Email: venugopalknair@gmail.com

DR JOSE CHACKO PERIAPURAM
(2017-2018)
Mob: 9847043224
Email: joseperiapuram@hotmail.com

DR P P MOHANAN (2018-2019)
Mob: 9846076006
Email: drppmohanan@yahoo.com

MEMBERS

DR C G BAHULEYAN
Mob: 9447344882
Email: bahuleyan2001@yahoo.co.uk

DR P CHANDRASEKHAR
Mob: 9443047152
Email: chanpad@gmail.com

DR COL JAMES THOMAS
Mob: 9892797060
Email: thomasdrjames@yahoo.in

DR JACOB ABRAHAM
Mob: 9847128123
Email: jacabraham1@gmail.com

DR JAYAGOPAL P B
Mob: 9847023777
Email: jaigopallakshmi@gmail.com

DR KARTHIK VASUDEVAN
Mob: 9845281450
Email: karvasudevan@gmail.com

DR C S HIREMATH
Mob: 9481119646
Email: hiremath.cs@sss.hms.org.in

DR MANOJ DURAIRAJ
Mob: 9822322072
Email: manojdurairaj@hotmail.com

DR RAJESH RAMANKUTTY
Mob: 9846005737
Email: drrajesh_mr@yahoo.com

DR V K CHOPRA
Mob: 9560898900
Email: chopravk@gmail.com

DR TALHA MEERAN
Mob: 9167048815
Email: talha.meeran@gmail.com