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Indian Journal of ECMO

1. Aims and Scope

Indian Journal of ECMO, the official publication of ECMO Society of India (ESOI) (https://www.ecmosocietyofindia.com), is a peer-reviewed print + online Quarterly journal. The *Indian Journal of ECMO* aims to publish Extracorporeal Membrane Oxygenation (ECMO) is an evolving branch in the critical care specialty. Recognizing the increasing need to consolidate the field and to promote awareness, continuing education, and research in this field, the "ECMO Society of India (ESOI)" was formed in September 2010 with the headquarters in Mumbai, India. Which will include editorials, original articles, case reports, review articles and a quiz.

2. Ethical Considerations

Manuscripts submitted for publication must comply with the following ethical considerations:

Informed Consent

Informed consent of the patients must be taken before they are considered for participation in the study. Patient-identifying information, such as names, initials, hospital numbers or photographs, should not be included in the written descriptions. Patient consent should be obtained in written and archived with the authors.

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From the Editors' Desk

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Critical Care at the Crossroads

Extracorporeal membrane oxygenation (ECMO) is evolving as a young science, which came into practice 5 decades ago. We are learning ways to make it more user-friendly and more biocompatible by reducing the interaction between the patient and the circuit.

Neonatal RCTs, adult ECMO RCTs (NIH, CESAR, EOLIA) trials, pandemics of H1N1 and COVID taught us many lessons. Learning from positive outcomes would be useful, but negative outcomes teach us much more important lessons about what should not be done. As we started to realize life between pandemics is exciting, realizing the importance of living in a free world, yet being conscious about the dangers posed by the germs having the potential to cause pandemics should help us prepare for the future. In May 2023, speaking at the annual health assembly in Geneva, the WHO chief, Dr Tedros warned that the world should be prepared for a future virus that could be even deadlier than COVID-19.[1]

Our journey towards making ECMO biologically compatible continues. In the international arena, studies are on to understand the importance of anticoagulation, direct thrombin inhibitors and heparin-free ECMO. Studies to make ECMO circuit surface mimic endothelium continue.

Since 2010, ECMO has seen tremendous growth in India. It is a pleasure to see the right professions from different disciplines from different states coming forwards to learn and practice ECMO in its true spirit. In our recent ECMO training course, we were pleasantly surprised to see clinicians in their sixties coming forward to learn ECMO as they identified its importance in their hospitals. We always encourage team participation. It is an opportunity to teach the learners and learn from them too.

Having practised ECMO for 25 years, I can identify the need for strengthening our services, building the bridges in our knowledge gap, embracing the right principles, and lying down deep foundations. In a country of 1.4 billion population, it is a herculean task, yet possible. We need to progress with our efforts in the indigenous production of ECMO consoles, oxygenators, and cannulas. We need to have the right combination of professionals coming together and investing. We should not lose this historical opportunity to help our society as well as stand as pioneers in spreading our knowledge to the entire ECMO community, more so to those in resource-limited countries.

Infection control has to be given due respect. If your ICUs are infested with nosocomial pathogens and multidrug-resistant bugs, I think it is not the suitable environment to treat your patients in that place. It is possible to change the microbial flora by adopting principles of antibiotic stewardship, by re-educating ourselves, by adopting no-blame policy and thorough introspection. As you adopt "zero tolerance" to the transmission of infection in operation theaters, you should extend the same practices to ICUs. Collective indulgence of the entire ICU team under the guidance of dedicated and understanding leadership can make this dream achievable. It will have a huge impact on our survival figures.

The number of pediatric and neonatal ECMOs done in our region are much less compared to adult ECMOs. The reasons for this phenomenon are multifactorial, ranging from awareness, technical expertise, availability of the services, and financial affordability, etc.

The establishment of regional centers of ECMO in different states in a big country like India would be a welcoming suggestion. Identifying ECMO centers of excellence and establishing critical care transport facilities from designated hospitals will help in sharing the protocols and the implementation of mobile ECMO facilities in a uniform manner. The establishment of the state chapters of ECMO is a positive move to identify individuals interested in practising ECMO and the communications going in different states.

We are grateful to the corporates for their role in encouraging ECMO facilities in the country. The practise of ECMO in state/central independent institutions such as AIIMS in different states; Nizam's Institute of Medical Sciences (NIMS); autonomous central institutions such as AIIMS Delhi; PGIMER; JIPMER; charitable organizations such as HERO DMC Heart Institute, Ludhiana; Major ESI hospitals and many other institutions should help in bringing the cost of ECMO closer to the affordable health care in the community. We hope, like cardiac surgery and oncology and transplantation services, ECMO will be available to the population in the years to come.

The importance of sharing knowledge cannot be over-emphasized. Learning from the cases and reporting your database with the Extracorporeal Life Support Organization (ELSO), ECMO Society of India (ESOI), and publication of your experience in journals will help in understanding and analyzing our own cases and developing our own database. It is the need of the hour.

1. https://www.livemint.com/news/world/deadlier-than-covid-who-chief-warns-threat-of-another-pandemic-emerging-11684895630062.html. Accessed on 30th June 2023.

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Greetings from the Desk of Journal Coordinator!

I feel both privileged and excited to bring out the second edition of the *Indian Journal of ECMO (IJECMO)*.

Publishing is the backbone of academic endeavors and is the traditional means of disseminating knowledge, research results and communicating new ideas and technology.

The aim is to provide a global platform to share extensive work and research related to this ever-expanding field of ECMO ranging from the evolution, physiology, equipment, ever- broadening indications, successful use, and its limitations. I would invite each one of you to share your valuable experiences to make our community stronger and enriched with knowledge.

The current edition includes the second part of our series on evolution of ECMO, a review article, research article and case reports. We have a special section on brief communications and a new addition of a crossword puzzle. I would like to invite suggestions on how to make the journal more useful to the students and interesting to the ECMO practitioners. I would like to bring new sections and keep on innovating and making our journal better with each published edition.

The full text of each article will be available online at https://www.ijecmo.com/journalDetails/IJECMO, where one can access the previous published editions of the journal as well as submit articles.

I hope each one of us make frequent use of this valuable resource and find it helpful in their clinical practice. I hope that this journal serves to stimulate a robust scientific understanding of ECMO with the long-term aim of improving the health of the public.

I would like to take this opportunity to thank the editors, associate editors and the reviewers for their hard work and enormous support to bring this edition in time. I am also grateful to the authors who have contributed their articles in our journal.

I would like to share a quote by Dr Leon Eydelman which I feel will be true for medical fraternity and public at large in the coming decades.

"ECMO is taking off. If you haven't seen it yet, you will."

Happy Reading, Happy Learning!

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Contents

ORIGINAL ARTICLE

Challenges Faced During Extracorporeal Membrane Oxygenation (ECMO) Management of COVID-19 Patients in India: A Retrospective, Multicentered, Observational Study

Vinayak Patki[1], Pranay Oza[2], Suneel Pooboni[3], Arpan Chakraborty[4]

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Abstract

Background: Very limited data have been published for Extracorporeal membrane oxygenation (ECMO) in patients of COVID-19 from India. We have conducted this survey-based study to understand the challenges faced during ECMO management of COVID-19 patients in India.

Materials and methods: This was a retrospective, multicentered, observational study conducted through a questionnaire-based survey. The survey addressed hospital characteristics, their experience of ECMO, and the various challenges faced during ECMO management of COVID-19 patients. The main four categories were technical challenges, operational challenges, clinical challenges, and major complications during ECMO of these patients. These challenges were probed in relation to the first and second waves of COVID-19 pandemic separately. The questions related to challenges faced during ECMO were ranked questions.

Results: In total, 22 hospitals have responded to the survey. Almost 60% of the participant hospitals were doing less than 10 ECMOs per year before COVID-19 pandemic. Limited availability of ECMO machines and the cost of ECMO therapy were the major technical challenges faced, both in the first and second waves. Resistance from staff to work and risk of getting cross-infection with other team members were serious operational challenges during the first wave, while high workload, limited staffing, and difficulty in transporting patients were challenges in the second wave. Difficulty in counseling, an apprehension/hesitancy in medical colleagues, lack of public awareness, and limited evidence in favor of ECMO therapy were the clinical challenges faced during the first wave, while complications during ECMO, and poor outcomes were the common clinical challenges faced during the second wave. Hospital-acquired sepsis was the most severe complication faced in both waves.

Conclusions: Managing ECMO in COVID-19 patients was found to be a challenging task. Sharing pre-ECMO strategies and protocols across usual referral centers and increased collaboration between ECMO centers is warranted to improve the outcome of patients.

Keywords: COVID-19 challenges, COVID-ECMO in India, ECMO, ECMO in COVID.

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Introduction

The role of Extracorporeal membrane oxygenation (ECMO) in the management of patients with COVID-19 adult patients has evolved over the last 2 years of the pandemic.[1,2] Many recently published articles describe the cohorts of COVID-19 patients supported by ECMO.[3–5] Earlier reports from Wuhan, China reported high mortality of 83% in COVID-19 acute respiratory distress syndrome (CARDS) was managed with ECMO.[6] More recent data, however, revealed improved survival of CARDS ECMO patients.[7] Recent Individual institutional reports and data from multi-institutional registries presented detailed analysis with promising results.[8] Very limited data have been published for ECMO in patients of COVID-19 from India. ECMO for COVID-19 in resource-intensive therapy requiring multidisciplinary teamwork. It itself is very challenging as there is a limited number of available centers with experienced personnel and well-equipped facilities, protection of team, difficult communication through PPE kits, cannulation problems, and COVID-19-related thromboembolism.[9,10] ECMO program in India has done tremendous development in the last 10 years and overcame many hurdles. Many centers in India have been offering ECMO for COVID-19.[11]

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Conflict of interest: Dr Vinayak Patki, Pranay Ozha, Suneel Pooboni and Arpan Chakraborty are associated as the Editorial board members of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of these Editorial board members and their research group.

Aims and Objectives

Aims and objectives of the study were to know the challenges faced during ECMO management of COVID-19 patients in India with reference to technical, operational, clinical challenges and complications other than the routine ECMO cases.

Materials and Methods

This was a retrospective, multicentered, observational study conducted through questionnaire-based survey. We have created a questionnaire consisting of 30 questions and was circulated through the available Internet Survey platform (SurveyMonkey Inc., San Mateo, CA, USA) to many of the ECMO Centers from India who were treating COVID-19 patients. The Ethical Committee (ESOI) waived the need for formal approval since the questionnaire did not retrieve any actual patient-identifiable data.

The first part of the survey consisted of preliminary information on Hospital and Intensive care units. The hospital details included were the type of hospital (government, nongovernment or mixed), whether affiliated with ECMO Society of India (ESOI) or Extracorporeal Life Support Organization (ELSO), the level of care the hospital has been providing, viz. tertiary care, nonacademic or community hospital and the number of beds in the hospital. The experience of the hospital in terms of the total number of patients managed on ECMO prior to COVID-19 was also asked. The ICU details included were the type of ICU (Interdisciplinary or multidisciplinary) and ICU bed capacity. The second part of the survey was about the different types of challenges the hospital has faced during the ECMO management of COVID-19 patients. The challenges were divided into four broad categories. These challenges were probed in relation to the first and second waves of COVID-19 pandemic separately. For the survey purpose, ECMO done in the calendar year 2020 was considered as the first wave, and the ECMO done in the calendar year 2021 was considered the second wave. The main four categories were technical challenges, operational challenges, clinical challenges, and major complications during ECMO of these patients. The technical challenges included were the availability of the equipment, disposables, and the cost factor. The operational challenges included were about staffing, workload, transport issues, administrative issues, and safety issues. The clinical challenges included were about the awareness and acceptance of therapy in public and in medicos, difficulty in initiation of ECMO, and outcomes. The last part of the survey was regarding the various complications faced during the ECMO run in COVID time.

For conformity reasons and to facilitate participation in the survey, most of the questions were multiple choice (MCQ) with two to nine possible answers per question. The first part items had requested the participants to express concern about their extent of agreement with specific statements about ECLS therapy in the context of COVID-19 on an analog scale. The questions related to challenges faced during ECMO were ranked questions. The participants were requested to put grades in front of all options from one to maximum. Grade one was considered the most challenging one and the maximum grade was considered the least challenging one. From these ranking questions, the average ranking was calculated for each answer choice to determine which answer choice was most preferred overall. The answer choice with the largest average ranking was the most preferred choice, that is, the most challenging. The average ranking is calculated as follows [$(x^1w^1 + x^2w^2 + x^3w^3 + \ldots\ldots x^nw^n)$/Total response count], where w = weight of ranked position and x = response count for answer choice).[12] Weights were applied in reverse. In other words, the respondent's most preferred choice (which they rank as #1) has the largest weight, and their least preferred choice (which they rank in the last position) has a weight of 1. You can not change the default weights. For example, if a Ranking question has five answer choices, weights are assigned as follows:

- The #1 choice has a weight of 5
- The #2 choice has a weight of 4
- The #3 choice has a weight of 3
- The #4 choice has a weight of 2
- The #5 choice has a weight of 1

The survey questions and multiple choice responses were discussed and consented to by two expert ECMO specialists who had experience of more than 10 years in the field of ECMO. When consensus on all questions and answers was reached, the survey was transferred to an online platform (Survey Monkey Inc.). Automatic data retrieval and descriptive statistics were retrieved through this platform. More than one answer from centers was avoided with mutual close-loop communication between the person-in-charge of the ECMO program and other associated departments. Results from multiple choice questions are expressed in the median, participant's extent of agreement or disagreement in mean, and the standard deviation in percent. A time frame of 3 weeks will be given to the participant center to complete the survey. The survey was launched on December 1, 2022; the deadline for return was December 20, 2020. The final analysis of results was performed using an extrapolation tool provided by SurveyMonkey as well as SPSS.

Fig. 1: Stagewise distribution of participating centers for the survey

Results

Hospital Characteristics

In total, 23 hospitals agreed to participate in the survey. Out of which 22 have participated and 1 center has declined. All 22 hospitals responded to the survey. The participated hospitals belonged to 11 states of India as shown in Figure 1. These eleven states have 780 million of the population which is 60% of the Indian population.

Twenty (90.90%) hospitals were tertiary care/academic hospitals and nongovernment each. Fifteen (61.18%) hospitals were registered under the ECMO Society of India, while 14 (63.63%) were registered under the Extracorporeal Life support organization. Twenty (90.90%) hospitals had multidisciplinary ICUs. Thirteen (59.09%) hospitals have done less than 10 ECMO cases, 5 (22.72%) have done ECMO between 11 and 29 cases, while 4 (18.18%) hospitals have done more than 30 ECMO runs per year before the COVID-19 pandemic period (Table 1).

Challenges Faced

Challenges faced by these hospitals in managing ECMO patients were categorized under four headings – Technical, operational, clinical, and complications.

Table 1: Participant hospital's characteristics

Type of hospital	
• Tertiary care/University Hospital/Academic	20 (90.90%)
• Nonacademic	01 (4.54%)
• General Hospital	01 (4.54%)
Type of organization	
• Nongovernment	20 (90.90%)
• Government	01 (4.54%)
• Mixed	01 (4.54%)
Whether the hospital is ELSO (extracorporeal life support organization) registered center?	
• Yes	14 (63.63%)
• No	08 (36.37%)
Whether the hospital is ESOI (ECMO Society of India) registered center?	
• Yes	15 (68.18%)
• No	07 (31.82%)
Type of ICU	
• Interdisciplinary	02 (9.10%)
• Multidisciplinary	20 (90.90%)
Total Number of ECMO cases done (per year) (Before COVID)	
• <10	13 (59.09%)
• 11–29	05 (22.72%)
• >30	04 (18.18%)

Technical Challenges

Limited availability of ECMO machines was the most common technical challenge encountered followed by the cost of ECMO therapy and limited availability of cannulas and/or circuits. Limited oxygen supply was the least common challenge faced by the hospitals. The trend was the same in both waves as shown in Figure 2.

Operational Challenges

The trends of operational challenges were different in the first and the second waves as seen in Figure 3. During the first wave, the resistance from staff to work was the most common challenge faced, followed by the risk of getting cross-infection with the team members, managing the patients with PPE kits, limited staffing, difficult communication with PPE kits, high workload, difficulty in transporting patients, and interventions from the regulatory authority in decreasing order. Hospital administrative issues (allocating multiple responsibilities, meetings, maintaining coordination between different departments, etc.) were the least common challenges faced in the first wave.

But during the second wave, different trend of challenges was observed. Limited staffing and the high workload was the most common operational challenge faced, followed by difficulty in transporting the patients, risk of getting cross-infection to the team members, interventions from regulatory authorities, and hospital administrative issues in decreasing order. The resistance from the staff to work and managing patients with PPE kits was the least challenges.

Interference from Regulatory Authorities

In both waves, there was an operational challenge of interference from local regulatory authorities for managing ECMO in COVID-19 patients. Fifteen (68.18%) hospitals have faced interstate restrictive policies for crossing the state borders, 13 (59.09%) had financial interference, and 11 (50.00%) hospitals had transport interference from regulatory authority.

Challenges Faced While Transporting COVID-19 Patients for ECMO

Transporting COVID-19 patients for ECMO was also a common challenge faced in both waves. The cost of transport by 13 (59.09%) was the most common challenge faced. Other challenges while transporting are given in Table 2.

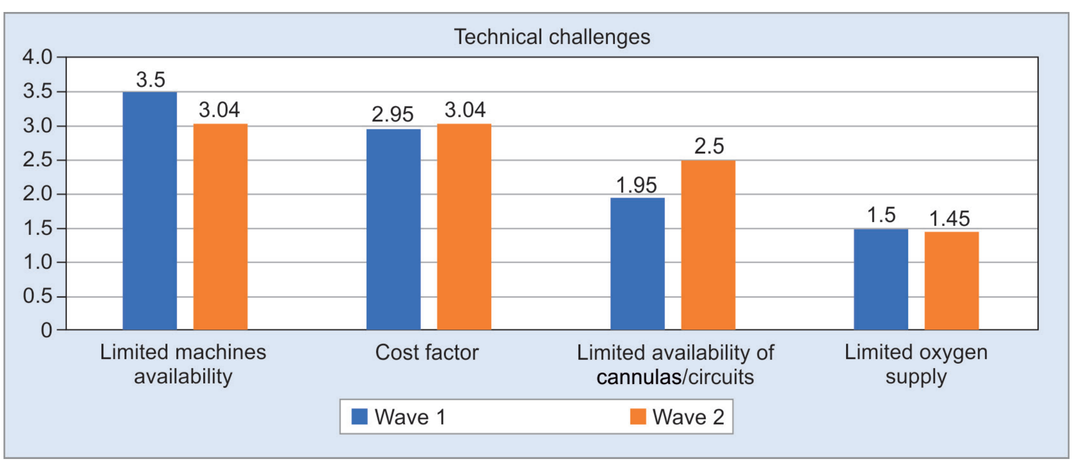

Fig. 2: Technical challenges faced in the first and second waves (Numbers above each bar indicate weighted average rank)

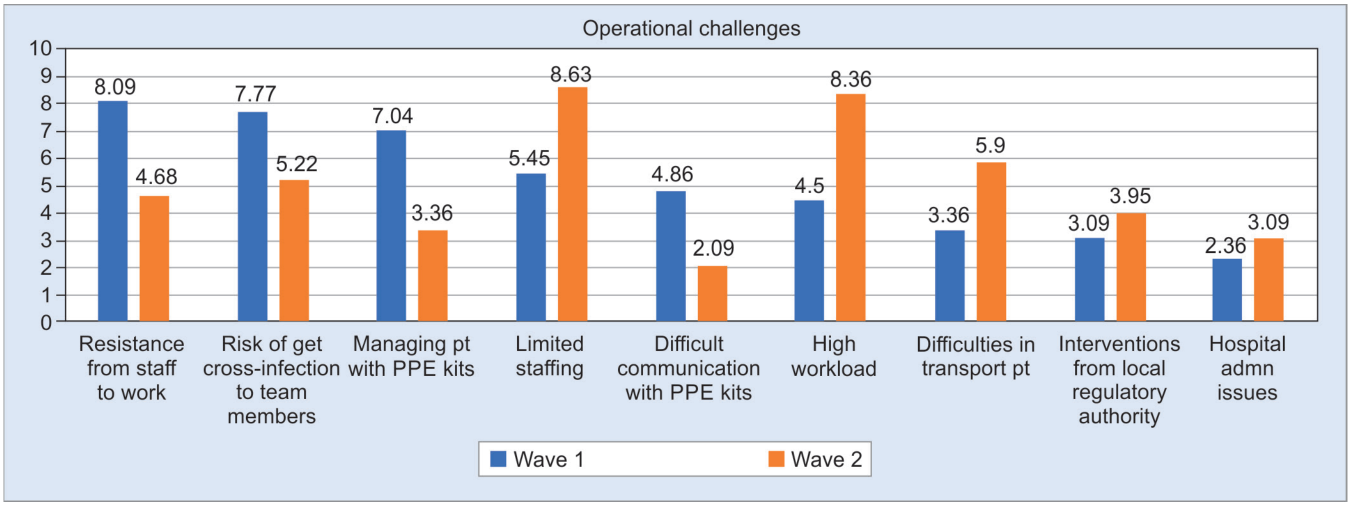

Fig. 3: Operational challenges faced during the first and the second wave (Numbers above each bar indicate weighted average rank)

Table 2: Challenges faced while transporting COVID-19 patients for ECMO

	N (%)
Cost of transport	13 (59.09%)
Availability of air ambulance	12 (54.54%)
Interstate/Intrastate restrictions	11 (50.00%)
Resistance from reference center	9 (40.90%)
Safety of transport team from COVID-19 cross-infection	6 (27.27%)
Availability of ground ambulance	5 (22.72%)

Clinical Challenges

In the first wave, difficulty in counseling and hesitancy among medical colleagues were the most serious clinical challenges, followed by lack of public awareness about ECMO, limited evidence of ECMO treatment, complications of ECMO as other challenges in decreasing order. Difficult cannulation, poor outcome, and thromboembolic phenomenon were the less common challenges faced.

The second wave has different clinical challenges. Complications during ECMO were the most serious challenge faced followed by thromboembolic phenomenon, difficulty in counseling, and lack of public awareness as other challenges in decreasing order. Limited local evidence of ECMO treatment and difficult cannulation were the less common challenges faced during the second wave (Fig. 4).

Complications During ECMO

The trends of complications during ECMO remained more or less the same in the first and second waves (Fig. 5). Hospital-acquired infections were the most common challenging complication followed by seizures, CNS bleeding and/or infarcts, hemolysis, hemorrhages from other sites in decreasing order. Pump failure, circuit changes, or clots in circuits were less common complications observed.

ECLS Providers Opinion on ECMO in COVID-19

In the last part of the basic survey, eight questions were designed to investigate participant's opinions on certain statements about ECMO and COVID-19, measured in percentage of agreement. Participants agreed to 84% on the statement that managing ECMO on COVID-19 was more challenging in the first wave than non-COVID-19 patients but agreed to 89% on COVID-19 patients were longer on ECMO compared with other influenza patients. About 81% agreement on the circuit/circuit components in COVID-19 patients was required more often than non-COVID-19 patients, but 65% agreement on disturbed coagulation in COVID-19 patients makes ECMO more difficult than non-COVID-19 patients on ECMO. Regarding preparedness on ECMO for COVID-19 patients in the future, there was 80% agreement and more utilization of ECMO for COVID-19 in the future, agreement was 90% (Table 3).

Discussion

The COVID-19 pandemic was one of its kind which is seen once in a century when almost the entire world was affected by the severity of disease spread. It has led to significant mortality and morbidity in many resourceful countries also. The magnanimity of its involvement and the unpreparedness of the world to face such a situation has caused panic state, fear, and also resource limitations. This is compounded by the lockdown and no cross-border movement. Indian scenario was worse due to limited ECMO experience in the pre-COVID-19 arena (nearly 60% of the hospitals were low-volume centers), a limited number of centers practicing ECMO pre-COVID-19 era and the availability of ECMO equipment and none of the units were manufacturing disposables in India. This study was done with the aim to find out what are the problems faced and then to draw a conclusion and recommendations for future pandemics.

Data collected from this survey are from 22 tertiary care hospitals with most of them having multidisciplinary ICUs. Looking at the geographical situation, the participant hospitals were representing major centers from 11 states of India which were also offering ECMO services to the nearby 4–5 states and almost more than 65% of the Indian population. This survey thus roughly represents the overall experience of ECMO management of COVID-19 patients in India. Out of these hospitals, only 20% of the hospitals were high-volume centers (more than 30 cases/year), while nearly 60% were low-volume centers (less than 10 cases/year) in the pre-COVID-19 era. This indicates that ECMO services were underutilized in the pre-COVID era in India and led to the

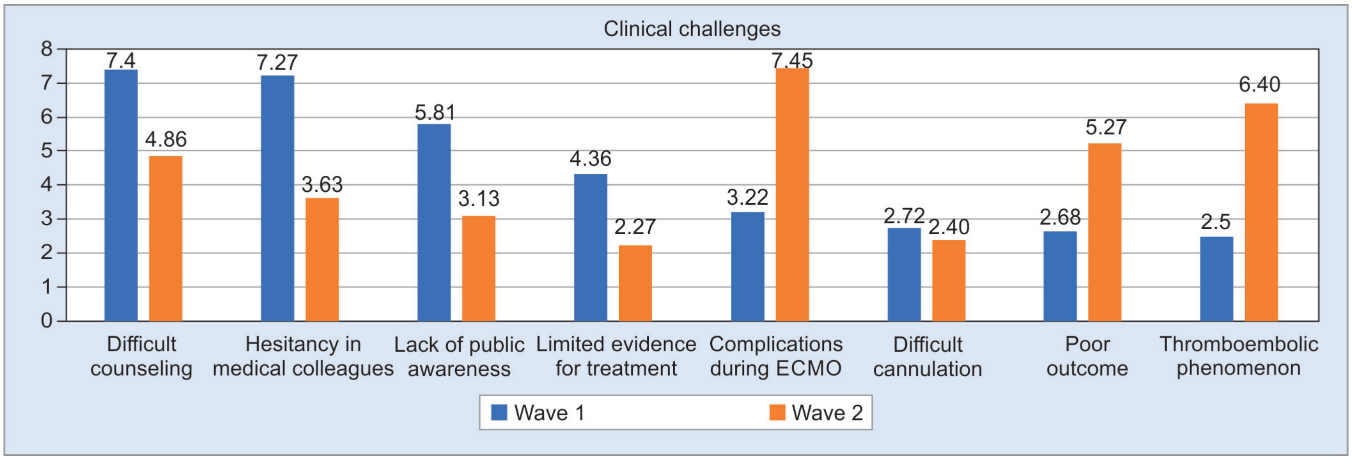

Fig. 4: Clinical challenges faced during the first and the second waves (Numbers above each bar indicate weighted average rank)

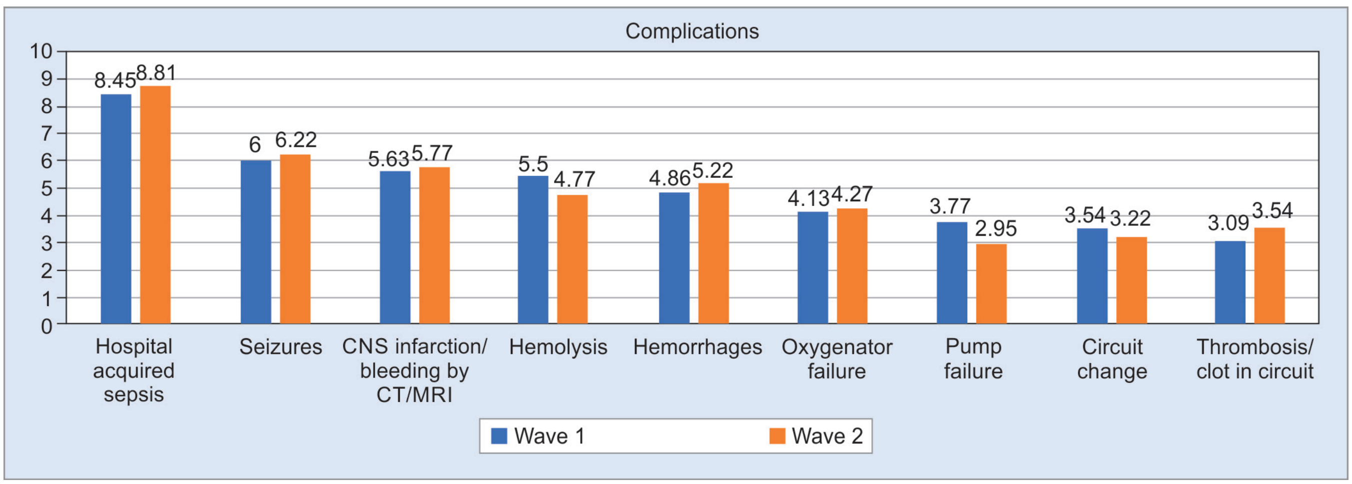

Fig. 5: Complications during ECMO (Numbers above each bar indicate weighed average rank)

Table 3: ECLS provider's opinion on ECMO in COVID-19

Participant's opinion	*Percentage of agreement*
Managing ECMO on COVID-19 was more challenging in the first wave than non-COVID-19 patients?	84
Overall, COVID-19 patients were longer on ECMO compared with other influenza patients	89
Overall, the circuit/circuit components in COVID-19 patients were required more often than non-COVID-19 patients	81
Overall, disturbed coagulation in COVID-19 patients makes ECMO more difficult than non-COVID-19 patients on ECMO	65
At our hospital, we were now fully prepared for many COVID-19 ECMO patients	80
In the next wave of COVID-19 I will use more ECMO as we are more prepared	90

limited exposure of ECMO management in respondent hospitals also. A retrospective, multicentered international, observational study published by Rabie et al.[13] also has a similar picture, out of 19 centers, 14 were established centers and 5 were new centers. Out of 14, only 4 centers were high-volume centers (managing more than 20 ECMO patients/year) pre COVID era.

Challenges Faced

1. Technical Challenges

During the COVID-19 pandemic, there was a significant mismatch between the demand and supply of oxygen, drugs, and ventilators for routine ICU patients, and because of the surge of infectivity, the situation became worst. When the option of ECMO was considered for these sick patients, the challenges were immense as very limited centers were offering ECMO services to non-COVID-19 patients, a sudden peak of patients qualifying the need for ECMO in COVID, and the need for ECMO has increased substantially.

When participants were asked to grade the severity of the above technical problems, limited machine availability was responded to as the most serious, followed by the cost of therapy and limited availability of circuits/cannulas. The limited availability of machines was the most serious challenge. The major problem of limited availability of ECMO machines and circuits is that most of these are manufactured outside India and because of the global lockdown, procuring via transport was a major hurdle. Sudden high demand and limited supply from overseas countries during global lockdown may be the reason in the first wave, and an exponential increase in patients for ECMO in the second wave again made scarcity of availability in the second wave.

The cost of ECMO therapy remained a serious challenge in both waves. High cost of disposables, higher recurring or maintenance changes per day, increased length of ICU stays, need for higher antibiotics and blood products and involvement of multiple professionals were the main factors responsible for high cost. Even in non-COVID times, the cost factor was the major hinderance in the development of the ECMO program in India.[11] In COVID-19 pandemic, the cost factor become more serious, and many of the family members were admitted to ICUs at the same time, high burden of simultaneous medical expenses at the same time was not allowing families to opt for very high-cost ECMO therapy.

Limited oxygen supply was found to be a less serious technical challenge. As the pandemic went worst, oxygen supply became the major limiting factor for all ICUs and naturally for ECMO too. The fact that the majority of these centers were tertiary centers and had their own in-house oxygen production units, can explain oxygen supply was not a major constraint for them.

2. Operational Challenges

A total of nine operational challenges were asked to grade severity in the survey. These were staff-related (limited availability of staff, resistance from staff to work, high workload), PPE kit-related (discomfort to work, difficult communication), transport-related, and other administrative-related challenges. The last two challenges were probed in greater detail.

During the first wave, the challenges were more related to fear, panic, and lack of experience scenario in managing such a highly communicable disease. This has led to unwillingness from the staff to work in critical care unit and more for managing ECMO patients. This resistance was a probable mixture of many components, such as the risk of getting cross-infection, risk of higher exposure due to the high demand of monitoring and nursing care required for these patients, and negative mind setup besides apprehension as many of their colleagues and relatives have lost lives during COVID-19 management.

The other challenges were the risk of getting cross-infection with the team members, managing the patients with PPE kits, limited staffing, difficult communication with PPE kits, high workload, and difficulty in transporting patients and interventions from regulatory authorities in decreasing order. Hospital administrative issue was the least common challenge faced in the first wave.

Managing ECMO patients even for non-COVID-19 indications is a high skill demanding job.[14] Managing circuits, pump, lines, and ventilators require the involvement of at least 2–3 nursing staff with respiratory assistants. The task became more difficult wearing a PPE kit for looking after COVID-19 patients. Discomfort, suffocation, sweating, fog on goggles, and difficult communication through the kit were extremely challenging.

Administrative issues like interference at the level of local hospital administration and local regulatory authority and transport issues were less serious challenges in the first wave. This can be explained by limited ECMO experience in the first wave for all, as majority of the ECMOs were initiated at the participant tertiary centers only.

But during the second wave, different trend of challenges was observed. The fear and panic factors have settled and staff even got acclimatized for working with PPE kits. Also, the overall awareness and experience about COVID-19 ECMOs have increased, and positive reports about the survival rate from published literature and data from different centers in India have increased the demand for ECMO. Secondly, the number of critically ill patients was more, and many of them were younger patients. These two factors caused huge demand for ECMO all across the country with limited centers practicing ECMO, which led to a shortage of staff. Dave et al. observed similar challenges in their study.[9]

Another major problem faced was transporting the patients, as there were huge demand and limited ECMO centers, many patients were retrieved from the nearby states and from the two-tier cities. Also, there were many patients on prolonged ECMO who were transported to other institutes for probable lung transplants. These transports for lung transplants were usually long-distance transport and most of them required airlifting. In most cases, transporting patients on ECMO for a very long distance was a herculean task due to the limited availability of air ambulance services in India and also the cost of transport itself. Inter and intrastate restrictions forced by local regulatory authorities made transport more challenging. Wearing PPE kits, limited space in ambulances made the job of ambulance staff highly challenging. Sen et al., in 2021,[15] shared the practical considerations and the outcome of interfacility ECMO transfer of COVID-19 patients from the Mayo Clinic. They concluded that good collaboration with transport partners is of paramount importance during ECMO transport. However, the creation of a checklist, tabletop exercise and necessary steps of donning and doffing PPE and transport logistics has reduced staff exposure. Role clarity, situational awareness, and backup behavior were the other key factors for event-free transfers.

The other challenges like the risk of getting cross-infection with the team members, resistance from the staff to work, interventions from regulatory authorities, managing patients with PPE kits, and hospital administrative issues were noted in decreasing order.

In both waves, there was an operational challenge of interference from local regulatory authorities for managing ECMO in COVID-19 patients. Inter- and interstate restriction was a serious challenge faced due to regulatory authorities which have reflected in the transport of COVID-19 patients for ECMO or with ECMO. There were more restrictions during the first wave compared with the second wave. Many permissions were required from local authorities to overcome interstate restrictions and for transport also. Financial interference was another serious challenge faced because of the ceiling of charges by different state governments through local regulatory authorities.

3. Clinical Challenges

In the first wave clinical challenges were again like lack of awareness and lack of statistics supporting ECMO leading to difficulty in counseling and hesitancy among medical colleagues to refer for a costly therapy like ECMO. This was compounded by Lack of public awareness about ECMO. The initial data published from China during the first wave have shown that the mortality of severe COVID-19 patients treated with ECMO was relatively high ranging from 57.1 to 100%, although the sample size of all these studies was very small,[6,16,17] Complications of ECMO and thromboembolic phenomenon were the other challenges seen in decreasing order. Difficult cannulation was the least common challenge faced during both the first and second waves.

Before the second wave, the large sample size data on patients with severe COVID with ECMO found 90 days mortality of 39%,[7] which has changed the outlook of intensivists from India toward ECMO in COVID-19. This fact has reflected in the increased turnover of ECMO in the second wave, and hesitancy was not the major concern after that time. So, during the second wave, difficulty in counseling, lack of public awareness, and limited evidence of ECMO treatment were fewer of the challenges faced. The commonest clinical challenges faced were the common complications during ECMO run such as thromboembolic phenomenon. The other challenge faced was the poor outcome of ECMO in the second wave compared with the first wave. Also, the number of ECMO days was more, and many required prolonged ECMO. To some extent, the poor outcome and prolonged duration of ECMO were related to the delayed initiation of ECMO. Awareness among the medical fraternity and public is essential to initiate ECMO at the right time. There is increased awareness about ECMO among physicians and Intensivists after H1N1 epidemic in 2009, but still a long way to go with respect to increasing awareness among the Indian public.[11] because of the limited awareness of ECMO in the Indian population, counseling them about ECMO and its consequences still remains a challenge in ECMOs for COVID as well as non-COVID-19 reasons.

In 2021, Shah et al.,[9] in their experience of 40 COVID-19 patients on VV-ECMO, have reported lessons learned from COVID-19 about ECMO planning and clinical management. They found the safety of the ECMO team was of paramount importance during the cannulation of COVID-19 patients. They stated that establishing consensus criteria for COVID-19 ECMO support should be based on institutional and/or state-level discussion. They also stated that the prothrombotic state in patients and the potential subsequent coagulopathy from ECMO were challenging to manage. A similar challenge to thromboembolic phenomenon was faced by many hospitals in the second wave of our study.

Lawrence et al.[18] conducted a survey for challenges in initiating ECMO for patients with COVID-19. They found that cannulating COVID-19 patients for ECMO was more challenging with rapid decompensation during cannulation and dislodgment or migration of the cannula after repositioning the patient on ECMO. In the current survey, cannulation was not found to be a serious challenge, both in the first as well as in the second wave.

4. Complications during ECMO

Complications during ECMO were the important clinical challenges faced in both waves and were more or less the same. Hospital-acquired infection remained a major challenge. Secondary bacterial and fungal infections in patients on prolonged ventilators, ECMO and with a greater number of ICU days were common in both COVID and non-COVID-19 era. Serious challenges of hospital-acquired infection in ECMO of COVID-19 patients can be attributed to multiple factors like longer duration of ECMO therapy, higher use of glucocorticoids, anti-cytokines medicine before ECMO, limited staff, and high workload which decreases the quality of care.

In their study of multicentric retrospective cohort of 31 ECMO in COVID-19 patients, Xuyan Li[19] found similar findings to our study with the majority (71%) of patients had the hospital-acquired infection. Hemorrhages (gastrointestinal and tracheostomy wound bleeding) were observed in 29% and thrombosis of circuit in 13% of cases.

Failure of the components of circuit either pump or oxygenator requiring a change of components or circuit was another problem faced but it came lower down in the list. The change of circuits or components required was slightly more during COVID era as compared with non-COVID-19 era. This was also seen in international statistics. In 2020, Barbaro et al.,[7] in an international cohort study of the ELSO registry of 1035 COVID-19 patients who had received ECMO, found circuit change as the most common complication in 15% of cases, followed by membrane lung failure in 8% of cases, CNS hemorrhage in 6% and hemolysis in 5% of cases. The ELSO registry, till May 2022,[8] reported that 21% of cases had oxygenator failure as the most common complication, while 12% has circuit change and 7% had CNS hemorrhage as other complications. Seizures (1%), CNS infarct (2%), and pump failure (3%) were minor complications.

Participants of the survey have almost 80–90% conscience that managing COVID ECMO was more difficult, ECMO was prolonged (especially in the second wave), more circuit-related issues as compared with non-COVID-19 patients. Sulakshana et al. (2023),[20] in their study also have similar findings of prolonged ECMO run during COVID compared with non-COVID ECMO patients. Our results have an overall percentage of agreement that is comparable with the results of Mang et al.[21] study. Disturbed coagulation resulting in increasing difficulty in ECMO management was the point of less agreement in both studies.

Also, the participants of the survey after having good exposure were found to be more confident and prepared in managing ECMO in further pandemics.

Conclusions

Managing ECMO in COVID-19 patients was found to be a challenging task. In the first wave, the challenges were related to a lack of awareness, fear, and resistance from the workforce along with inadequate data to support ECMO use. While in the second wave, the challenges were related to more clinical issues and outcome-oriented. Exchanging pre-ECMO strategies across usual referral centers and increased collaboration between ECMO centers is warranted to improve the outcome of these patients and even in future pandemics.

Recommendations

Management of ECMO in COVID-19 patients was a big lesson to learn and has highlighted key elements of emergency preparedness. These should not only include the reserves of personal protective equipment, intensive care unit (ICU) devices, consumables, and pharmaceuticals, but also include effective supply chains and efficient utilization protocols along with good education of therapies and improving awareness of the public as well as the treating personnel. While planning to effectively face any pandemic, it is recommended to have an online national registry of cases, availability of beds and equipment along with the outcome data with different therapies and their role. This can be achieved with the active involvement of medical councils, and critical care societies, such as the Indian Society of Critical Care Medicine (ISCCM), the Indian Academy of Pediatrics (IAP), the ECMO Society of India (ESOI), and the international societies. There should be guidelines/recommendations, protocols, or conscience statements from all the concerned medical bodies and societies. We need to improve interstate restriction practices during pandemics like COVID. In future, the availability of supportive care during follow-up should be evaluated.

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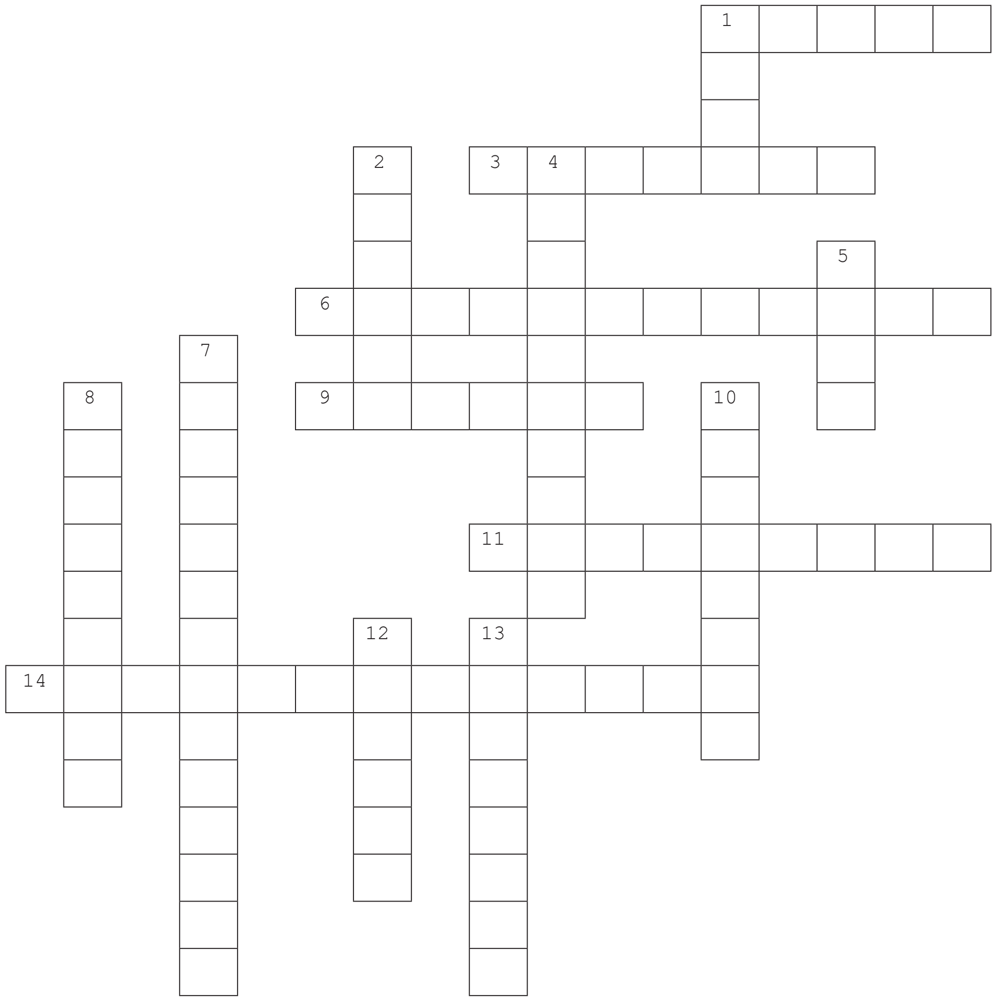
CROSSWORD



ACROSS

1 - Gas flow in an ECMO circuit is referred to as what (4)

3 - Thromboelastography was developed by (7)

6 - Which form of ECMO involves a complete lung bypass? (12)

9 - Factor X is also called as (6)

11 - Differential oxygen saturation is observed between the upper and lower parts of the body in patients on VA ECMO (9)

14 - Condition in VV ECMO in which reinfused oxygenated blood is withdrawn through the drainage cannula without passing through the systemic circulation (13)

DOWN

1 - Scoring for prognostication of patients on VA ECMO (4)

2 - Trial showing improved neurological outcomes in OHCA patients on ECPR (6)

4 - Anticoagulation of choice in ECMO patients developing Heparin induced thrombocytopenia (10)

5 - Immune-mediated coagulation side effect of heparin therapy characterized by thrombocytopenia and by a paradoxical prothrombotic state (4)

7 - Principle of CO monitoring by pulmonary artery catheter (14)

8 - Echocardiography sign of massive pulmonary embolism (9)

10 - Most common complication on all types of ECMO (8)

12 - Lung injury score in severe ARDS (6)

13 - Father of ECMO (8)

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RESEARCH ARTICLE

Venoarterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock in Aluminum Phosphide Toxicity

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Abstract

Introduction: Aluminum phosphide (ALP) toxicity causes high mortality, often implicated for suicidal purposes since it has no specific antidote. Release of phosphine upon ingestion leads to refractory cardiogenic shock and multiorgan failure, which are the highest predictors of mortality. Compared with conventional treatment, extracorporeal membrane oxygenation (ECMO) plays a significant role in such unsolved problems.

Materials and methods: Retrospective study of 9 cases from 2021 to 2022 with an undetermined number of tablets consumed. On examination, all patients had arrhythmias, hypotension, ejection fraction (EF 10–20%), and severe metabolic acidosis. We divided our patients into groups A and B based on the time taken for initiating ECMO. In group A (4 patients) VA-ECMO was initiated within 6 hours. Group B (5 patients) patients had a delay in arrival and the late decision worsened their condition and ECMO was initiated after 8 hours of ingestion.

Conclusion: Early initiation of ECMO seems to improve survival rates in ALP toxicity.

Keywords: Aluminum phosphide, Cardiogenic shock, Extracorporeal membrane oxygenation, Mortality, Toxicity.

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Introduction

Aluminum phosphide (ALP) is often implicated in suicidal purposes and has high mortality of 80–100%. Release of phosphine upon ingestion leads to refractory cardiogenic shock and end up with multiorgan failure.[1] Poor outcome is largely due to delay in arrival, diagnosis, comorbidities, doubtfulness in the minds of clinicians, and patient relations for decision-making.[2,3] Our single-center retrospective study found that conventional treatment for ALP poisoning can be supported by ECMO in earlier toxic periods, which may reduce mortality.

Materials and Methods

A Retrospective study of 9 cases from 2021 to 2022 with no known psychiatric illness admitted to our emergency department after alleged ingestion of ALP with suicidal intent. The number of tablets consumed, the time interval between arrival and ECMO initiation, total duration, the severity of preexisting comorbidities, and their complications were analyzed. On comparative time interval between earlier ECMO initiation, cohorts were divided into two groups respectively (Table 1).

Observation

On examination, all patients had mean arterial pressure (MAP <60 mm Hg), heart rate >110 b/min, saturation ≤95%, ECG of the patients shows ventricular arrhythmia and fibrillation, echocardiography revealed EF 10–15% with global hypokinesia. Arterial blood gas analysis showed severe metabolic acidosis with PH ≤7.0 and lactate ≥80 mg/dL. Inotropic supports like adrenaline, noradrenaline, and vasopressin were started along with magnesium sulfate, sodium bicarbonate, potassium chloride, and xylocard infusion. Upon early resuscitation in group A, VA-ECMO was initiated within 6 hours of ingestion. Femoral artery and vein were percutaneously cannulated and an 8Fr sheath was placed for distal limb perfusion. Inotropes were titrated for maintaining target pressure. Bedside echo and doppler scan were done in alternate hour for monitoring EF and peripheral blood flow. Three patients developed acute kidney injury (AKI) due to toxic severity and required sustained low-efficiency dialysis (SLED) (Fig. 1) with or without fluid removal based on volume status and negative pressure of the access line. One patient had undergone a left heart vent via right superior pulmonary vein (RSPV) for myocardial stunning (Table 2). Despite the intensive treatment, one patient died because of irreversible brainstem injury.

In group B, delay in arrival and late decision worsened the condition and VA-ECMO was initiated after 8 hours of ingestion. Most of them required intermittent cardioversion (upto 40 hours) during ECMO support, In this, one patient was ECMO retrieval and required LV vent for myocardial distension. Arrhythmia

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Table 1: HTN – hypertension, DM – diabetes mellitus, AKI-acute kidney injury

	Group A (n = 4)	*Group B (n = 5)*
Tablets	Fatal dose	Fatal dose
Age	29–45 years	35–60 years
Gender	Male	Male
ECMO initiation	Within 6 hours	>8 hours
Suspected mortality	60%	80%
EF	10–20%	10–15%
Past history	HTN	HTN, DM, AKI

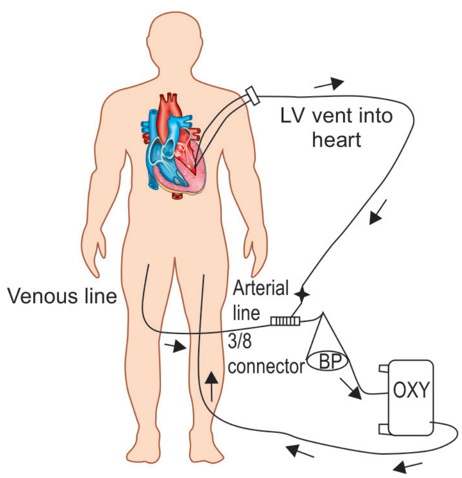

Fig. 1: LV vent diagrammatic representation
BP, centrifugal pump; OXY, oxygenator

Table 2: Special intervention

	Group A	*Group B*
LV vent	1 patient	1 patient
SLED	3 patients	4 patients
Retrieval	–	1 patient

and ventricular fibrillation settled gradually and decannulated within 3 days, and discharged at 28th day of his admission. Four patients required SLED for renal failure (Table 2) but succumbed subsequently. ECMO was discontinued in one patient on insistence of family after poor prognosis and critical condition was explained. Multiple complications arose in both groups and all were treated as per protocol. After 6–12 months of follow-up range all the survivors of both groups did well with normal organ function.

Discussion

Aluminum phosphide is the most common poison in India owing to easy availability and cheaper cost. Phosphine is a protoplasmic poison, which disrupts mitochondrial oxidative phosphorylation, inhibit cytochrome C oxidase, is lethal to cell enzymes and leads to cellular hypoxia.[4,6] The clear mechanism is multifactorial and includes myocardial damage, peripheral vasodilation, fluid loss, cellular energy, or cytokine-mediated dysfunction.[1,5] Since there is no specific antidote, treatment was based on general poison management like early resuscitation, gastric lavage with coconut oil, fluid administration, and inotropic supports to maintain normal hemodynamics[7] (Table 3).

Table 3: Target maintenance in ECMO

	Target
Pulse pressure	>10 mm Hg
MAP	>60 mm Hg
Cerebral saturation	Not less than 50%

In case of refractory cardiogenic shock VA-ECMO was initiated with intent of avoiding organ damage and providing adequate time for heart to rest and recover.[8,9] All the patients were under strict monitoring including near-infrared spectroscopy (NIRS) and supports were titrated accordingly. Phosphine causes damage to renal tubules, parenchymal cells which result in renal dysfunction.[10] Most patients developed oliguria (output <5 mL/hour) and required SLED with or without fluid removal for several days even after decannulation till the toxic metabolites are excreted. One patient from each group had severe LV distension with EF <15% multidisciplinary team inputs were obtained and patient shifted to OT immediately for insertion of LV vent, 16Fr vent catheter was placed through RSPV and an hourly drain was noted. Within a few days, left ventricular function started improving with EF >25% and normal aortic valve opening, then gradually weaned from ECMO with minimal inotropic support and decannulated uneventfully within 5 days, and finally discharged with normal organ function.[11] Despite intensive treatment, multiple complications aroused, and one patient from group A, underwent fasciotomy for compartment syndrome and succumbed due to irreversible shock and septicemia. Three patients of group B with preexisting comorbidities further exacerbated the toxicity and died because of severe lung consolidation and septicemia (Table 4). This led us to believe that earlier initiation of ECMO might mitigate cardiovascular and other organ adverse effects, thereby assist in early recovery and favorable survival rates in this highly mortal condition.

Limitations

This is a single-center retrospective study and has a small sample size. Thus, it is likely to have biased outcome. Patients who were not reverted even after receiving multiple shock at initial management and financially not affordable for further treatment and ECMO support were excluded in this study. Further research with large number of patients is required to validate this result.

Conclusion

There are no definitive guidelines indicating appropriate timing for ECMO initiation in poisoning cases. Decision-making depends upon the family's willingness and the clinical judgement of the multidisciplinary team concerment.

It is important to understand that ECMO should be initiated before irreversible end organ damage occurs. Earlier ECMO as bridge to recovery, a timely intervention for the refractory cardiogenic shock seems to increase survival rate in aluminum phosphide toxicity cases.

Table 4: Comparison of outcome between groups

	Group A		*Group B*	
ECMO initiation	<6 hours		>8 hours	
Mortality	Upto 70%		>80%	
Total ECMO hours	≤80 hours		125 hours	
Comorbidities	30%		30%	
ICU stay	<10 days		16 days	
Hospital stay	18 days		28 days	
Discharge alive	3 patients		1 patient	
Survival rate	80%		30%	
Post-ECMO complications	–		Bilateral watershed infarcts – left hemiparesis	
	Admission	*Discharge*	*Admission*	*Discharge*
EF	10–20%	40%	10–15%	>35%
Arterial blood gas and electrolytes	HCO_3^-: <15	HCO_3^-: ≥25	HCO_3^-: <10	HCO_3^-: 23
	lactate: >75	Lactate: <17	Lactate: >90	Lactate: 18
	K^+: upto 5.5	K^+: upto 4	K^+: >5.0	K^+: 3.9
	Cr:>1.5	Cr: 1.3	Cr: >2.0	Cr: 1.5

Cr, creatinine (mg/dL); EF, ejection fraction; HCO_3^-; Lactate (mg/dL); K^+, Potassium (mmol/L); Sodium bicarbonate (mmol/L)

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EXPERT VIEW/REVIEW PAPER

Evolution of Extracorporeal Membrane Oxygenation

Suneel Kumar Pooboni

Keywords: Brunkhonencko, Cardiopulmonary bypass, ECMO, Evolution, History, John Gibbon, Walton lillehei.
Indian Journal of ECMO (2023): 10.5005/jaypee-journals-11011-0012

In continuation of Part 1

Part 2: Evolution of Concepts of Extracorporeal Membrane Oxygenation

To understand the basic concepts of Extracorporeal Membrane Oxygenation (ECMO), the true foundation for the anatomic, physiological, and surgical understanding and adaptation should be established. An open mind with creative thinking can help in finding the way as these new ways of treating human disease are innovations. It's important to realize that this transformation did not happen overnight. Generations of free thinkers and researchers worked together over the past four centuries leading to the perfection of a new technique, Extracorporeal membrane oxygenation. Although we credit a few clinicians for the discovery of a new process (innovation), it is important to recognize the hard work of their predecessors in helping them to build their hypothesis and test it. Thinking in novel ways with a free mind and developing new ideas about the utilization of artificial oxygenation for providing gas exchange and building devices for mechanical circulatory support was crucial for understanding the growth of this segment of the medical field during human civilization.

Extracorporeal oxygenators are mechanical devices that take over the function of gas exchange in case of lung or heart and lung failure. On reviewing the medical history, Robert Hooke (1635–1703) seems to be the first person to record his thoughts about the process.

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Richard et al, in their article, quoted Robert Hooke's statement as follows: "I shall shortly further try, whether the suffering the Blood to circulate through a vessel, so as it may be openly exposed to fresh air, will not suffice for the life of an Animal; and make some other Experiments, which, I hope, will thoroughly discover the Genuine use of Respiration; and afterwards consider what benefit this may be to Mankind."[21,22] The thought process behind this clearly implies the search for a mechanism to achieve gas exchange.

I am briefly summarizing the contributions of researchers/Physicians from 1667 to 1935 in the following table. This period is illustrating the genesis of concepts and animal experiments

Year	*Name*	*Contribution*
1667	M Hooke	Oxygenation of blood in a vessel by exposing it to fresh air: Gas exchange.
1812	César Julien Jean Le Gallois (1770–1814)	By continuously injecting arterial blood into the heart of animals even after decapitation, keeps the function active.
1828	James Phillips Kay	In the pursuit of initial perfusion experiments, this surgeon from Edinburgh injected the blood drawn from carotid arteries into the abdominal aorta of a rabbit while observing muscular contractions. He tried to differentiate the favorable nature of the oxygenated blood from the venous blood.
1849	Carl Eduard Loebell	Performed isolated perfusion of an organ, kidney.
1858	Eduard Brown–Séquard	He made early attempts at artificial oxygenation by shaking the venous blood with oxygen and injecting this blood into the hands of decapitated criminals. He was able to induce reflexes on stimulation of these perfused hands.
1862	Ernst Bidder	Ernst devised a model of perfusion equipment. Although it was primitive, it explains the thought processes about building artificial perfusion devices.
1867	Alexander Schmidt	He conducted further research on mixing venous blood with oxygen. He also established approaches for measuring the proportion of oxygen and carbon dioxide content in venous and arterial blood.

1868	Ludwig and Schmidt	He did research on conducting perfusion experiments with muscle tissue in canine species.
1876	Bunge and Schmiedeberg	His experiments involved attempts at artificial oxygenation by mixing dark venous blood with air until the color changed to bright red suggesting gas exchange.
1882	Waldemar von Schröder	His research was focused on the perfusion of individual organs. He built apparatus for oxygenating venous blood on mixing with air. These experiments paved the way for developing the first form of bubble oxygenators.
1883	M Abeles	He used von Schröder's apparatus but experimented with oxygen instead of air.
1885	Max von Frey and Max Gruber	He demonstrated the first closed artificial circulation system. This marks the beginning of the development of later heart–lung machines.
1890, 1895, 1923	Jacobj	Closed circulatory systems were constructed for experimental organ perfusion. In the next four decades from 1890 to 1932, researchers improved the design of artificial devices for supporting circulation. Some of the precise details signifying their contribution to the construction of these devices have been mentioned below.
1903	Brodie	
1905	Embley and Martin	
1908	Mandel	
1910	Friedmann	
1910	Neubauer and Groß	
1910	Hooker	
1915	Richards and Drinker	
1920	von Skramlik 1922 Dixon	
1932	Bauer, Dale, Poulsson, and Richards	
1903	TG Brodie	He endeavored in building a device that would mimic the ideal equipment for perfusing the organs. He developed an interchanging pump and was able to achieve "aeration" by mixing defibrinated blood and air in the pump chamber.
1907	Johannes Bock	First electrically powered syringe pumps
1908	O Zeller	Established the fact that a lack of red blood cells, resulting in hypoxia, damages the brain and the central nervous organs.
1913	Fröhlich	First demonstrated the usage of an electrically driven rotary pump for prolonged perfusion of organs.
1915	Richards and Drinker	Developed equipment for the perfusion of isolated organs with defibrinated or anticoagulated blood. They used hirudin as an anticoagulant.
1916	Jay McLean	Discovery of heparin.
1926	A Bornstein	Conducted experiments demonstrating gas exchange by using a film across a large surface for achieving oxygenation.
1927	Brukhonenko	Reported experiments with artificial circulation.
1935	Carrel and Lindbergh	Developed a model which helped in maintaining a pulsating circulation with serum, blood, and growth-stimulating substances. This system demonstrated the ability of an organ to live extracorporally (outside the body).

supporting artificial gas exchange, supporting individual organs, supporting circulation, and gas exchange when the heart has stopped.

History of Extracorporeal Circulation: The Conceptional and Developmental Period[23]

Brukhonenko from Russia was touched by the casualties he witnessed in the World War I (Fig. 1). Thinking about solutions for saving lives at the time of mass casualties, he considered ways of supporting severe bleeding while the surgeries are being done. He worked on research in supporting artificial circulation on isolated heads and the entire body as well.[24] Along with S. Tchetchuline, he has been working on shaping an apparatus called the "autojector" (Fig. 2) since 1926; aiding artificial circulation. The design of autojector included two main components: two mechanical diaphragm pumps with a valve system and rhythmically ventilated lungs of an animal, which served as oxygenators (as shown in the above picture).

One pump helped in moving deoxygenated blood *via* the lungs while the second pump was used for pumping blood through the systemic circulation. In the initial run, they supported the circulation for a couple of hours. After conducting further trials, Brukhonenko documented that it should be possible to take over the function of a temporarily stopped heart for a few hours [such as for helping cardiopulmonary bypass during cardiac surgery or venoarterial (VA) ECMO].[25] Brukhonenko patented his technology in 1928, in Russia and in 1929 in Germany. In 1931, he also experimented with deep hypothermic cardiac arrest by bringing the temperature of the dogs to 3°C. By using autojector, Nikolai Terebinski, a pioneer of open valve operation operated for the first time on the valves of the open heart in animal experiments between 1926 and 1937.[26] He performed more than 250 open valve operations, which were the first of their kind. Surgical techniques for creating and correcting tricuspid and mitral valve stenosis and insufficiency-related lesions were invented by Terebinski, and are in use even today.[26] In 1936, Brukhonenko replaced the donor lung of the autojector with a bubble oxygenator, which was developed by him. He registered it in 1937.[27–31] Meticulous insight into maintaining pulmonary and systemic circulations and achieving gas exchange as well as using

Fig. 1: Microscope used by Robert Hooke
Source: https://medicalmuseum.health.mil/micrograph/index.cfm/posts/2019/microscopical_investigation_hookes_microscope; Public domain: https://commons.wikimedia.org/w/index.php?curid=9583064

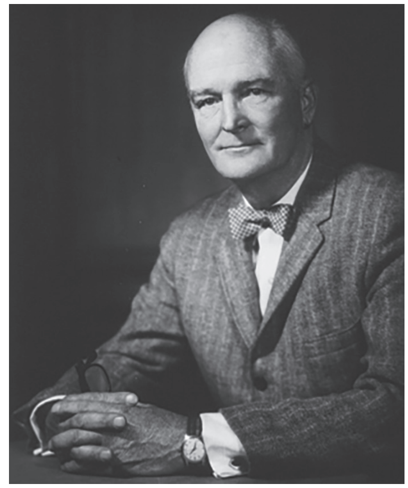


Fig. 3: Dr. John Heysham Gibbon
Source: By Unknown author – http://resource.nlm.nih.gov/101441395; Public domain: https://commons.wikimedia.org/w/index.php?curid=89545994

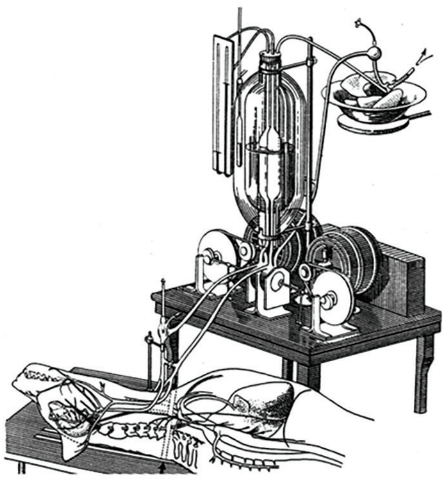


Fig. 2: Brukhonenko's Autojektor
Source: https://commons.wikimedia.org/wiki/File:Patent_autojektor.gif Briukhonenko S.S., Public domain *via* Wikimedia Commons

Fig. 4: Mayo–Gibbon Heart–lung machine
Source: https://www.si.edu/object/mayo-gibbon-heart-lung-machine%3Anmah_1213038

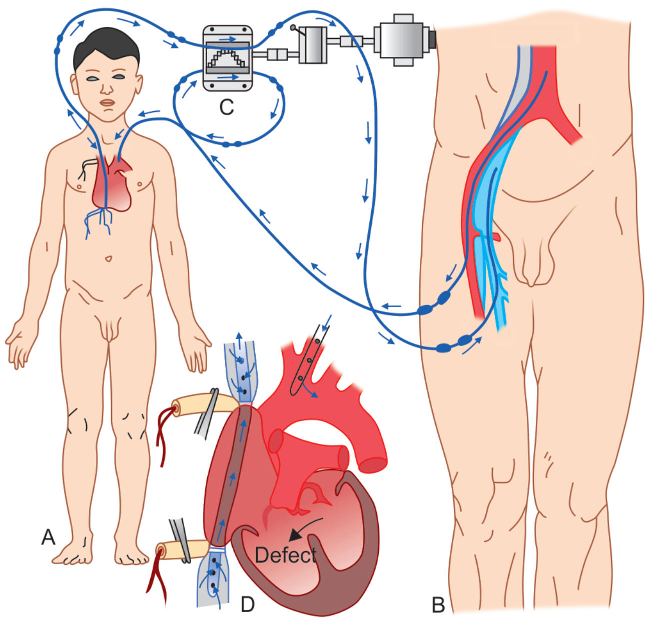
deep hypothermia in animal experiments was already accomplished by this time.

Era of Cardiopulmonary Bypass on Human Subjects

John Heysham Gibbon (Fig. 3) was a surgeon of American origin, credited with the invention of the heart–lung machine, leading the way for performing subsequent open-heart surgeries in humans. Dr. Gibbon successfully finished his research fellowship in surgery at Harvard Medical School under Dr. Edward Delos Churchill from 1930 to 1931 and 1933 to 1934.

When he was a fellow, he was looking after a patient who was operated for cholecystectomy and developed massive pulmonary embolism. The patient demised. The loss of this patient made Dr. Gibbon think about developing an alternate mechanism for bypassing the function of the lungs and providing the patient with oxygenated blood till the recovery of the lungs and heart.[32] He joined Pennsylvania Hospital as an Assistant Surgeon, participated in World War II, and returned to his base. He continued his research at the University of Pennsylvania on building the prototype of a heart–lung machine and experimented with cats in the initial stages. In 1937, he published his results about keeping these cats alive for hours. He continued to work on this project along with his assistant Mary, who later became his wife. In 1953, Dr. Gibbon successfully used his heart–lung machine for operating on an 18-year-old lady for ASD closure using a cardiopulmonary bypass. Heparin was used for anticoagulation. The surgery was successful. Thus, he laid the foundation for the era of open-heart surgery for complex cardiac surgical procedures using cardiopulmonary bypass.[33]

After his initial success story, the subsequent four patients operated by Dr. Gibbon did not survive.[34] He abandoned cardiac surgery until Mayo Organization came forward to make changes to his design. Four years later, John Kirklin and his associates at the Mayo Clinic in Rochester, Minnesota began using and improved upon the Gibbon-type heart–lung machine (Fig. 4).[35]



Figs 5A to D: Controlled cross-circulation. (A) Patient with sites of arterial and venous cannulations. (B) Donor with sites of arterial and venous cannulations. (C) Motor pump to control exchange of blood between the patient and donor. (D) Closeup of the patient's heart, showing canula to draw venous blood from both the superior and inferior venae cavae. Arterial blood from donor entered patient's body through canula in the left subclavian artery
Source: Punjabi and Taylor

In 1954, Walton Lillehei introduced the practice of controlled cross-circulation (Fig. 5). In this procedure, a patient, usually a child, will be connected to a donor (usually one of his biological parents), whose heart and lung served as a pump and oxygenator, permitting the performance of open-heart surgery. Soon after, in 1955, Dr. Lillehei introduced the bubble oxygenator, making open-heart surgery practicable surgery to all surgeons around the world.

Although the research was ongoing for decades prior to Dr. Gibbon's cardiopulmonary bypass machine, the fundamental difference was, most of the other pioneers focused on the perfusion of single organs rather than the whole body. This can be explained by the limited capacities of their equipment. The organs tolerated bypass for a longer period of time. The limiting problem was the perfusion of the brain, in the absence of the pumping action of the heart. Hypoxia of the brain results in severe neurological damage or death. In 1939, Dr. Laurence Frederick O'Shaughnessy (1900–1940, London) published his experiments on perfusing the brains of cats and dogs with Ringer lactate solution and blood, approximately 5% of the blood volume of the patient.[36] O'Shaugnessy ended his publication on the future of cardiac surgery with this visionary message: "This method of cerebral perfusion is clearly unfitted for immediate clinical application, but it is presented as an example of the sort of work necessary for the further advance of the surgery of the heart." His early demise at the age of 40 was a serious blow to the development of cardiac surgery. He was blown to pieces in May 1940, while watching an air raid in Flanders.

With the advances and refinements in the process of cardiopulmonary bypass, the stage is set for further thoughts on the development of ECMO technology.

Part 3: Evolution of Extracorporeal Membrane Oxygenation

(The story continues)

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CONFERENCE REPORT

Conference Report: 9th Annual International Conference SWAAC ELSO, 2023 and 12th Annual National Conference ECMO Society of India, Ludhiana, India, 10th–12th March, 2023

Vivek Gupta[1], Tanveer Singh[2], Pranay Oza[3], Venkat Goyal[4], Suneel Pooboni[5], Vinod Singh[6], Poonam Malhotra[7], Yatin Mehta[8], Bishav Mohan[9], Gurpreet Singh Wander[10]

Abstract

The recent past has seen a surge in extracorporeal membrane oxygenation (ECMO) usage and awareness among health care professionals. However, It is still thought that these complex modalities for managing critically ill patients is restricted to metros. Moreover awareness among healthcare professionals is crucial who are primarily managing these critically ill patients for timely advice for ECMO support. The best way to create awareness and encourage for research among the professionals is conferences. However, this is always challenging to organize an international event beyond the metros. This was the first ever South West Asian and African chapter Extracorporeal Life Support Organization (SWAAC ELSO) conference that was organized successfully from 10th to 12th March 2023 with high academic standards involving multiple specialties involved in ECMO management and care.

Keywords: Conference, Report, South West Asian African chapter extracorporeal life support organization.

Indian Journal of ECMO (2023): 10.5005/jaypee-journals-11011-0011

Introduction

Extracorporeal membrane oxygenation (ECMO) has gained significant attention during COVID-19 pandemic.[1] However there is lack of awareness not only regarding the usage but appropriate time for initiation of ECMO among the health care professionals working in acute or critical care settings. Conferences may be one of the best method to create awareness, sharing the experiences and ideas along with provoking the thought for future research in a scientific manner. This was an honor for the organizing team for an opportunity to organize an international event of South West Asian and African Chapter of Extracorporeal Life Support Organization (SWAAC ELSO) as 9th Annual Conference at Dayanand Medical College and Hospital, Ludhiana, Punjab, India. India was hosting this event 4th time, however, the mannerism was that this mega event was organized for the first time in 2-tier city with air connectivity limitations. However, the national and international participation was phenomenal during this academic event. The participation of various medical specialties and integration of different extracorporeal therapies was another unique feature of this congress. The theme of this conference was ***Learn – Practice – Sustain Lives***. It is a matter of great pride that 20 countries from SWAAC ELSO region along with the United States, United Kingdom, Singapore, and Australia participated physically in this conference. However, faculty from few countries participated virtually such as Germany, Prague, etc.

Keynote

The inaugural session was scheduled on the first day of the conference, inaugurated, and addressed by chief guest Mr Sunil Kant

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Munjal, an Indian entrepreneur, the chairman of Hero Enterprise and serving as the chancellor of BML Munjal University. The guest of honor Dr Mathew Paeden kept his view as ELSO representative and spoke about the importance and growth of ECMO in recent past across the globe. The main events during the inaugural session included fellowship awards of ECMO Society of India to all successful candidates. Another milestone was the launch of ECMO Journal of India, the official journal of ECMO Society of India. The inaugural ceremony was concluded with the experience of ECMO survivors.

Scientific Committee

The scientific committee was a mixture of experts from various specialties who are leading the ECMO program across the globe. The scientific committee met several times on a virtual platform to shape up the scientific program. The incorporation of various specialties such as critical care specialists, cardiologists, cardiac surgeons, pediatricians, pediatric intensivists, anesthesiologists, neonatologists, physicians, chest physicians, and perfusionists helped to design a scientific program in such a manner to involve both beginners and the experts in the field of ECMO. The scientific committee also agreed along with SWAAC ELSO executive body to start International ECMO Quiz every year during SWAAC ELSO annual conference.

Workshops

There were four preconference workshops that were tailored for both basic and advanced training in ECMO therapies along with continuous renal replacement therapies (CRRT). Since acute kidney injury is quite common in patients requiring ECMO support and CRRT is another form of extracorporeal therapy, incorporation of CRRT would provide additional confidence to ECMO specialists to manage acute kidney injury leading to acute metabolic derangements.[2] Theoretical components of these workshops were covered online prior to workshop day to provide more time to participants for simulation and hands-on training. These four workshops were attended by more than 200 both national and international participants. All the workshops were focused on routine management, troubleshooting, and problem-oriented focused discussions with an opportunity to perform the procedures (Table 1).

Conference

The scientific program during the conference presented a unique model of interdisciplinary involvement and addressed every aspect of ECMO management with recent advances and research. The sessions were arranged both physical and virtual for speakers to involve more international faculty. Two parallel sessions were continued on 11th and 12th March 2023 to cover the various aspects of ECMO management. The program was attended by 498 delegates from India, Dubai, Oman, Kuwait, Saudi Arabia, Nepal, and Qatar. Nearly 100 experts from 20 countries, including SWAAC ELSO region, the United States, Australia, France, European countries, Singapore, Bangladesh, and Sri Lanka, participated as faculty and shared their views, researches, and experiences (Table 2).

The total number of received abstracts were 43, however, after initial screening, 32 abstracts were relevant to the extracorporeal therapies. All the abstracts were sent to abstract committee and each abstract was reviewed by at least two experts before finalizing and choosing 10 best papers for award category. However, the remaining abstracts were chosen for podium and e-poster presentations. These presentations included original research, case series, and case reports (Tables 3 and 4).

Table 1: Pre conference workshops

Name of workshop	*No. of participants*	*Workshop director*
Basic ECMO for paramedics	62	Mr Ali Boroujerdi Mr Deblal Pandit
Advance ECMO simulation training	86	Dr Pranay Oza Dr Arpan Chakraborthy
Procedures during ECMO: Hands on training	34	Dr Venkat Goyal Dr Dipanjan Chatterjee
Continuous renal replacement therapy (CRRT) and other extracorporeal therapies	26	Dr Ranajit Chatterjee Dr Vinay Singhal

Table 2: Scientific deliberation during congress

Scientific session	*Number of presentations*
Critical care and ECMO	4
Case-based discussion	3
Complications on ECLS	2
Weaning session	2
Anticoagulation	4
Respiratory care on VV ECMO	3
Troubleshooting and challenges during ECMO	12
Prolonged ECMO run	4
ECMO nursing session	3
ECMO perfusionist's session	3
Education, research, and quality	5
Ethical issues	3
Neonatal and pediatric ECMO	6
ECPR and transport	4
Monitoring during ECMO	4
Recent advances and updates	4
Renal issues and other extracorporeal therapies	4
Cardiac ECMO	9
Infection and nutrition during ECMO	6

Quiz Session

Another unique addition of this academic event was quiz competition, which included preliminary elimination round and final round. Teams from different countries participated in the event. The questions included various aspects of ECMO, including history, pictorial, and identification of complications.

Sponsors

The success of this event was possible only due to generous educational support by various partners, including Getinge Medical India Pvt. Ltd. as platinum partner and Baxter (India) Pvt. Ltd. as gold sponsors along with other sponsors.

Table 3: Podium presentation (award category)

Presentation topic	*Primary speciality*	*Place*
Extracorporeal membrane oxygenation in COVID-19-Indian scenario	Anesthesiology and critical care	Varanasi, India
The use of VV ECMO in infant with human Metapneumovirus pneumonia and ARDS	PICU and adult ICU	Farwaniya area, Kuwait
VV ECMO cannula shattering	Pediatrics ICU	Farwaniya area, Kuwait
Problems faced during VV ECMO of a dengue patient with severe ARDS: a case report	Internal medicine	Lucknow, India
Neurodevelopment outcome in children undergoing extracorporeal membrane oxygenation	Pediatric critical care	Trivandrum, India
ECMO oxygenator change out during COVID-19 pandemic	Perfusion	Kolkata, India
Association of pre-intubation noninvasive mechanical ventilation and the hospital mortality of critically ill COVID-19 patients received extracorporeal membrane oxygenation (ECMO) support: a retrospective cohort study	Critical care	Riyadh, Saudi Arabia
ECMO as a life-saving modality in near-fatal asthma, Najran experience	Cardiothoracic surgery	Najran, Saudi Arabia
Incidence and outcomes of neurological complications in H1N1 respiratory failure patients on ECMO: a retrospective study	Critical care	Mumbai, India
Rapid establishment of ECMO program during COVID-19 pandemic	Cardiothoracic surgery	Najran, Saudi Arabia

Table 4: Podium presentation (others)

Presentation topic	*Primary speciality*	*Place*
Fulminant myocarditis	Pediatric intensivist	Jaipur, India
The savior of reversible toxic myocarditis – a case report	Critical care	Salem, India
Severe ARDS in a kyphoscoliotic patient – application of VV-V ECMO – a case report	Critical care and anesthesiology	Hyderabad, India
Extracorporeal membrane oxygenation in pregnant women – case series	Adult critical care medicine	Riyadh, Saudi Arabia
ECMO for polytrauma patients: a blessing in disguise or a trail of fiction?	Critical care	Riyadh, Saudi Arabia
Combined VV ECMO and independent lung ventilation for hydatid cyst – case report	Critical care	Riyadh, Saudi Arabia
Combined use of VA ECMO and IMPELLA in patients with acute coronary syndrome and cardiogenic shock (ACS-CS)	Critical care	Riyadh, Saudi Arabia
Successful VV ECMO in post-CPR pediatric patients with ARDS and pneumothorax	Anesthesiology and critical care	Secunderabad, India
Novel approach to ECMO troubleshooting (hypoxia) management utilizing two ECMO circuits in parallel – a case report	Critical care	Riyadh, Saudi Arabia
Lifesaving starts with BLS and ends with ECPR	Internal medicine	Najran, Saudi Arabia

Impact and Perspective

Extracorporeal membrane oxygenation technology has significant impact on management of critically ill patients. The practice of ECMO is not restricted to any specific medical specialty; moreover, the successful management requires multidisciplinary team approach, including multiple medical streams. Professional education and research are a cornerstone for involving interdisciplinary professionals to enhance ECMO awareness. This SWAAC ELSO event was the first time organized in a 2-tier city since the inception of the organization with the theme to create awareness and bring the ECMO services to remote areas to serve more and more critical patients. Recently, the service sectors and industries are focusing on two- and three-tier cities due to saturation in metro. Moreover, better connectivity through road and air, improved infrastructure, and development have significantly contributed to growth of these cities. Although, there are some challenges such as language difficulties and restricted air connectivity, but enthusiasm and support by national and international participants including experts were phenomenal and will definitely help the professionals for development of the ECMO program and participation in research. Since conferences are an excellent platform to review and evaluate scientific findings and to develop a roadmap for future projects.[3] SWAAC ELSO 2023 was an exceptional model of international interdisciplinary education and research, in which several recent advances, technological innovations, and medical findings were presented, reviewed, and commented.[4] Several constructive scientific debates were collected and moderated by professional experts in the field of critical care and ECMO. The success of the conference was measured by the participant's feedback and several suggestions were collected from the participants of the conference for future improvement.

Conclusion

ECMO is a growing field and requires not only training and education to develop future ECMO specialists, but awareness among the specialists of various specialties for appropriate identification of patients at the right time. Organizing this international annual conference was challenging in a 2-tier city due to several limitations, but has definitely put an impact that such events can be organized successfully beyond metros and can be helpful in creating awareness to help more and more patients requiring ECMO support.

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Vivek Gupta https://orcid.org/0000-0003-4319-6843

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Conference Report Photo Gallery


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Neurologic complications after ECMO initiation. Are they inevitable?
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ECMO SUPPORT FOR HIGH
RISK CARDIAC
INTERVENTION
EVIDENCE & REALITY
Professor
Alia Abd El Fattah, MD.
Critical Care Department,
Cairo University
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SWAAC ELSO-2023


Critical Illness During Pregnancy
Incidence of critical illness in pregnancy is low (<3/1000 maternities)
Critically ill obstetric patients is rarely encountered and depends on the volume of admissions (both ICU and obstetric)
Those who require ECMO is even less common
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Divine Chants of Lord Ganesh


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ELSO Registry, ELSO Community
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CASE REPORT

Successful Venovenous Extracorporeal Membrane Oxygenation (VV-ECMO) for Acute Respiratory Distress Syndrome (ARDS) and Air Leak in a Child with Severe Traumatic Brain Injury: Lessons Learned

Shivakumar Shamarao[1], Harshini Bolabail Parthasarathy[2], Hari Prasath Madhu[3], Ashwath Ram[4], Jahnavi Kare[5], Dev Ananda[6], Murali Krishna[7], Ilin Kinimi[8]

Received on: 04 July 2023; *Accepted on*: 24 July 2023; *Published on*: 14 August 2023

Abstract

Background: We report a case of severe traumatic brain injury with acute respiratory distress syndrome (ARDS) and air leak, in a child, who was successfully managed with venovenous extracorporeal membrane oxygenation (VV-ECMO) and made a good recovery.

Patients and methods: This is a single case report from the pediatric intensive care at Manipal Hospitals, Bengaluru, Karnataka, India.

Conclusion: We conclude that ECMO is feasible and safe for children with ARDS in the setting of severe traumatic brain injury (TBI). Timely initiation of ECMO can enable good recovery in children with severe ARDS and air leak complications, in the setting of trauma.

Keywords: Case report, Severe traumatic brain injury, Severe acute respiratory distress syndrome, Pneumomediastinum, Venovenous extracorporeal membrane oxygenation.

Indian Journal of ECMO (2023): 10.5005/jaypee-journals-11011-0007

Introduction

Adopting lung protective ventilation strategies minimizes lung injury which contributes to the development of multi-organ dysfunction syndrome (MODS) and mortality in children with severe pediatric acute respiratory distress syndrome (P-ARDS). However, in a subset of children with severe P-ARDS, and traumatic brain injury (TBI), accepting permissive hypoxemia and hypercapnia can be counterproductive, and not neuroprotective. Despite the lack of grade-1 evidence, there is a strong agreement to consider extracorporeal membrane oxygenation (ECMO) to support gas exchange and provide rest to lungs to enable recovery in children with severe but potentially reversible lung injury in the absence of any serious contraindications.[1] Severe TBI with intracranial hemorrhage is considered a relative contraindication for ECMO due to the need for anticoagulation which can potentially worsen the intracranial bleed.[2]

We present the case of a child of age 3 years 10 months with severe TBI who developed severe ARDS and air leak and made a good recovery with venovenous extracorporeal membrane oxygenation (VV-ECMO) support.

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Source of support: Nil

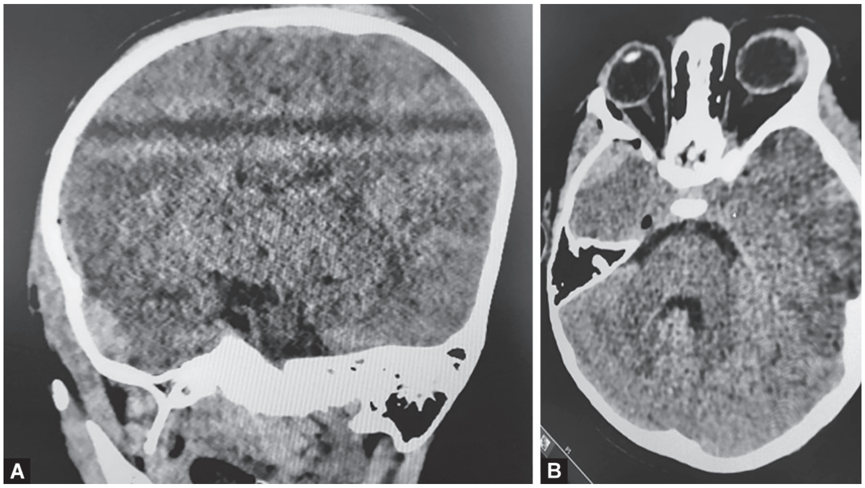
Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

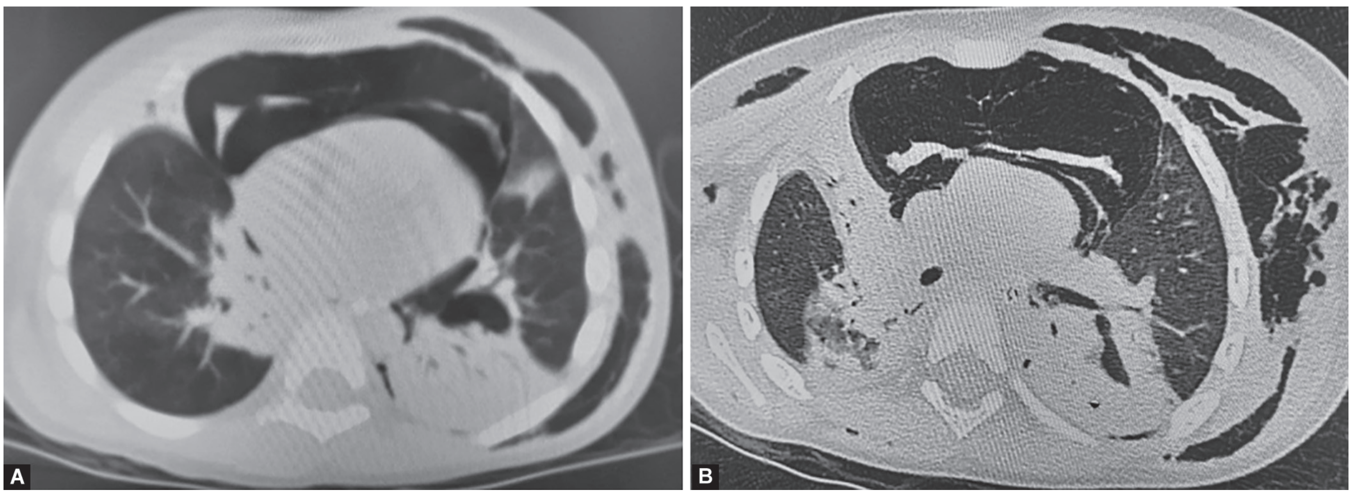
Case Description

Background History and Presentation

A child of age 3 years and 10 months was treated elsewhere for an alleged history of (h/o) fall from second floor at home. At admission, the Glasgow coma scale (GCS) was 6/15 and he was intubated for the same. Computed tomography (CT) brain showed focal extradural hemorrhage (EDH) along the right temporal convexity with a maximum thickness of 9.6-mm indenting the adjacent temporal lobe, thin rim of acute subdural hemorrhage (SDH) along the right frontotemporal convexity with few air pockets, focal EDH along central frontal convexity measuring 3 mm in maximum thickness, and a focal small hemorrhagic contusion in the left temporal lobe (Fig. 1). He was treated with supportive neuroprotective measures. On day 4 of admission, he developed methicillin resistant *Staphylococcus aureus* (MRSA) pneumonia with moderate-to-severe ARDS (OI = 12–13). He also developed air leak syndrome with pneumomediastinum, progressive subcutaneous emphysema, and pneumopericardium (Fig. 2). At this stage, he was referred to us for further management.



Figs 1A and B: CT brain coronal and sagittal imaging showing intracranial bleed



Figs 2A and B: Showing collapse consolidation, lung contusion and pneumomediastinum

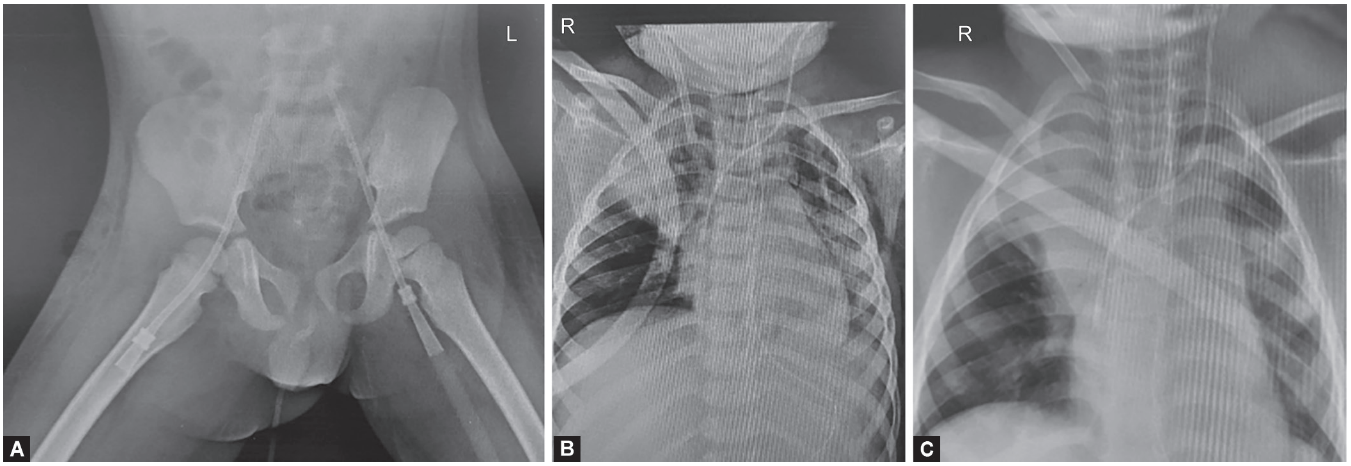
In view of progressive air leaks and persistent hypoxemia, the decision was made to institute ECMO. Neurosurgical clearance was obtained and on day 7 of admission, the child was put on VV-ECMO.

Extracorporeal Membrane Oxygenation Details

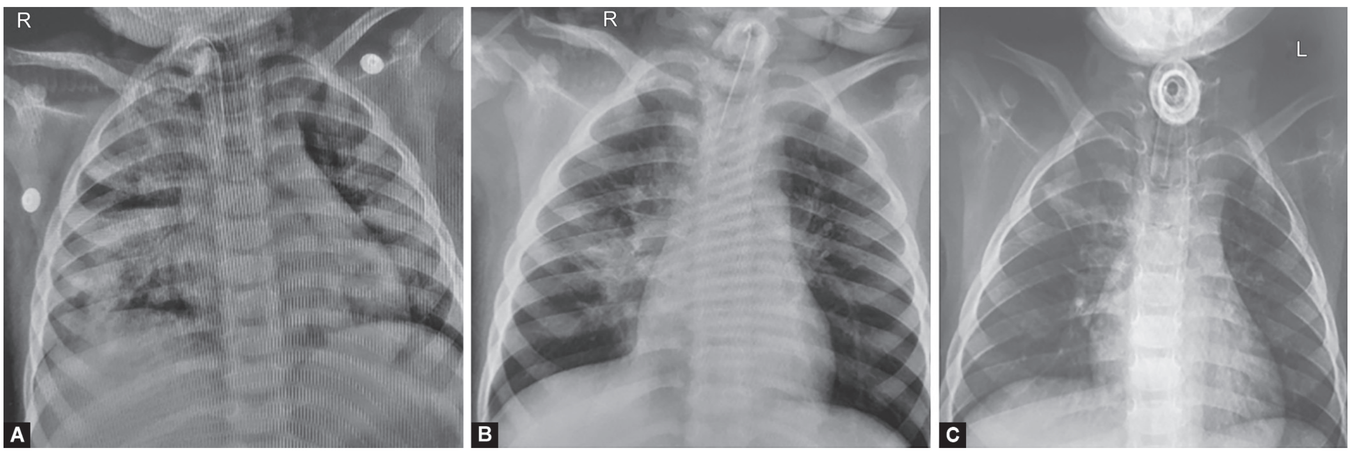
The child was cannulated with bilateral femoral cannulas (10-Fr Medtronic cannulas for drainage) (Fig. 3A) and right internal jugular vein (IJV) (12-Fr Medtronic cannula) for return (Fig. 3B). He was connected to ECMO with a Sorin oxygenator and rotaflow pump with flows of 0.98 L and 2300–2600 rpm. The Fio_2 on ECMO was 100% and sweep gas was around 3 L. Unfractionated Heparin was used for anticoagulation with a target ACT of 160–180 seconds. The rest settings on the ventilator were pressure-control mode with peak pressure of 10 cm H_2O, rate of 20/m, Fio_2 weaned to 0.4, positive end-expiratory pressure (PEEP) of 8–10, and generating tidal volume (TV) of around 1–2 mL/kg. On day 2, chest radiography (CXR) showed that the right IJV cannula had migrated upward (Fig. 3C) without any flow implications and was changed uneventfully with a 12-Fr Edwards cannula. Oxygen saturation was maintained in the range of 85–92% throughout the ECMO course with brief desaturations to as low as 77%, related to ECMO flow fluctuations. We could maintain an average flow of 0.8 L on ECMO during the entire ECMO run which lasted 8 days. The child underwent bronchoscopy twice to clear thick mucopurulent secretions causing the collapse of the lungs. N-Acetylcysteine and Levosalbutamol nebulization's were administered for the same. Gradually, there was an improvement in the lung condition with a resolution of air leak and he was decannulated on day 8 of ECMO.

Post-extracorporeal Membrane Oxygenation Course

He underwent a tracheostomy on day 10 of admission to enable faster weaning from ventilator support. On day 5 post-decannulation, he developed pulmonary hemorrhage despite a normal coagulation profile with blood culture growing *Burkholderia* and *Candida guillermondi* same time. His lung condition deteriorated on conventional ventilator support needing peak pressures of 30, mean airway pressure (MAP) of 21 and Pao_2/Fio_2 Ratio (P/F) ratio of 67, and oxygenation index (OI) of 31 (Fig. 4A). The family was counseled on the potential need to go back on ECMO. He was started on high frequency oscillator ventilation (HFOV) with settings of MAP of 30, ΔP of 60, Fio_2 of 1, and frequency of 9. Inhaled nitric oxide therapy was also tried and discontinued with no benefits. After 3 days of HFOV, prone ventilation on a conventional ventilator was done, which seemed to aid lung recruitment (Fig. 4B).



Figs 3A to C: (A) Bilateral femoral cannulas (showing femoral cannula position); (B) IJV cannula [showing cannula internal jugular vein (IJV)]; (C) IJV cannula migrated upwards (showing the upward migration of IJV cannula)



Figs 4A to C: (A) The CXR at the time of deterioration with pulmonary hemorrhage; (B) Post-prone position; (C) The CXR at discharge

He could be weaned off ventilator support on day 28 of admission. Off sedation, he was noticed to have visual deficits (absent focus/follow/Menace reflex). Magnetic resonance imaging (MRI) brain showed multifocal areas of microhemorrhages in bilateral centrum semiovale, corona radiata, splenium of the corpus callosum, genu of the corpus callosum, posterior periventricular area, and a few along the cortical and subcortical location of bilateral hemispheres. Fundus examination was normal. Stimulation exercises with brightly colored objects were recommended. His vision was normal at discharge. He was discharged home on day 47 of admission with normal-looking lungs (Fig. 4C) and subsequently, tracheostomy decannulation was done at follow-up.

Discussion

The above-mentioned case of a child on ECMO for severe P-ARDS with air leak though seemingly straightforward was challenging in many aspects.

Dilemma on Initiation of Extracorporeal Membrane Oxygenation

The incidence of ARDS in isolated TBI is around 20–30% and is known to contribute significantly to mortality and worse neurological outcomes.[3] There is definite evidence that hypoxemia adversely affects outcomes in TBI.[4] Lung protective ventilation targets may not be neuroprotective in the setting of TBI. The need for high PEEP can have a detrimental effect on cerebral perfusion and venous drainage from the brain which can be unpredictable in the absence of intracranial pressure (ICP) monitoring. Although ECMO provides an option for treating severe ARDS, TBI is a relative contraindication.[5] Children on ECMO support need anticoagulation at high doses in order to prevent circuit clotting and prolong oxygenator life. Along with the need for anticoagulation, they can also develop thrombocytopenia which predisposes to an increased risk of bleeding. We had the following concerns regarding the initiation of ECMO in the index case. The first was the risk of causing expansion of the already existing bleed in the brain with ECMO and heparinization. Second was the uncertainty regarding the candidacy for ECMO due to a severe form of primary brain injury causing diffuse axonal injury which could independently lead to poor neurological outcomes. MRI brain was not possible given his unstable condition. We had a multi-disciplinary team (MDT) discussion involving the neurologist, neurosurgery team, and ECMO team and had close consultations with other centers doing pediatric ECMO. The family was counseled regarding the challenges of bleeding on ECMO and uncertainty with regard to neurological outcome. The decision to initiate ECMO was jointly done with the family and the MDT. We decided to accept lower anticoagulation targets given the concern for bleeding. There are different anticoagulation strategies in the literature for such situations. The availability of pre-heparinized or heparin-coated circuits, more efficient membrane oxygenators, centrifugal pumps, miniaturization of circuits, and heparin-bonded circuitry has allowed ECMO use with little or no anticoagulation, making it possible for heparin free runs, as discussed in the literature.[6]

Alternating Lung Atelectasis

This child had thick and copious secretions despite adequate humidification causing airway obstruction and lung atelectasis. The progression of the lung condition with additional MRSA lung infection warranting high ventilator pressures resulted in air leaks. Periodic bronchoscopies were performed for clearing secretions from the lungs due to persistent lung atelectasis despite non-invasive measures that included NAC nebulization, positioning, physiotherapy, and adequate humidification. Bronchoscopy on ECMO needs to be balanced with the risk of causing airway trauma, bleeding, and introducing infections. Flexible bronchoscopy is reported to be safe on ECMO when done by an experienced team with adequate precautions to prevent bleeding and infections.[7,8] Pediatric patients pose further challenges with the small size of endotracheal tube (ET) tube which may make bronchoscopy challenging in the absence of small-sized scopes. Our bronchoscopy is done by our pediatric pulmonologist with a 2.8-mm Olympus scope *via* the ET. Additional measures taken to tackle the secretions were nebulization's with N-acetyl cysteine, cautious periodic position changes, suctioning, and gentle chest physiotherapy.

Refractory Systemic Hypertension with Transient Vision Loss

Systemic hypertension is the most common cardiovascular complication seen in 94% of cases of VV-ECMO.[9] Positive fluid balance, presumed alteration of the renin–angiotensin axis, and alteration of circulating levels of endothelin-1 are some of the proposed causative theories. The clinical implications of hypertension with anticoagulation on ECMO are the increased risk of bleeding (mainly intracranial), and the need for increased sedation and analgesia (due to presuming increased awareness and pain). In the index case, systemic hypertension was controlled with a combination of multiple intravenous (IV) and enteral antihypertensive medications. In our observation, there seemed to be better control with the enteral route of administration of anti-hypertensives compared to the IV route. However, there is no literature evidence to explain the same. A combination of different groups of antihypertensives was employed simultaneously to address hypertension, which resolved once off ECMO. The evaluation for transient visual impairment showed normal fundus exam and multifocal microhemorrhages in the brain. The MRI findings could be related to the possible primary injury to the brain. Subclinical changes in MRI scans are reported in ECMO survivors with the incidence of cerebral microhemorrhages in as high as 50% of cases, which made us wonder if it was related to ECMO.[10,11] The cause for the transient visual impairment was possibly related to the microhemorrhages noted along the optic radiation bilaterally. He had regained normal visual functions at discharge with conservative management.

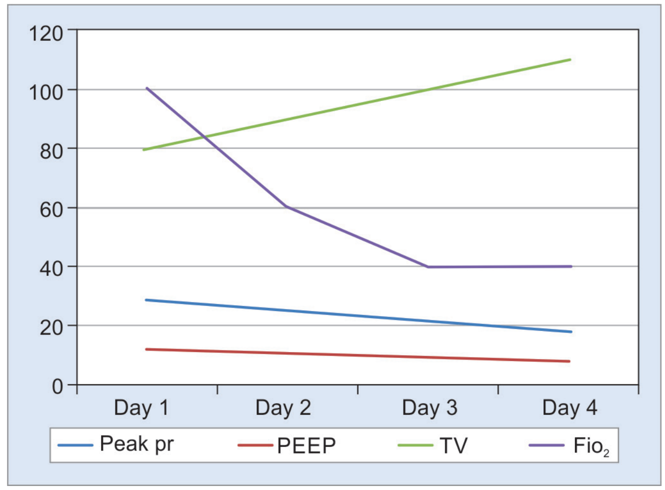


Fig. 5: Graphic depiction of the improvement in the lung parameters and ventilator settings post-prone position. Day of proning depicted on the *x*-axis

Pulmonary Hemorrhage post-ECMO Decannulation

Post-ECMO decannulation, with a fresh tracheostomy, and pulmonary hemorrhage associated with bacteremic sepsis causing refractory hypoxemia and hypercapnia on a conventional ventilator and later HFOV seemed like we were heading toward another ECMO requirement. Prone ventilation was done with tracheostomy in our child which was highly challenging, as it was a <7 days old tracheostomy when proning was undertaken. At our institution, we generally re-intubate children with a conventional cuffed ET tube if we need to prone them on tracheostomy. The challenges in proning children with a tracheostomy are the high risk of tube dislodgement due to the short length of the trachea and the tube itself, the fear of delayed recognition of tube-related complications, and the undue torsion of the short neck during the positioning making access to airway very difficult. On the contrary, the positive practice with tracheostomy in children at our institute is stay sutures and maturation sutures which make re-cannulation less cumbersome in the event of any dislodgement. We ensured high sedation and paralytic infusions during this period to minimize the risk of tube dislodgement and regular suctioning to prevent tube block. Proning brought about a significant improvement in lung condition (Figs 4B, C and 5).

Conclusion

In the setting of severe TBI with intracranial bleeding with severe ARDS, failure of maximal conventional management for ARDS need not prevent us from offering ECMO support in the appropriate clinical setting. Assessing risks vs benefits, multi-disciplinary support, and shared decision making with the family may ultimately prove to be a winner under such dire circumstances.

Prone ventilation in children with a tracheostomy, though logistically challenging, can be performed safely with adequate preparation and precautions.

Flexible bronchoscopy, when undertaken in the presence of clear indications, is a useful tool and can be safely done in children on ECMO, even on heparin, but warrants appropriate expertise, equipment, and strict asepsis precautions to prevent iatrogenic infections.

Severe refractory systemic hypertension, of unclear etiology, is a common problem in children on VV-ECMO and can be very challenging due to drug resistance.

Acknowledgments

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Authors' Contributions

HB, HM, SS, AR, JK, DA, MK, and IK: Contributed to the clinical management of the patient.
SS: Drafted the manuscript.
All authors approved the final version of the manuscript.

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CASE REPORT

Managing Hypercapnia in a Coronavirus Disease 2019 Acute Respiratory Distress Syndrome with Extracorporeal Carbon Dioxide Removal Using Continuous Renal Replacement Therapy Machine: A Case Report

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Received on: 30 June 2023; *Accepted on*: 28 July 2023; *Published on*: 14 August 2023

Abstract

Coronavirus disease-2019 (COVID-19) acute respiratory distress syndrome (ARDS) management remains challenging for intensivists, especially during limited resource availability. We report a COVID-19 ARDS case who had hypercapnia in spite of appropriate ventilatory management. This case was successfully managed with the use of extracorporeal carbon dioxide removal ($ECCO_2R$) device with attaching pediatric oxygenator with continuous renal replacement therapy (CRRT).

Keywords: Acute respiratory distress syndrome, Continuous renal replacement therapy, Extracorporeal carbon dioxide removal, Pediatric oxygenator.

Indian Journal of ECMO (2023): 10.5005/jaypee-journals-11011-0008

Introduction

The coronavirus disease-2019 (COVID-19) has been associated with high mortality due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), however, the treatment is grossly restricted to supportive therapies due to lack of specific treatment.

Pathologically ARDS may lead to diffuse alveolar damage (DAD) which is initially an acute inflammatory phase causing edema, hyalinization, and interstitial inflammation. The next phase is an organizing phase with fibroblast proliferation in the alveolar septa and hyperplasia of pneumocytes.[1] Finally, the ARDS may progress to pulmonary fibrosis, however, a protective lung ventilation strategy may reduce this risk and abnormal radiographic findings following ARDS.[2]

The dysregulated immune response in the form of cytokine storm enhances the risk for progression to pulmonary fibrosis. The release of various inflammatory mediators may lead to epithelial and endothelial injury during the acute phase of ARDS. The fibroblasts and myofibroblasts proliferation and accumulation of collagen enhance the chance of pulmonary fibrosis.[3]

So far, no specific treatment for the virus has been proven its efficiency. The current management is aimed at giving supportive care to the lungs.

Case Description

A 54-year-old male, a known hypertensive, who presented with shortness of breath and fever was evaluated and RTPCR tested positive for COVID-19 around 15 days back. He was managed initially with oxygen, low-molecular-weight heparin, methylprednisolone along with other supportive therapies, however, oxygen requirement and work of breathing kept increasing and he required non-invasive ventilation. In spite of increasing support his oxygen saturation kept worsening and he required intubation and mechanical ventilation with proning 2 days before shifting to our hospital. We initiated a lung protective ventilatory strategy with positive end expiratory pressure (PEEP) 12. He remained hemodynamically stable and was maintaining oxygen saturation (SpO_2) around 90–92%; however, his arterial blood gas showed hypercapnia in spite of appropriate ventilatory settings, [arterial blood gases (ABG) pH 7.35, PaO_2 68; $PaCO_2$ 54]. In the next few hours, patients became hemodynamically unstable with tachycardia and hypotension, a fluid bolus and vasopressors did not improve the hemodynamics much and urine output started falling. Two-dimensional echocardiography was unremarkable with normal ejection fraction (55%); however, ABG showed severe respiratory acidosis ($PaCO_2 > 115$ and pH 6.82), ensuring adequate sedation,

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Source of support: Nil

Conflict of interest: Dr Vivek Gupta is associated as Editor-in-Chief of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of the Editor-in-Chief and his research group.

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Table 1: Effect of $ECCO_2R$ using CRRT along with pediatric oxygenator on hemodynamics, arterial blood gases, and ventilatory setting

Time (hour)	*HR*	*BP*	*pH*	*$PaCO_2$*	*PaO_2*	*Minute ventilation*	*RR*	*IP*	*Mode*	*Vasopressor*
0	146	86/43	6.86	109	64	12.6	36	32	Bilevel	High doses
6	118	104/52	7.18	84	58	12.2	36	32	Bilevel	Reduced
	12	128/68	7.24	63	76	13.2	28	28	Bilevel	Reduced
	18	122/64	7.50	49	67	11.9	24	28	Bilevel	Reduced
24	92	144/80	7.30	53.2	74	10.4	16	22	Bilevel	Stopped
36	88	156/74	7.32	47	76	9.8	14	20	Bilevel	No

BP, blood pressure; HR, heart rate; IP, inspiratory pressure; RR, respiratory rate

normothermia, patency of airway and ruling out other causes, the minute ventilation was increased by increasing both tidal volume and ventilation rate further. This also did not improve the respiratory acidosis and $PaCO_2$ remained high (108 mm Hg, pH 6.86 with PaO_2 59) and vasopressors requirement further increased. The family was reluctant to venovenous (VV) extracorporeal membrane oxygenation (ECMO) support. We initiated extracorporeal carbon dioxide removal ($ECCO_2R$) by connecting a pediatric oxygenator in series with continuous renal replacement therapy (CRRT) circuit using a Prismaflex® machine (Baxter India Ltd). Also, $ECCO_2R$ was initiated using M100 set with blood flow of 300 mL/minute and sweep gas flow of 1000 mL/minute; however, CRRT was kept on (slow continuous ultrafiltration) SCUF with zero balance. Anticoagulation was maintained using heparin infusion. Hemodynamic parameters and respiratory acidosis started improving followed by ventilatory parameters (Table 1). The $ECCO_2R$ with CRRT was stopped after 36 hours. Percutaneous tracheostomy was performed and further weaning from mechanical ventilation was initiated. Decannulation was done after successful weaning. The total duration of mechanical ventilation was 24 days and was discharged from the hospital after 30 days. His HRCT showed significant lung fibrosis prior to discharge. However, the patient required 2–3 L/minute oxygen at the time of discharge.

Discussion

The COVID-19 mainly involves the respiratory system. There is high prevalence of progression to ARDS in elderly patients especially with comorbidities. Timely management and intervention can avoid and circumvent the fatal morbidity and mortality in these high-risk patients. Various institutions have released showing various management protocols on lung protective ventilation low tidal volume, prone positioning, use of high flow nasal cannula, and use of higher PEEP by using existing data on ARDS management but there is limited data available on the use of carbon dioxide removal methods despite its proven efficacy in the management. $ECCO_2R$ is basically a method that artificially removes the CO_2 from the blood through an extracorporeal circuit connected with a gas exchange device.

In our patient, early implementation of an $ECCO_2R$ therapy prevented further acceleration of the invasiveness of therapy requiring the need for ECMO. This was integrated along with CRRT support and showed effective results in settling down the hypercapnia and improving oxygenation by lowering the ventilator requirement in our patient.

The progression of ARDS has been evaluated through 159 autopsies showing DAD and they found that these DADs may either recover to normal lung tissues or may lead to fibrosis.[4] The low-flow extracorporeal carbon dioxide removal has been used in patients with moderate ARDS receiving ultraprotective ventilation in patients and has been found safe, effective, and feasible in preventing carbon dioxide retention due to low tidal volume (4 mL/kg) ventilation in these patients.[5] Similarly, Parrilla et al.[6] also evaluated the use of ultralow tidal volume ventilation along with use of Hemolung® RAS as low flow CO_2 removal device in ARDS patients and concluded $ECCO_2R$ will be helpful in preventing respiratory acidosis with ultralow tidal volume ventilation strategy.[5]

In another study with a group of 15 patients where $ECCO_2R$ was used, the aim was to avoid intubation in 5 patients, which was achieved in 4 patients; the other 10 patients were supported with $ECCO_2R$ and managed successfully with lung-protective ventilation. The average requirement of the $ECCO_2R$ device was 5 days (range: 3–7 days). The pH and PCO_2 could be stabilized within 6 hours of initiating $ECCO_2R$, even with a significant reduction in minute ventilation. The results were encouraging with 67% survival to hospital discharge, though 93% of patients were weaned from $ECCO_2R$ and 73% were discharged from ICU. The author concluded $ECCO_2R$ can be used safely and effectively in this group of patients.[6–9]

Conclusion

COVID-19 ARDS management is a challenging task for intensivists as the extent of fibrosis of the lung involved goes undetermined. Clinical trials still undergoing to find out any effective treatment and so far have failed to show any specific drug. Furthermore, ECMO may be a standing practice to manage the severe cases, however, with limited resources; this can be managed with protective lung ventilation along with carbon dioxide removal artificially using cheaper options in crisis situations. As the mortality due to COVID ARDS is higher more and more studies and clinical trials are needed to target the efficacy of various lung protective ventilation strategies along with the use of carbon dioxide removal

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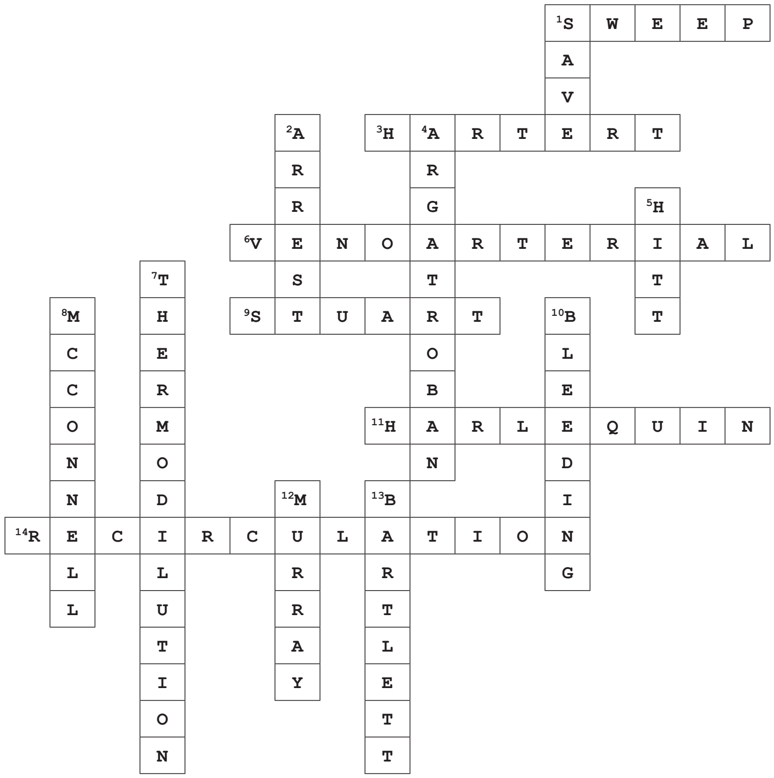
CROSSWORD ANSWERS



ESOI – COURSES

ECMO Society of India (ESOI) is running 2 courses since 2019, the details of the courses are as below:

- **Duration**
  - Fellowship – 1 yr
  - Certificate – 6 months
- **Eligibility**
  - ***Fellowship***
    - Postgraduate degree in critical care, medicine, cardiology, CVTS, chest medicine, pediatrics
    - MBBS with additional qualification (with 2 years experience in critical care after PG diploma)
  - ***Certificate course***
    - MBBS
    - Paramedicals – Respiratory therapist, Perfusionist, Nursing staff—BSc Nurse and GNM
- **Fees**
  - Fellowship – ₹40,000; For overseas students – $750
  - Certificate course – ₹25,000; For overseas students – $500
- Objective of the course – To transfer knowledge, make ECMO care and practise standardized in India
- Regular and alternate course in 10 affiliated institutes in 7 different states
- There will be entrance exam of 100 marks (MCQ type on basic critical care)
- Entrance Exam will be on 25 Dec 2023
- Courses start from January 2024
- Last day of Submission of Entry Form is 20 Dec 2023
- For details, click on www.ecmosocietyofindia.com, www.esoi-courses.com
- For queries, write to us on ecmosocietyofindia@hotmail.com or contact:
  - Dr Pranay Oza – 9821214971, 9223186518, Dr Vivek Gupta – 9815398993, Dr Arpan Chakravarty – 9432062377
  - Dr Suneel Pooboni and Dr Venkat Goyal
  - *NB:* We, the teachers of ECMO Society of India or the Society, are not related to any other ECMO-related course in India

SHORT COMMUNICATION

Minimally Invasive Venovenous Extracorporeal Carbon Dioxide Removal: How I do it?

Arpan Chakraborty

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Abstract

Extracorporeal carbon dioxide removal ($ECCO_2R$) is a technique used in hypercapnic respiratory failure without much hypoxia. Here we have depicted a simple reproducible method of CO_2 removal using a conventional dialysis machine and oxygenator.

Keywords: Acute respiratory distress syndrome, Chronic obstructive pulmonary disease, Decap, Extracorporeal carbon dioxide removal.

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Hypercapnic respiratory failure is usually managed by non-invasive or invasive ventilation depending on severity. In this communication, we are going to depict a technique for managing hypercapnia by using extracorporeal technology both in chronic obstructive pulmonary disease (COPD) and in adjunct to the ultraprotective ventilation strategy in acute respiratory distress syndrome (ARDS). Extracorporeal carbon dioxide removal ($ECCO_2R$) is a technique of partial respiratory support that achieves the removal of CO_2 from the blood through a low blood flow extracorporeal circuit, without significant effect on blood oxygenation. There are several methods of $ECCO_2R$, such as arteriovenous $ECCO_2R$, venovenous $ECCO_2R$, etc.; among these methods, the venovenous method is mostly popular and has been followed by different systems of CO_2 removal. Because of low flow, the anticoagulation target is kept higher than the conventional extracorporeal membrane oxygenation (ECMO) circuit.

The device of CO_2 removal essentially is a membrane lung (artificial gas exchanger) through which blood is passed. A flowing gas (sweep gas) runs along the other side of the membrane. The sweep gas contains little or no CO_2 (usually oxygen is used), which creates a diffusion gradient, and CO_2 comes out of the blood accordingly. Apart from the sweep gas, CO_2 removal also depends upon the blood flow to the membrane. The steep slope of the CO_2 dissociation curve means that a small variation in PCO_2 causes a significant variation in CO_2 levels in the blood. This helps in removing CO_2 from blood with much lesser blood flow than that needed for oxygenation.

In COPD patients, who are getting admitted recurrently for hypercapnic respiratory failure and the clinicians want to avoid invasive ventilation, an $ECCO_2R$ can be helpful to come down on CO_2 levels. This will help the patient to regain a pH of more than 7.25 and consciousness, thereby avoiding intubation and ventilation and its complications. Many times, even if they are intubated, using $ECCO_2R$ will be helpful in early extubation and avoid ventilation-associated injuries and pneumonia. The venovenous form is more commonly used and considered the conventional form of $ECCO_2R$.[1] Despite its pathophysiological rationale, studies regarding the use of $ECCO_2R$ in this subgroup of hypercapnic patients are still rare.[2] In the supernova study, $ECCO_2R$ in ARDS with ultraprotective ventilation strategy has given an outcome of 62% discharge with a mean duration of 5 days of $ECCO_2R$.[3]

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Decap System of VV-$ECCO_2R$

This system contains a roller pump. In this device, the membrane lung is connected in series to a hemofilter. The advantage of this assembly is as follows:

- Enhance the performance of the extracorporeal device by extracting the carbon dioxide dissolved in the plasmatic water separated by the hemofilter and recirculated through the membrane lung.
- Minimize the need for heparin by diluting the blood entering the membrane lung by recirculating the plasmatic water separated by the hemofilter.
- Increase the pressure inside the membrane lung by adding the downstream resistance given by the hemofilter and therefore reduce the risk of air bubble formation.

We use a modified decap method (Fig. 1) in which a double-lumen venous catheters/cannulas are placed in the right internal jugular or femoral vein and hemodialysis tubing is connected in the dialysis machine (Fig. 2), but instead of hemofilter, only pediatric oxygenator remains in the circuit which allows a low flow system to work efficiently. The roller pump of the dialysis machine (Fig. 3) is used to ensure blood flow. Sweep gas is usually kept between

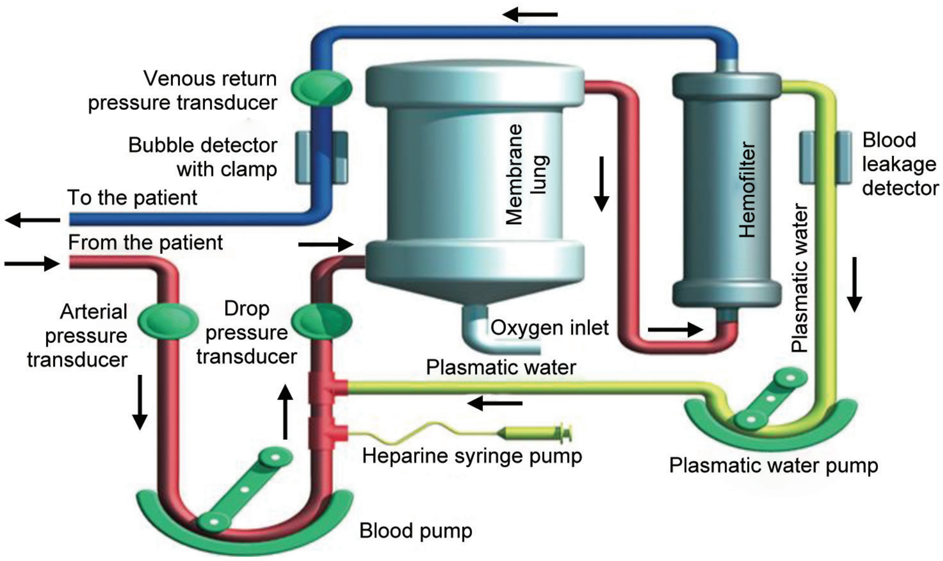

Fig. 1: Modified decap method

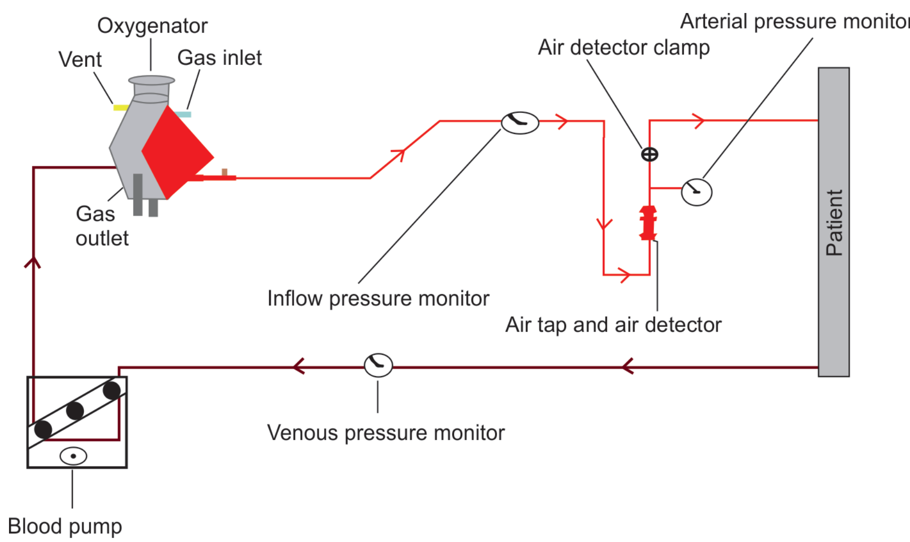

Fig. 2: Schematic representation of dialysis machine

Fig. 3: In-process machine

4 and 8 L/minute. Blood flow is maintained between 300 and 600 mL as the hemodynamics tolerates. The requirement of heparin or other anticoagulation is there to maintain activated partial thromboplastin time (APTT) >2 or activated clotting time (ACT) around 200. This method is less invasive than ECMO and is reproducible at non-ECMO centers without much expertise around.

Fig. 4: Venovenous $ECCO_2R$ is getting practiced in respiratory critical care

Though $ECCO_2R$ has been found beneficial in ARDS with low-tidal volume strategies and acute exacerbations of COPD with type II respiratory failure, large trials are needed to prove its evidence. The modified decap technique is getting popular in different Indian centers due to the low-cost reproducible method. Awake venovenous $ECCO_2R$ is getting practiced in respiratory critical care (Fig. 4) for COPD with recurrent admissions as an adjunct to non-invasive ventilation.

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