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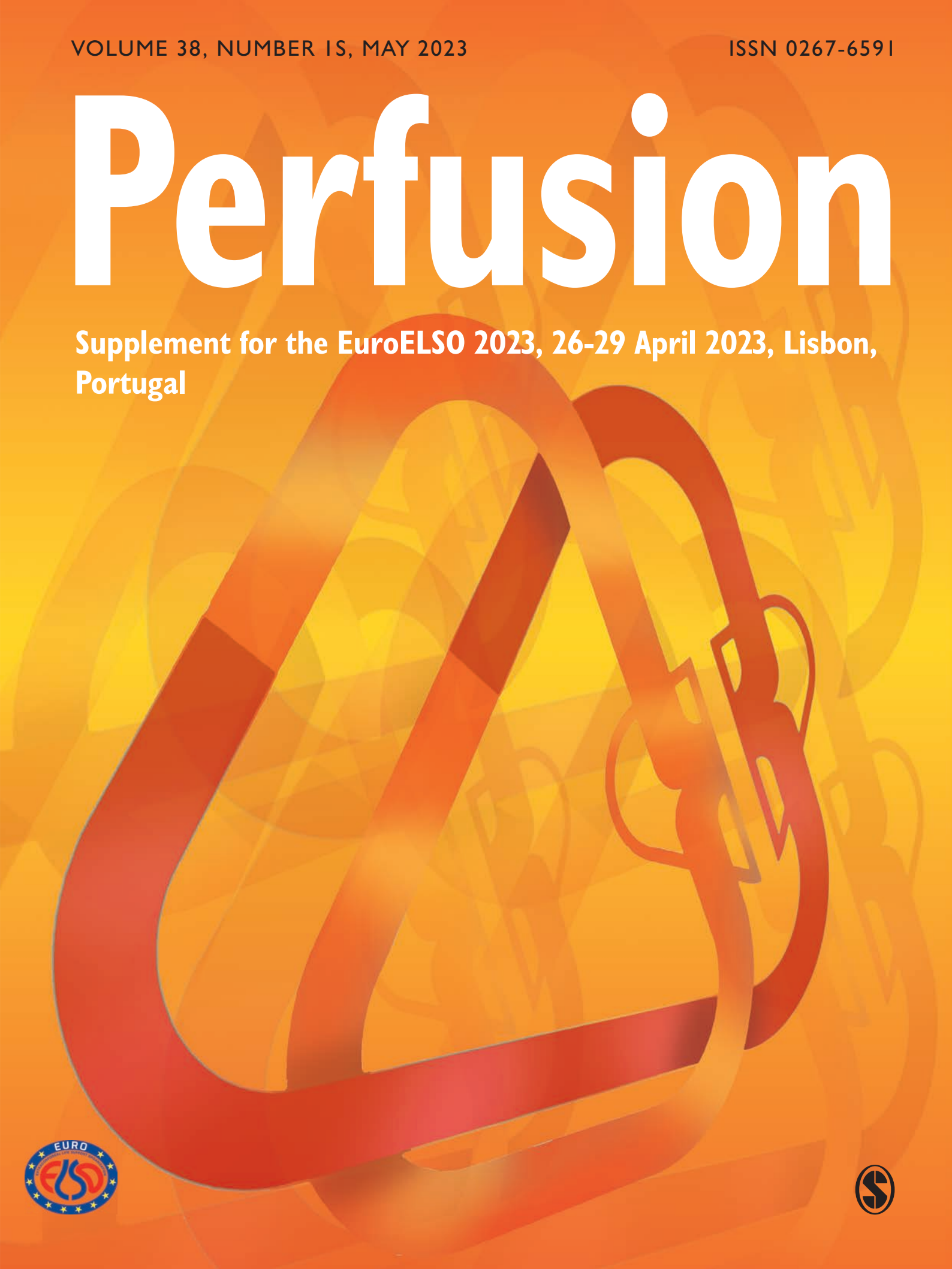
Perfusion

Supplement for the EuroELSO 2023, 26-29 April 2023, Lisbon, Portugal



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Special Issue: EuroELSO 2023

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Special Issue: EuroELSO 2023

Perfusion

"Bridging the Gap" international ECLS training and simulation - evaluation of the 10th educational corner on EuroELSO congress 2022 in London, United Kingdom

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Abstract

Introduction: Simulation training offers an authentic team-based learning opportunity without risk to real patients. The Educational Corner at the annual congress of the European Branch of Extracorporeal Life Support Organisation (EuroELSO) provided an opportunity for multiple simulation training sessions facilitated by experts from all over the world.
Aim: We aimed to review the educational impact of EuroELSO Educational Corner and whether it provides a quality ECLS training to a wide spectrum of multidisciplinary international attendees utilising high and low fidelity simulation, workshops and hands on sessions.
Methods: During the congress, 43 sessions were conducted dedicated to ECLS education with identified educational objectives. The sessions focused on management of adults and children on V-V or V-A ECMO. Adult sessions covered

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emergencies on mechanical circulatory support with management of LVAD and Impella, managing refractory hypoxemia on V-V ECMO, emergencies on ECMO, renal replacement therapy on ECMO, V-V ECMO, ECPR cannulation and performing perfect simulation. Paediatric sessions covered ECPR neck and central cannulation, renal replacement on ECMO, troubleshooting, cannulation workshop, V-V recirculation, ECMO for single ventricle, PIMS-TS and CDH, ECMO transport and neurological injury.

Results: The Educational Corner was attended by more than 400 participants over the two congress days. Majority of responders (88%) reported that training sessions met the set educational goals and objectives and that this would change their current practice. Almost all (94%) reported that they received useful information and 95% would recommend the session to their colleagues.

Conclusion: The Educational Corner, as an integral component of the annual EuroELSO congress, achieved the set educational goals and provided quality education based on the recipient survey. Structured multidisciplinary ECLS education with standardised curriculum and feedback is an important key step in delivering quality training to an international audience. Standardisation of European ECLS education remains an important focus of the EuroELSO.

Keywords

education, extracorporeal membrane oxygenation, extracorporeal life support, extracorporeal cardiopulmonary resuscitation, mechanical life support

Introduction

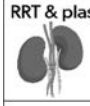
Simulation for extracorporeal life support (ECLS) has become an important modality for education of the multidisciplinary ECLS care team. ECLS care is delivered by teams of providers, therefore establishing optimal educational strategies requires considerations of interprofessional collaboration, communication, and teamwork. Simulation-based training for ECLS has emerged as a valuable tool offering the opportunity to improve technical skills[1–5] and reduce the risk of human errors[6] potentiating training to an individual team member along with the whole interdisciplinary team, and it has found to be superior to traditional training.[7] An integration of both clinical and nonclinical skills is important to improve survival and complications in the high risk and complex patients that require ECLS.[8] Simulations can be provided in different environments: directly in hospitals (in situ, on site), in dedicated facilities (simulation rooms) or, on occasion, at scientific meetings, thus taking advantage of the delegates' motivation.[9]

The Educational Corner has been an integral part of the European branch of Extracorporeal Life Support Organisation (EuroELSO) - annual congress since the first meeting in Rome, Italy in 2012.[9] The Educational Corner is an area dedicated to active learning and training providing well organised high-quality simulation sessions, hands on sessions and didactic teaching focusing on the acquisition of both technical and behavioral skills facilitated by experienced experts from all over the world. It allows attendees to consolidate knowledge about ECLS alongside the congress activities. Historically, sessions organised by Educational Corner have been well attended with excellent structured feedback with the number of participants increasing each year. It is therefore key to develop structured ECLS courses and educational programs within EuroELSO.[9] Based on this, we aimed to review the impact of Educational Corner and whether it provides a quality ECLS simulation training to a wide spectrum of multidisciplinary international attendees utilising high and low fidelity simulation, workshops and hands on sessions.

Methods

The 10th EuroELSO Congress took place in London, United Kingdom in May 2022 and the Educational Corner was held during two main congress days. Previous Educational Corner feedback from 2019 was considered whilst planning for the sessions.[9] Feedback from 2019 was positive with recommendations to expand the Educational Corner to two full days through the length of the congress. During Educational Corner, a total of 43 sessions, 32 adult and 11 paediatric, took place in four different rooms. Each room hosted six sessions on 5th May and five sessions on 6th May with extensive educational programme. The topics for the simulations were advertised in advance on the EuroELSO website and via EuroELSO social media channels with outlined learning objectives, allowing the congress delegates to select and sign up for specific simulations (Table 1). The overall goals of the sessions were to increase knowledge base and competencies in managing adult and paediatric patients. Adult sessions covered emergencies on mechanical circulatory support with management of LVAD and Impella (Abiomed, Danvers MA, USA.), managing refractory hypoxemia on V-V ECMO, membrane failure and circuit change on ECMO, renal replacement therapy/

Table 1. Educational corner programme.

Title	Aims	Modality	Learning Outcomes
Emergencies on MCS 	provide an overview of contemporary advanced heart failure management and emergency management of patients with LVAD, Impella & ECMO	theoretical part & hands on simulation session	- Understand phatophisyology of heart failure and advanced heart failure - Understand heart transplantation - Understand ventricular assist devices - Implement mechanical Life Support algorithm
Managing refractory hypoxemia on V-V ECMO 	provide a systematic approach of analyzing patient-ECMO interactions that can lead to severe hypoxemia on V-V ECMO	theoretical part & high fidelity simulation with debriefing	- Define refractory hypoxemia during V-V ECMO - Understand refractory hypoxemia pathophysiology and review the possible etiologies - Explore all the potential interventions.
ML failure & circuit change 	give an understanding precipitants and mechanisms of membrane lung failure, and practicie circuit replacement under time pressure using mannequin.	practical scenario with case vignette & simulation of membrane clotting	- Understand the mechanisms leading to ML failure - Demonstrate ability/knowledge of team management of return obstuction due to ML thrombosis - Demonstrate good communication skills
RRT & plasmapheresis on ECMO 	give an understanding indications for and of the practical aspects of managing CRRT and plasmapheresis on ECMO	theoretical part & hands on	- Describe indications for connecting CRRT/ plasmapheresis to the ECMO circuit - Demonstrate safe connection/disconnection - Describe complications & challenges of different approaches & prevent/troubleshoot these
How to perform perfect simulation 	extend knowledge about simulation techniques and improve team performance related to ECMO	theoretical part & simulation	- Provide real-life scenarios for teams practice - Demonstrate debriefing - Evaluate what aspects of team performance needs improvement, feedback, and conversation from participants
Troubleshooting V-V ECMO 	provide an overview about common difficulties that clinicians may encounter while managing patients on V-V ECMO	high-fidelity simulation	- Understand common difficulties, medical complications and circuit malfunctioning which could be encountered while managing patients during V-V ECMO support
ECPR cannulation	provide insights how to perform cannulation via percutaneous vascular access to provide ECPR in patients experiencing CA	hands-on workshop	- Understand procedure to obtain vascular access to implement ECLS during cardiopulmonary resuscitation both in IHCA and OHCA - Discuss team logistics and requirements for ECPR
Adventure in pediatric ECMO 	acquire basic knowledge and competencies, and develop adequate multidisciplinary teamwork skills to manage children on ECMO	hands-on workshop & high fidelity simulation	· Identify the components of the ECMO circuit · Recognize major ECMO indications/ contraindications - Identify most appropriate modality and most effective cannulation strategy · Recognize and address complications · Recognize, identify, and assess inadequate DO_2 · Differentiate the interaction between ECMO and various patient organ systems · Understand multidisciplinary teamwork and basic pathway during ECPR

MCS: mechanical circulatory support; ECMO: extracorporeal life support; LVAD: left ventricular assist device; V-V: veno-venous; CRRT: continuous renal replacement therapy; ECLS: extracorporeal life support; ECPR: Extracorporeal Cardiopulmonary Resuscitation; IHCA: in hospital cardiac arrest; OHCA: out of hospital cardiac arrest.

plasmapheresis on ECMO, troubleshooting V-V ECMO, ECPR cannulation and sessions about performing of perfect simulation. Paediatric sessions covered ECPR neck cannulation, ECPR central cannulation, renal replacement on ECMO, troubleshooting, ECMO cannulation workshop, V-V recirculation, ECMO for single ventricle, ECMO in Paediatric Inflammatory Multisystem Syndrome Temporarily Associated with SARS CoV-2 (PIMS-TS), ECMO for CDH, ECMO transport and neurological injury on ECMO.

Educational Corner provided three sessions on performing a perfect simulation and helped developing adequate multidisciplinary teamwork skills whilst managing patients on mechanical life support. The sessions were facilitated by international, highly experienced faculty dedicated to education and training using various educational modalities. (Table 2). The leaders of the sessions and majority of the faculty had a formal medical simulation certificate. Each session had at least two formally certified debriefers present during simulations. Other members of the faculty were selected on their experience and special expertise.

All the sessions were set up according to the recognised simulation standards in non-threatening learning environment.[10] All the simulations and hands-on sessions were inspired by previous face to face Educational Corner in 2019[9] using the principle of the suspension of disbelief to help the attendees learn using scenarios similar to their clinical practice though in a controlled environment.[6,11] Each session started with briefing introduction where the trainers and trainees were presented, followed by explanation of the learning objectives and then an introduction to scenario to ensure engagement and active participation (Figure 1). Confidentiality was highlighted both for participants and cases discussed. The sessions lasted between 60 and

Table 2. Advanced sessions facilitated by international, highly experienced trainers.

Title and number of the sessions	Trainers	
Emergencies on mechanical circulatory support Six sessions	Alex Rosenberg Waqas Akhtar Sofia Da Costa Pinto Emanuele Gerlando	Chris Bowles Olaf Maunz Joe Hughes Agnieszka Wypych
Managing refractory hypoxemia on V-V ECMO Seven sessions	Ibrahim Fawzy Hassan Abdul Salam Saif Ali Ait Hssain	
Membrane Failure and Circuit Change on ECMO Four sessions	Chris Meadows Dan Taylor Peter Sherren Stephen Tricklebank Nicholas Ioannou Nicola Agnew Nigel Gooby	Kath Daly Maria Lozinski Simon Bateman Charlotte Belmonte Catherine Whitley Carl Von Dutch
Renal replacement therapy/plasmapheresis on ECMO Seven sessions	Jo-Anne Fowles Kerry Pooley	Andrew Hadley-Brown Laura Bowden
How to perform perfect simulation Two sessions	Justyna Swol Marek Dąbrowski	Sebastian Stefaniak Mateusz Puslecki
Troubleshooting V-V ECMO Three sessions	Justyna Swol Marek Dąbrowski	Sebastian Stefaniak Mateusz Puslecki
ECPR cannulation Three sessions	Justyna Swol Marek Dąbrowski	Sebastian Stefaniak Mateusz Puslecki
Adventure in paediatric ECMO Eleven sessions	Mirjana Cvetkovic Maura O'Callaghan	Heidi Dalton Jon Lillie
ECPR neck cannulation	Aparna Hoskote	Lars Mikael Broman
ECPR central cannulation	Matteo Di Nardo	Lindsey Pulford
CRRT on ECMO	Velia Marta Antonini	Malaika Mendonca
Troubleshooting	Ajay Desai	Marisa Vieira
ECMO Cannulation Workshop	Alex Robertson	Peter P. Roeleveld
V-V recirculation	Alice Hutin	Ravi Thiagarajan
ECMO for Single Ventricle	Arun Beeman	Robert Jan Houmes
ECMO PIMS-TS (MIS-C)	Chris Harvey	Roberto Chiletti
ECMO for CDH	Giacomo Cavallaro	Sylvia Belda
ECMO Transport	Gillian Wylie	Uri Polak
Neurological injury on ECMO	Hannah Staines	

ECMO: extracorporeal life support; V-V: veno-venous; ECPR: extracorporeal cardiopulmonary resuscitation; CRRT: continuous renal replacement therapy; PIMS-TS: Paediatric Inflammatory Multisystem Syndrome Temporarly Associated with SARS CoV-2; MIS-C: Multisystem inflammatory syndrome in children; CDH: congenital diaphragmatic hernia.

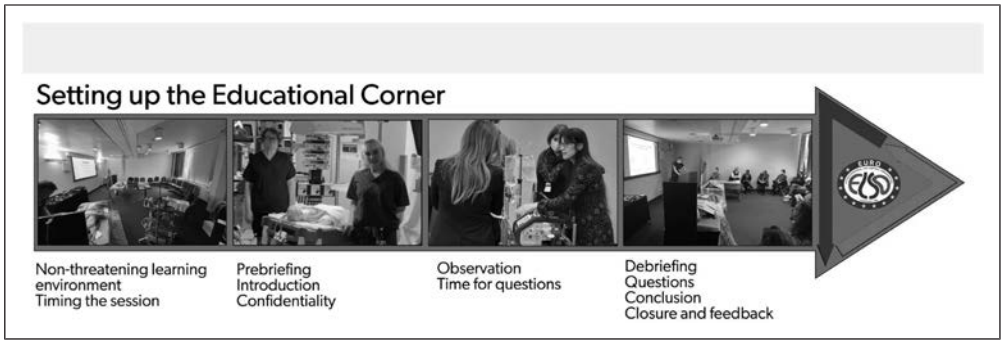


Figure 1. Setting up the educational corner.

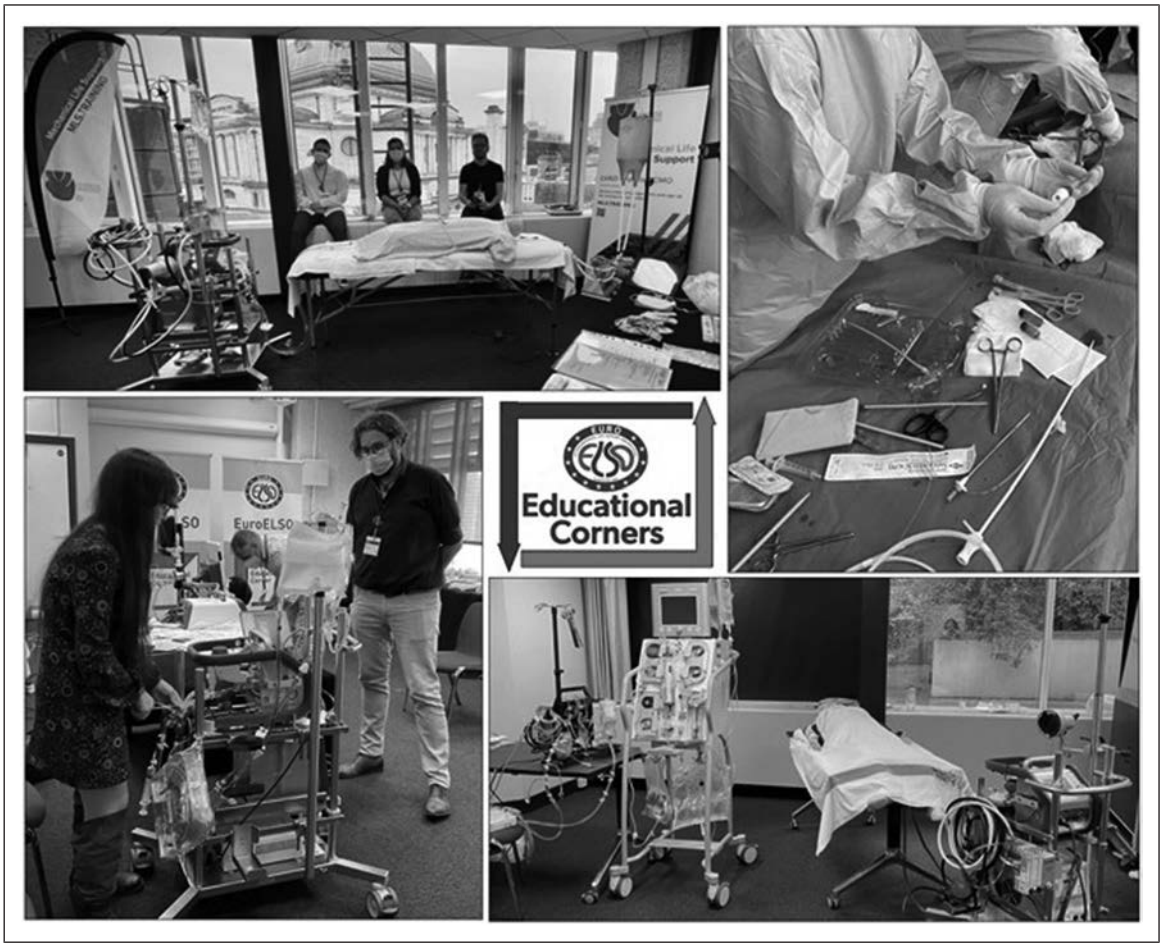


Figure 2. Different training modalities during educational corner.

90 min and covered one or two topics. Trainers were observing the sessions facilitating the requirements of attendees. Time for questions was allocated during and after the sessions. Sessions were built to cover not only technical skills but also behavioral skills maintaining professionalism during teamwork, leadership, call for help, closed loop communication, utilization of available resources etc. Sessions utilised high and low fidelity simulation mannequins, hands on sessions (Figure 2) Majority of the sessions 28 (65%) were simulation based, whilst 15% were hands-on workshops. At the end of each session, a debriefing was performed addressing clinical questions and teamwork, followed by a conclusion and feedback from the participants. A specially tailored questionnaire evaluating the quality of the simulation session was developed by the Working Group for Education of the EuroELSO (appendix 1). The aim was to evaluate the impact of this learning strategy on the attendees using a dedicated questionnaire after each simulation session. The questionnaire included three open-ended questions (with an option for a free response for suggestions and ideas) and five closed-ended questions with response options of 'yes', 'somewhat' or 'no', referring to the educational goals (Table 3). The questionnaire was distributed and collected by congress organisers.

Data analysis

All the data from the completed questionnaires were analysed using an Excel form (Microsoft™ Office Standard Excel version 2016) calculating the numbers, percentages and evaluating free text responses.

Results

The EuroELSO Congress 2022 in London, United Kingdom, was widely attended by 1225 face to face and 175 online international participants from 56 countries. The Educational Corner was attended by more than 400 participants (approximately 33% of face-to-face

Table 3. Feedback form.

Question	Answer
1. Have you received useful information during this workshop?	Yes/Somewhat/No
2. Will it change your current practice?	Yes/Somewhat/No
3. Did the workshop meet the set educational goals & objectives?	Yes/Somewhat/No
4. Do you have suggestions to improve the efficacy of the workshop you attended?	Free text
5. Would you recommend the workshop you participated to your colleagues?	Yes/Somewhat/No
6. Are there any new topics you would like to see included at the Educational Corner of the next EuroELSO Conferences?	Free text
7. Do you consider the Educational Corner – being a practical approach towards ECLS-related techniques – an important part of the EuroELSO annual meeting?	Yes/Somewhat/No
8. Do you have any other recommendations for future EuroELSO Educational Corner workshop?	Free text

ECLS: extracorporeal life support; EuroELSO: Educational Corner within European Chapter of Extracorporeal Life Support Organisation.

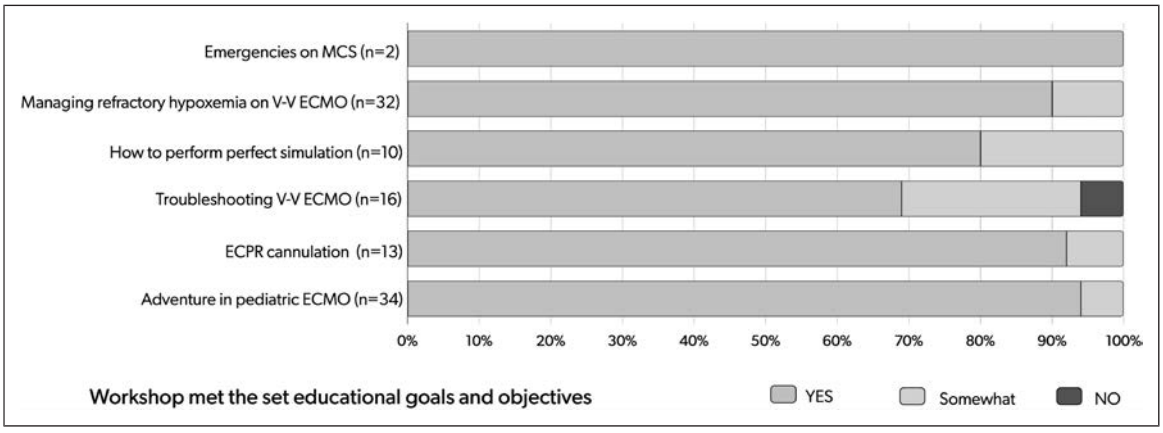


Figure 3. Educational corner goals and objectives. MCS: mechanical circulatory support: ECMO: extracorporeal life support: V-V: veno-venous: ECPR extracorporeal cardiopulmonary resuscitation.

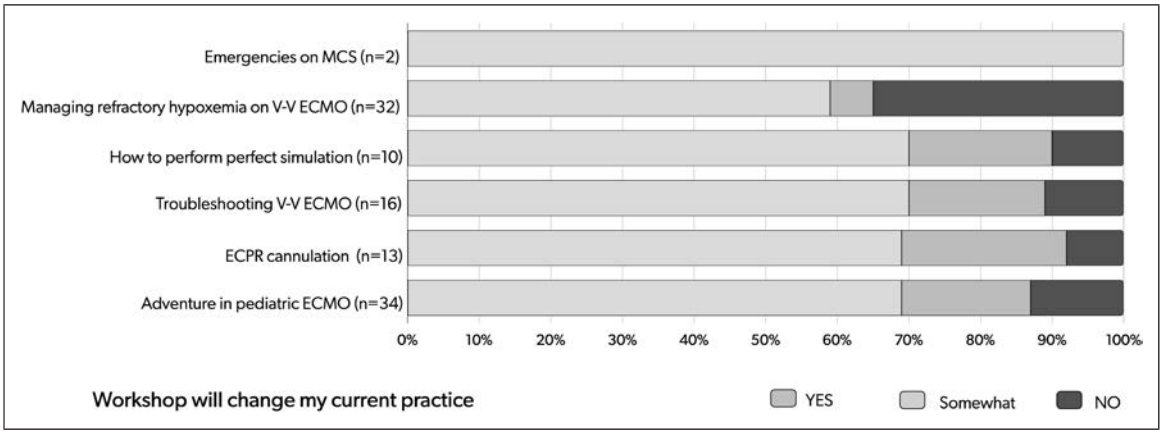


Figure 4. Does educational corner provide a change in current practice. MCS: mechanical circulatory support: ECMO: extracorporeal life support: V-V: veno-venous: ECPR extracorporeal cardiopulmonary resuscitation.

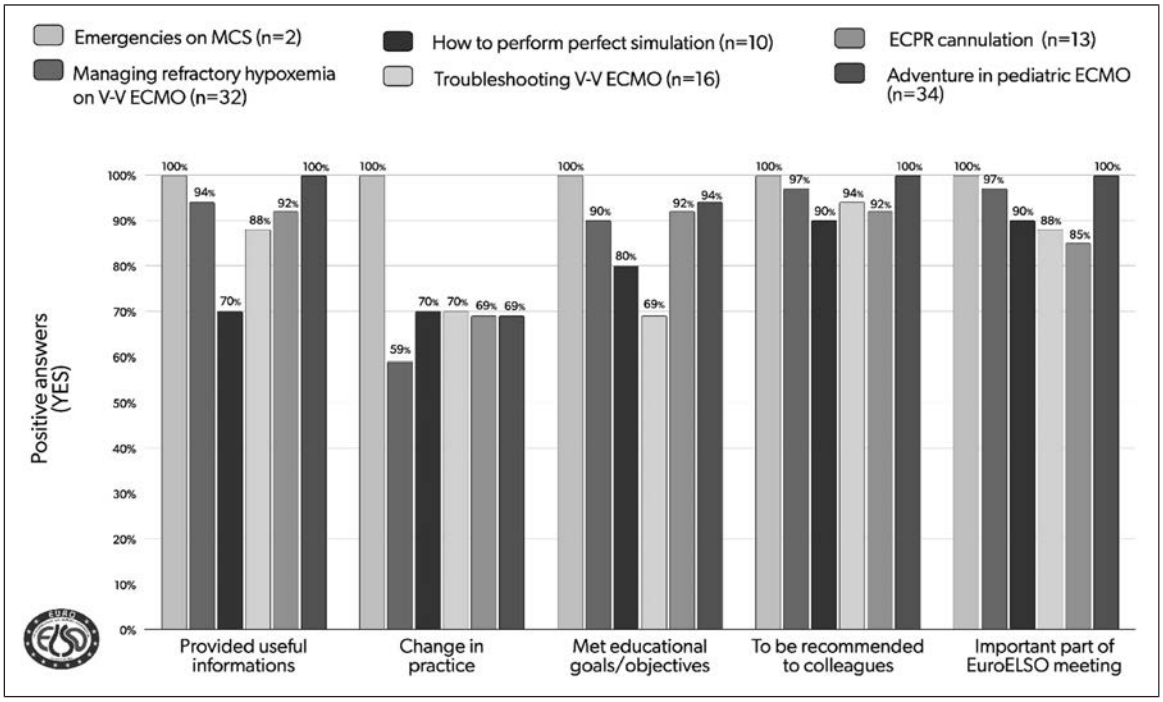


Figure 5. Number of positive answers to the five closed-ended questions. MCS: mechanical circulatory support: ECMO: extracorporeal life support: V-V: veno-venous: ECPR: extracorporeal cardiopulmonary resuscitation.

participants) over the two main congress days. During 43 sessions we collected 107 (approximately 27%) evaluation forms. The feedback for one session (CRRT on ECMO) were misplaced and consequently this session could not be analysed. On feedback form, one session was missing (Membrane Failure and Circuit Change on ECMO) and could not be added to the results. Out of 107 responders, 101 (94%) stated that the Educational Corner was an important part of the EuroELSO annual meeting providing a practical approach to Extracorporeal Life Support (ECLS) related techniques.

The majority of responders 94 (88%) acknowledged that training sessions within Education Corner met the set educational goals & objectives for all sessions (Figure 3). The comments were positive - 101 (94%) responders received useful information during Educational Corner, whilst the vast majority 102 (95%) of responders would recommend the workshop to their colleagues. Importantly, 94 (88%) stated that the workshops would change their current practice in both adult and paediatric settings (Figure 4). The session about troubleshooting V-V ECMO had 69% positive feedback. The participants stated in the free text that there was a time pressure to finish the scenarios and that the groups were large. The sessions about managing refractory hypoxemia had 59% positive feedback. Several participants stated in the free text that the time for simulation was limited. The responses to the five closed questions were extrapolated and compared (Figure 5). In the free text, participants commented that sessions simulating practical aspects, problem solving and emergency ECLS management, for example circuit emergencies, troubleshooting, complications on V-V and V-A ECMO were the most desirable.

Participants reported several potential suggestions for improvement for future sessions requesting more time for comprehensive case-based simulations, use of ultrasound for ECMO cannulations and providing workshop material and treatment algorithms. Furthermore, 20 (19%) participants suggested interesting topics for the next Educational Corner as ECPR, discussion about ECMO candidacy and targets for successful ECMO run, combination and transition from cardiopulmonary bypass to ECMO, daily ECMO management on intensive care unit, troubleshooting for ECMO emergencies and post-cannulation, V-V and V-A ECMO for specific diagnoses, ECMO weaning strategies, paediatric ECMO, hybrid configurations for ECLS support with rationale for changes of configuration and strategy during ECLS, ultrasound guidance in ECMO and more. Participants also suggested separating between basic and advanced training with multidisciplinary sessions providing the workshop material and treatment algorithms on the day. Topics on organisation and leadership in the ECMO Centre and comprehensive

training about simulation setup and handling challenges during simulation were suggested.

Discussion

Educational Corner is an integral ECLS educational platform within EuroELSO Congress. Study results from Educational Corner EuroELSO 2022 showed that the Educational Corner sessions met the set goals and learning objectives, provided useful information to participants and facilitated the changes in their ECLS practice. Majority of participants would recommend Educational Corner to colleagues, and they considered the Educational Corner to be an integrated part of EuroELSO Congress. The Educational Corner Team is aims to use the feedback constructively in further developing the standardised ECMO curriculum, course structure, certification criteria and research in line with the Education ELSO Statement on global ECMO education.[12]

Simulation was first applied to ECLS training in 2006.[13,14] Members of an interprofessional ECMO team have varying levels of experience, and therefore have different educational needs.[15] Several authors have demonstrated positive effects of ECMO simulation training on subsequent performance in simulated scenarios, as well as improved care delivered to patients.[3–5,7] With the significant increase in ECMO utilisation and wider understanding of the challenges for centers, teams, and individual providers, patient care is becoming a dynamic team effort requiring effective training, commonly via simulation.[1,4,6–9,16] Simulation-based training was beneficial in building a successful procedural chain, and to eliminate errors at the stage of identification, notification, transportation, and providing ECMO perfusion therapy.[17] In addition, simulation training is a valuable resource employed to implement novel procedures and pathways.[18,19] Free Open Access Medical Education (FOAM) on social media is a resource used during EuroELSO 2022. FOAM represents an important building block in the acquisition of information in the context of medical training being the ultimate resource for the background, logistics, and evidence for ECMO.[20,21] Simulation safety during the international medical conference was found to be feasible and very successful in increasing the knowledge alongside with understanding and accepting international differences.[22]

The Educational Corner has provided high-quality training utilising different teaching modalities during annual EuroELSO congress since 2012. The Educational Corner has gained popularity and was well described during the annual congress in Barcelona 2019.[9] The feedback results from attendees of international multidisciplinary background in Barcelona showed that Educational Corner training was an excellent way to improve attendees' motivation and knowledge about ECLS using an active learning environment, with a positive impact on their practice. The majority of the delegates expressed the wish to extend the duration of the offered simulation framework in order to demonstrate more types of circuits and increase the number of scenarios. The results extracted from this evaluation provided a framework for improving the efficacy of the workshops for the coming Educational Corners.[9] During COVID-19 pandemic, in 2020 and 2021, no in person training was available but some virtual tools had been offered during EuroELSO Virtual Congress.[23,24] The available direct feedback was excellent for the virtual sessions, but there were some limitations regarding essential training like skill stations - ECMO cannulation and the team-based simulation training which coud not be replaced virtually.

Educational Corner during EuroELSO congress in London 2022 took the previous feedback into account. Educational Corner expanded to 2 days, the number of the sessions increased from 17 to 43 and sessions included both technical skills and multidisciplinary team training. The Educational Corner was running in parallel in four different rooms including V-A and V-V ECMO modalities, cannulations, complications, emergencies and ECPR. The novel sessions included simulation training setup and tips from various international centres. Paediatric sessions expanded providing a large spectrum of high-quality simulation modalities with variety of topics specifically tailored for paediatric population. Current feedback results show an increasing satisfaction with simulation scenarios for all sessions including team training and simulation set up. Attendees from international multidisciplinary background also identified that the aims and goals were set and increasingly met (88%) during the Educational Corner 2022 training sessions. The number of the attendees stating that the sessions would change their current practice increased from 50–88%. This significant increase could be used as a non-specific marker for Quality Improvement facilitated by Educational Corner. Vast majority of the attendees (95%) stated that they would recommend Educational Corner to their colleagues, and that Educational Corner was perceived as an integrated part of the EuroELSO Congress. Spontaneous positive comments of the attendees suggested that expansion of Educational Corner would be desired. Simulation training during Educational Corner represents an ideal platform to deliver standardised training in the safe environment, allowing the rehearsal or unusual or infrequent life-threatening critical incidents.

The sessions on troubleshooting V-V ECMO had 69% positive feedback. The participants stated in the free text that there was a time pressure to finish the scenarios and that the groups were large. The sessions about managing refractory hypoxemia had 59% positive feedback. Several participants stated in the free text that the time for simulation was limited. This will be addressed for the next Education Corner EuroELSO 2023 in Portugal.

The advantages of Educational Corner during the congress include – no additional cost to delegate, delivered by highly experienced faculty, access to sessions without complex registration process, and user satisfaction as shown in the evaluation of feedback. The future developments of the Educational Corner will be aimed at standardisation of the educational programs and guidelines across Europe providing EuroELSO attendance certificate upon conditional feedback.

Limitations

The main limitation of this study was the low response rate. Due to missing forms, unfortunately, some attendees expressed their thoughts which could not be considered during the evaluation as the forms were lost. The forms for two topics in particular (Membrane Failure and Circuit Change on ECMO and CRRT on ECMO) were lost, however validation of the other sessions remained feasible. To address this, we will simplify the evaluation at future Educational Corners congresses using online feedback forms with shared QR code and providing EuroELSO standardised attendance certificate upon conditional feedback. Another significant limitation is that demographic data were not collected on the delegates who filled in the questionnaires nor the level of their ECMO experience. An important limitation was the difficulty in linking Educational Corner sessions with improved clinical practice or other local outcomes. With increasing standardisation of the training facilitated by Educational Corner, the clinical outcomes may become apparent in the future. Moreover, organising Educational Corner workshop is demanding regarding time invested, logistics and equipment needed. Hence, support from the industry and congress organisers is necessary to maintain the Educational Corner.

Conclusion

Educational Corner represents high-quality simulation based ECLS training and is seen as an integrated event dedicated to ECMO education and training during annual EuroELSO. Significant variability and limitations in global ECLS education is apparent.[25] Structured high quality ECLS based education with unified curriculum, evaluation, assessment tools and research are current focus for EuroELSO society.[12] The Educational Corner Team is aiming to follow and participate in further developing the standardised ECMO curriculum, course structure, certification criteria and research in line with the Education ELSO Statement ELSO on global ECMO education.[12]

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Declaration of conflicting interests

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Supplemental Material

Supplemental material for this article is available online.

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Extracorporeal life support provision in COVID-19 patients - An international EuroELSO 2022 update survey

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Abstract

Introduction: An analysis on the ECLS use for patients with respiratory or cardiac support in COVID-19 based on an international response to EuroELSO survey, aims to generate a more comprehensive understanding of ECLS role during the recent viral pandemic.

Methods: EuroELSO announced the survey at the 10th annual congress in London, May 2022. The survey covered 26 multiple-choice questions.

Results: The survey returned 69 questionnaires from 62 centers across 22 European countries and seven centers across five non-European countries. Most of the centers providing ECLS for COVID-19 patients had more than 30 runs for respiratory support since December 2019. In the same period, at least 31 runs in adult COVID-19 patients have been performed in 48 of 69 centers (69.6%). The reported pediatric data from 18 centers is limited to less than the patients per center.

Conclusion: Majority of the COVID-19 patients received respiratory ECLS support and adult patients dominated. The indications and contraindications are broadly aligned with available guidelines. Most of the centers considered age >65 or biological age as a relative or absolute contraindication for ECLS in COVID-19. ECLS withdrawal criteria in COVID-19 are controversial because the long-term outcomes after ECLS in COVID-19 and the impact of critical illness and the impact of long-COVID are still not known.

Keywords

ECMO, extracorporeal membrane oxygenation, ECLS, extracorporeal life support, COVID-19, SARS-CoV-2

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Introduction

A surge of patients with acute respiratory distress syndrome (ARDS) due to pandemic Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) disease 2019 (COVID-19) pushed healthcare systems, hospitals, emergency departments and intensive care units worldwide to a verge of collapse. Those most severely affected by COVID-19-related ARDS (CARDS) could be offered Extracorporeal Life Support (ECLS) as a bridge to lung recovery. Thus, ECLS experienced an increasing usage during the COVID-19 pandemic.[1–3] To generate a more comprehensive understanding of ECLS usage for adult and pediatric patients a survey was performed which aimed to provide an insight in the use of ECLS for patients with respiratory or cardiac support in COVID-19.

Methods

All members of EuroELSO Scientific and Steering Committees approved the survey questionnaire. The survey was largely promoted through the Organization Web site, newsletter, social media channels and during the 10th EuroELSO Congress in London, May 4th – 6th, 2022 (Suppl. File 1). Data entry was enabled between May 1st and 31 May 2022.

The questionnaire included various aspects of both clinical and organizational practices since the COVID-19 pandemic began in December 2019. The survey covered 26 multiple-choice questions available via an online platform (SurveyMonkey Version 3.0.1 San Mateo, California, United States). The first 10 questions focused on statistical details such as geographical location, center characteristics, patient age groups and number of runs in COVID-19 patients. Further 16 questions addressed various aspects of transport, contraindications, complications regarding COVID-19 patients supported on ECLS (Suppl. File 2).

Institutional Review Board review was waived since individual subjects cannot be identified and patient data was not asked for. In accordance with General Data Protection Regulation (https://gdpr-info.eu/), no respondent data were stored. Participation in the survey was voluntary. Results are presented as descriptive statistics. We acknowledged one response per each participating ECLS center. Duplicates were merged to one response (Suppl. File 3).

Results

The survey returned 69 questionnaires from 62 centers across 22 European countries, and seven centers across five non-European countries (among others United States, Australia) after excluding eight duplicates and

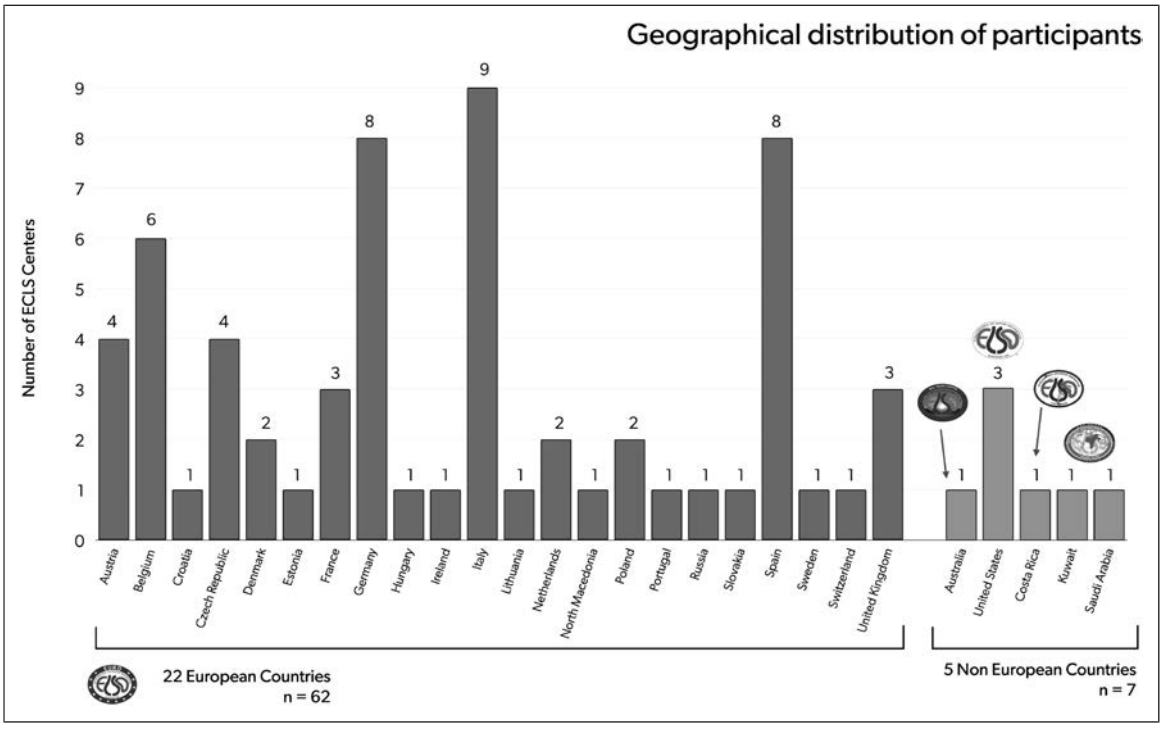

Figure 1. Geographical distribution of participants; ECLS – extracorporeal life support.

six implausible responses (Suppl. File 4). Most responses were from Europe and 40% of them from Italy (9), Germany (8) and Spain (8) (Figure 1). Fifty-nine centers (85.5%) provided both respiratory and cardiac support, but respiratory support in majority of runs. No geographical differences were recorded. Sixty-eight percent of centers performed 31 or more runs for respiratory support, and 10.1% of centers performed at least 31 runs or more of cardiac support in COVID-19 patients (Table 1).

More than 95% of participating centers performed ECLS for adults. Only two centers (2.9%) reported use of ECLS in neonates and 18 centers (26.1%) in pediatric COVID-19 patients, mostly less than 10 runs. Provided numbers were higher in adult patients: 21.7% reported 31–50 runs, 27.5% performed 51–100 runs and 20.3% more than 100 runs (Table 2). Almost 67% retrieval services included transfer on ECLS and around 26% retrievals without ECLS were followed by cannulation in referral hospital (Table 3, Figure 2). The hybrid configuration (V-AV ECLS) was used in about 23% (Table 4).

Mostly, patient's age was considered as a potential contraindication. Almost 50% of responders considered age above 65 years as a relative and nearly 16% as an absolute contraindication for ECLS in COVID-19. In more than 24% of responses no specific cut off was set, as individual decisions were based on the patient's biological age. Furthermore, 72.5% of responders considered multiorgan failure including cardiac failure with need for high-dose vasopressors in continuous resuscitation rate as a contraindication, and 69.6% considered prolonged invasive ventilation for more than 10 days as a contraindication (Table 5, Figure 3).

The majority of responders (68.1%) used dexamethasone 6 mg for at least 10 days as additive therapy. In 72.5% of the participating centers therapeutic

Table 1. Basic statistics: Center characteristics and number of runs in COVID-19 patients.

Questions	*N*	(%)
ELSO center (N = 69)		
Yes	43	(62.3)
No	21	(30.4)
I don't know	5	(7.2)
Type of support provided at the ECLS center (*N* = 69)		
Both cardiac and respiratory	59	(85.5)
Respiratory ECLS	7	(10.1)
Cardiac ECLS	3	(4.3)
Number of runs for respiratory support in COVID-19 patients since Dec 2019 (*N* = 69)		
>100	11	(15.9)
51–100	20	(29.0)
31–50	16	(23.2)
11–30	15	(21.7)
1–10	7	(10.1)
No runs	0	(0.0)
Number of runs for cardiac support in COVID-19 patients since Dec 2019 (*N* = 69)		
>100	2	(2.9)
51–100	3	(4.3)
31–50	2	(2.9)
11–30	19	(27.5)
1–10	32	(46.4)
No runs	11	(15.9)
Other programs provided at the ECLS center (*N* = 69) (multiple answers possible)		
Implantable VAD	40	(58.0)
Heart transplant	31	(44.9)
Lung transplant	15	(21.7)
None of above	29	(42.0)
Age groups of COVID-19 patients treated at the ECLS center (*N* = 69)		
Adult only	50	(72.5)
Pediatric and adult	11	(15.9)
Neonatal, pediatric and adult	5	(7.2)
Neonatal and pediatric	2	(2.9)
Pediatric only	1	(1.4)
Neonatal only	0	(0.0)

Table 2. Number of runs in different age groups (adult, pediatric, neonatal).

Questions	*N*	(%)
Number of runs in neonatal COVID-19 patients since Dec 2019 (*N* = 69)		
>100	0	(0.0)
51–100	0	(0.0)
31–50	0	(0.0)
11–30	0	(0.0)
1–10	2	(2.9)
No runs	67	(97.1)
Number of runs in pediatric COVID-19 patients since Dec 2019 (*N* = 69)		
>100	0	(0.0)
51–100	0	(0.0)
31–50	0	(0.0)
11–30	1	(1.4)
1–10	17	(24.6)
No runs	51	(73.9)
Number of runs in adult COVID-19 patients since Dec 2019 (*N* = 69)		
>100	14	(20.3)
51–100	19	(27.5)
31–50	15	(21.7)
11–30	14	(20.3)
1–10	4	(5.8)
No runs	3	(4.3)

anticoagulation was routinely performed, and 56.5% used heparin with a goal of aPTT (activated partial thromboplastin time) of 50–60 s. Higher need for circuit changes due to clotting was observed in 63.8% of the centers despite widely administered therapeutic anticoagulation (Table 4, Figure 4).

Heterogenous interventions and configuration changes were preferred in hypoxic patients

Table 3. Regional distribution and transport modalities for COVID-19 patients.

Statements	*N*	(%)
The following statement best describes the indicated ECLS center regarding COVID-19 patients (*N* = 69) (multiple answers possible)		
ECLS is provided for COVID-19 patients from across the region/country; a retrieval service is offered and this includes transport on ECLS when indicated	46	(66.7)
ECLS is provided for COVID-19 patients from across the region/country; a retrieval service is offered but this does not include transport on ECLS	18	(26.1)
ECLS is provided only for COVID-19 patients originating in this center; no retrieval service is offered	4	(5.8)
ECLS is provided only for COVID-19 patients originating in this center; patients are cannulated and referred to specialized centers for further ECLS	0	(0.0)
None of above	0	(0.0)
Further services	3	(4.3)

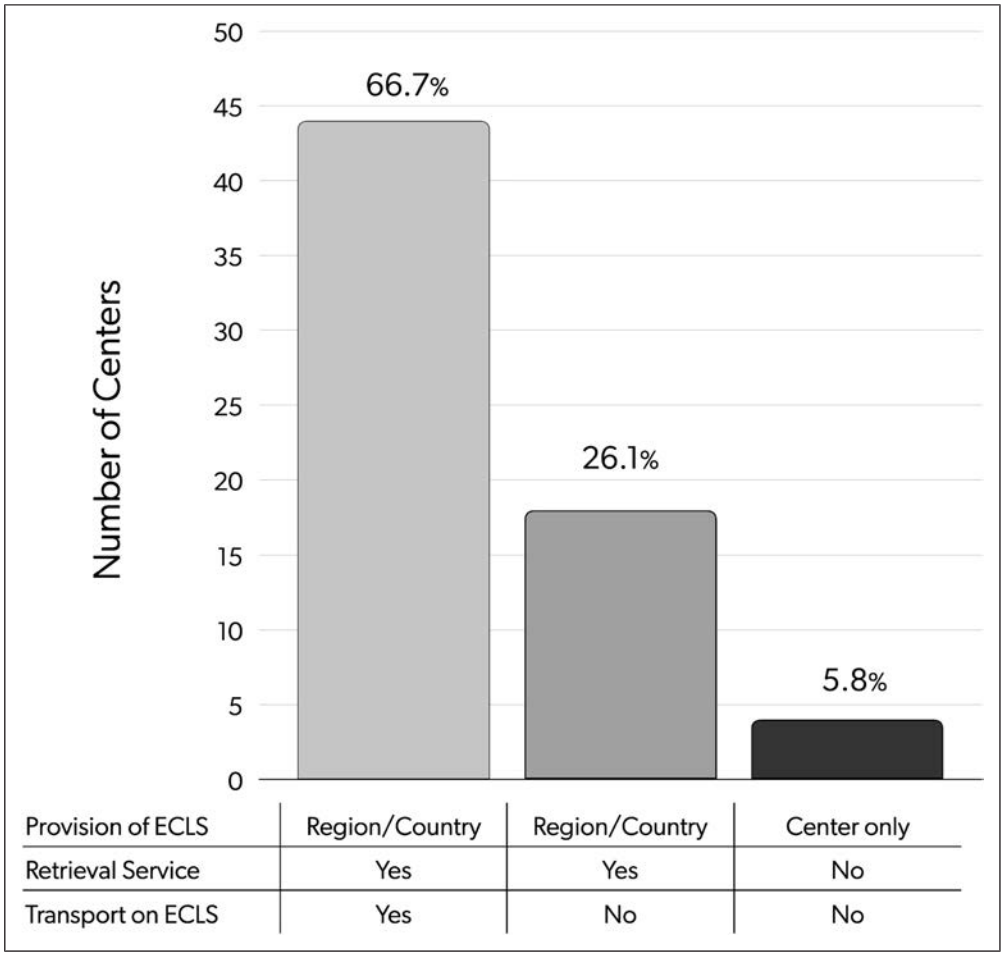

Figure 2. Regional distribution and transport modalities for COVID-19 patients; COVID-19 – Corona Virus Disease 2019, ECLS – extracorporeal life support.

Table 4. Medical treatment of COVID-19 patients with need of ECLS support.

Statement	*N*	(%)
Following immunosuppressive therapy would be initiated in ECLS center for COVID-19 patients supported on ECLS (*N* = 69) (multiple answers possible)		
Dexamethasone 6 mg for at least 10 days	47	(68.1)
Tocilizumab	34	(49.3)
Methylprednisolone	24	(34.8)
A higher dose than 6 mg of dexamethasone	20	(29.0)
Baricitinib 4 mg	7	(10.1)
Anakinra	4	(5.8)
Other	6	(8.7)
The routine management of COVID-19 patients on ECLS in the indicated center includes the following actions (*N* = 69) (multiple answers possible)		
Therapeutic anticoagulation	50	(72.5)
Bronchioalveolar lavage or aspirate if signs of co-infection	36	(52.2)
Bronchioalveolar lavage or aspirate before ECLS cannulation or right away after	30	(43.5)
Bronchioalveolar lavage or aspirate once a week to monitor for SARS-CoV-2, aspergillus, bacterial and viral co-infections	28	(40.6)
Single thorax CT scan before ECLS cannulation or right away after	28	(40.6)
Whole body CT scan (cranial, thorax and abdomen) before ECLS cannulation or right away after	18	(26.1)
Routine antifungal therapy even if no proof of fungal infection	7	(10.1)
Other	7	(10.1)
The anticoagulation goals and their monitoring in COVID-19 patients on ECLS include the following combination (*N* = 69) (multiple answers possible)		
Anticoagulation with heparin, goal of aPTT (activated partial thromboplastin time) of 50–60 s	39	(56.5)
Anticoagulation with heparin, goal of anti Xa (anti-factor Xa-activity) of 0.3–0.4 IU/mL	12	(17.4)
Anticoagulation with argatroban, goal of aPTT of 50–60 s	10	(14.5)
Anticoagulation with heparin, goal of anti Xa of 0.2–0.3 IU/mL	8	(11.6)
Anticoagulation with bivalirudin, goal of aPTT of 50–60 s	5	(7.2)
Other	13	(18.8)
Despite therapeutic anticoagulation, there are higher needs for circuit changes due to clotting in COVID-19 than in non-COVID patients (*N* = 69)		
Yes, that was observed at our center	44	(63.8)
No, I don't agree	21	(30.4)
I do not know	3	(4.3)
Other	1	(1.4)
Cerebral bleeding is more common in COVID-19 patients compared to non-COVID patients (*N* = 69)		
No, I don't agree	39	(56.5)
Yes, that was observed at our center	21	(30.4)
I do not know	8	(11.6)
Other	1	(1.4)
Interventions in COVID-19 patients, who are hypoxic (PaO2 < 60 mmHg) and/or raising levels of lactate occur during respiratory support on VV-ECLS (*N* = 69) (multiple answers possible)		
Deep sedation Ramsay score at least −4	40	(58.0)

(continued)

Table 4. (continued)

Statement	*N*	(%)
Increase in ECLS blood flow at least to 6 L/min	38	(55.1)
Betablocker use to decrease cardiac output	34	(49.3)
Configuration change	25	(36.2)
Red blood cell transfusion with goal of hemoglobin at least of 12 g/dL	23	(33.3)
Mild hypothermia of 35°C	22	(31.9)
None of above will be performed	5	(7.2)
Other	12	(17.4)
Configuration change in COVID-19 patients, who are hypoxic and/or raising levels of lactate occur during respiratory support on VV-ECLS (*N* = 69) (multiple answers possible)		
Cannulation with additional drainage cannula (venous site)	32	(46.4)
No configuration change will be performed	19	(27.5)
Configuration change to veno-arterialvenous ECLS (V-AV ECLS)	16	(23.2)
Configuration change to peripheral veno-arterial ECLS (V-A ECLS)	13	(18.8)
Configuration change to adding a second oxygenator	9	(13.0)
Configuration change to central V-A ECLS	1	(1.4)
Other	4	(5.8)
Adjuvant therapies or interventions routinely used in COVID-19 patients supported on ECLS (*N* = 69) (multiple answers possible)		
Use of neuro-muscular blockage	56	(81.2)
Prone positioning	55	(79.7)
Recruitment (open the lung) maneuvers	37	(53.6)
Inhaled nitric oxide	29	(42.0)
Inhaled prostacyclines	8	(11.6)
Almitrine	0	(0.0)
Other	6	(8.7)
The routine management of COVID-19 patients on ECLS in the indicated center includes one of the following actions (*N* = 67)		
Tracheotomy between day 7 and 13 on ECLS	18	(26.9)
Early tracheotomy (<6 days on ECLS)	16	(23.9)
Late tracheotomy (>14 days on ECLS)	15	(22.4)
Aim to extubate if failed late tracheotomy (>14 days on ECLS)	12	(17.9)
Extubation (no need for tracheotomy)	3	(4.5)
Other	3	(4.5)
Performance of awake ECLS in COVID-19 patients supported on ECLS; awake = RASS 0 to -1 (*N* = 68)		
Awake ECLS is considered to be rarely possible because of very limited compliance of the lungs in COVID-19 patients and high respiratory drive	35	(51.5)
Awake ECLS is tried in every patient	20	(29.4)
Awake ECLS is not tried in any patients on ECLS at all	7	(10.3)
Awake ECLS is considered to be rarely possible because of very overwhelming context and/or deficit of personnel	4	(5.9)
Other	2	(2.9)

(continued)

Table 4. (continued)

Statement	*N*	(%)
Mobilization and physiotherapy in COVID-19 patients supported on ECLS (*N* = 68)		
Mobilization out of bed is not done in patients on ECLS	26	(38.2)
Mobilization out of bed is tried in selected patients	24	(35.3)
Mobilization out of bed is tried in many patients (<50%)	17	(25.0)
Other	1	(1.5)
ECLS would be stopped in COVID-19 patients generally in the following cases (*N* = 68) (multiple answers possible)		
Irreversible brain damage (bleeding, ischemia) occurs	63	(92.6)
Multi-organ failure (e. g. due to sepsis) developed after more than 14 days of ECLS	37	(54.4)
Need for high-dose vasopressors (adequate to resuscitation) due to irreversible heart failure	33	(48.5)
There are signs of pulmonary fibrosis in the CT-scan and progressive right heart failure occurs	24	(35.3)
COVID-19 patient will be evaluated for bridging to lung transplantation if no recovery occurs before evaluating futility	22	(32.4)
No improvement in lung function after 8 weeks	13	(19.1)
No improvement in lung function after 12 weeks	11	(16.2)
No improvement in lung function after 4 weeks, and lung compliance is below 15 mL/cmH2O	5	(7.4)
We never stop ECLS due to futility	5	(7.4)
There is proof of invasive aspergillosis	4	(5.9)
Other	2	(2.9)
Following co-infections were observed in the ECLS center in some of the COVID-19 patients supported on ECLS (*N* = 68) (multiple answers possible)		
Klebsiella pneumoniae	55	(80.9)
Pseudomonas aeruginosa	54	(79.4)
Staphylococcus aureus	48	(70.6)
Aspergillus	45	(66.2)
Escherichia coli	34	(50.0)
Stenotrophomonas maltophilia	31	(45.6)
Acinetobacter baumannii	30	(44.1)
Herpes simplex virus	23	(33.8)
Cytomegalo virus	22	(32.4)
Mucor-/Cygomyces	4	(5.9)
Other	5	(7.4)

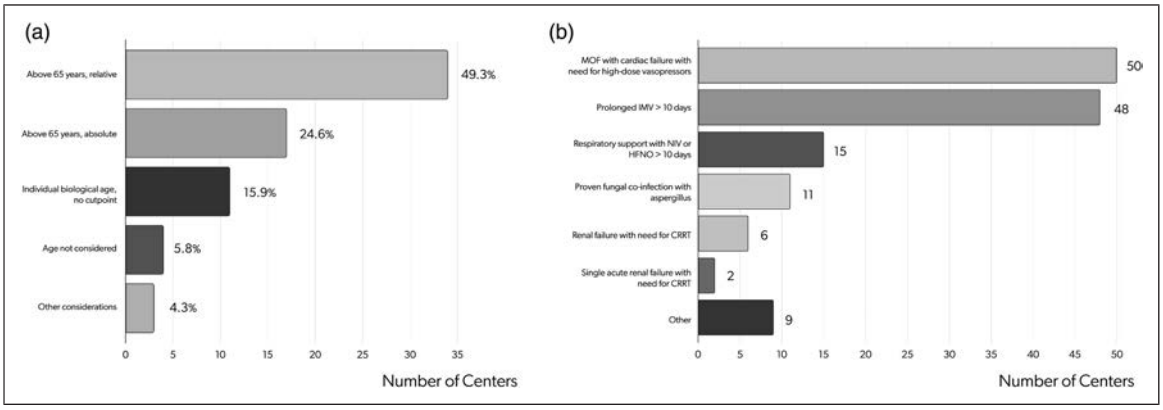

Figure 3. Contraindications for the use of ECLS in COVID-19 patients; ECLS – extracorporeal life support, COVID-19 – Corona Virus Disease 2019, MOF – multiorgan failure, IMV – invasive mechanical ventilation, NIV – non-invasive ventilation, HFNO – high-flow nasal oxygen, CRRT – continuous renal replacement therapy.

(PaO_2 < 60 mmHg), and/or patients with raising levels of lactate occurring during respiratory support on VV ECLS. Deep sedation (Ramsay score at least −4) in 58.0% and increase of blood flow at least to 6 L/min in 55.1% were performed in such situations. Cannulation with an additional drainage cannula was the mostly performed configuration change (46.4%). Use of neuromuscular blockage (81.2%), prone positioning (79.7%), open lung recruitment maneuvers (53.6%), and inhaled nitric oxide (42.0%) were used as additive procedures (Table 4).

Tracheotomy, mobilization, or physiotherapy as well as implementation of awake ECLS also showed wide practice variability among responders. For instance, awake ECLS was considered rarely possible according to 51.5% of responders due to limited lung compliance and high respiratory drive. In contrast, awake ECLS was aimed for in all patients in 29.4% of participating centers (Table 4, Figure 4).

Few individual responders (7.4%) considered withdrawing ECLS if there was no improvement in lung function after 4 weeks or lung compliance was persistently below 15 mL/cmH2O, or in cases of proven invasive aspergillosis (5.9%). However, a substantial number of centers (92.6%) withdrew organ support in cases of irreversible brain damage (e. g. bleeding, ischemia) (Table 4).

Discussion

The results were not surprising and quite similar to previous published findings.[1–9] The previous EuroELSO approved survey was performed in 2 June020[3] and was based on questionnaire consisting of 45 questions and distributed to 4193 physicians with response rate of 9%. At that time, it was highly unlikely that ECLS would be broadly recommended to critical care providers for COVID-19, given its high demands on personnel and resources.[4] Also, COVID-19 pathophysiology was still poorly understood, and little was known about how to tailor ECLS to meet COVID-19 specific challenges, such as hypercoagulability or how long ECLS should be continued when patients failed to improve. Experience with ECLS for COVID-19 was then still very limited as only two to six patients with COVID-19 had received ECLS in 30% of responding centers, with 85% of all centers having supported a maximum of 15 patients on ECLS in the previous survey.[3] Extracorporeal Life Support Organization Registry and COVID-19 Addendum reported outcomes for 1035 patients with COVID-19 supported on ECLS before May 1st in 2020, with cumulative incidence of in-hospital mortality 90 days after starting ECLS of 37.4%.[10] After 2 years of pandemic, the care of patients with COVID-19 and ECLS criteria for those patients has significantly changed[11] and the use of ECLS has increased.[1,2] Thus, the numbers in the current survey were much higher in adult patients: 21.7% centers reported 31–50 runs, 27.5% performed 51–100 runs and 20.3% more than one hundred runs.

The majority of the patients received respiratory support and adult patients dominated. The indications and contraindications are broadly aligned with ELSO guidance.[11] A substantial proportion (67%) of retrievals was for patients on ECLS and around 26% of retrievals without ECLS, followed by cannulation in referral hospital. This proportion differs from the previous survey, when ECLS has mostly been initiated in the participants' hospitals (63%).[3] The majority of ECLS cannulations were performed in VV

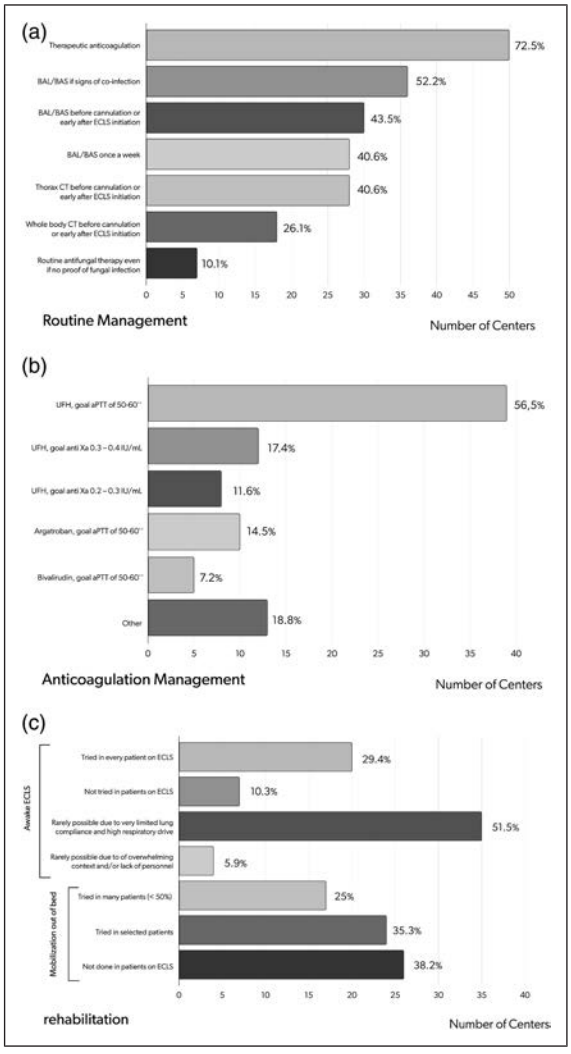

Figure 4. Routine management, anticoagulation, and rehabilitation in COVID-19 patients on ECLS; COVID-19 – Corona Virus Disease 2019, ECLS – extracorporeal life support, BAL/BAS – bronchoalveolar lavage or aspirate, CT – computed tomography, UFH – unfractionated heparin, aPTT – activated partial thromboplastin time, antiXa – anti-factor Xa-activity.

configuration for respiratory support similar to previous reports.[1–3,5,7] The current survey showed increasing trends in use of ECLS for cardiac support and in use of hybrid configuration compared to previous findings.[2,3] The hybrid configuration (V-AV ECLS) was used in about 23%, e. g. for refractory hypoxemia, and about 10% of centers performed at least 31 runs or more of cardiac support. Regarding COVID-19 pathophysiology as systemic disease inclusive cardiomyopathy and coagulopathies, the use of cardiac support might be still underutilized.[8,12]

The use of heparin is within a usual practice. Interestingly, the loss of circuits in COVID-19 patients is higher compared to non-COVID-19 patients with ARDS, likely due to the inflammatory and procoagulant nature of the disease. Surprisingly, that evidence-based treatments were not used consistently, and it is worth exploring reasons for this, e. g. significant sepsis and MOF with concerns about deteriorations. Predominantly, Gram negative bacteria were detected in case of prolonged pneumonia. Broadly, the similar favor rescue therapies for refractory hypoxia aligned with the guidelines.[10,11]

Physiotherapeutic interventions during and after ECLS in COVID-19 patients were described as feasible and safe,[9] however personal protection and wearing masks were considered an additional burden. The optimal physiotherapy approach depends on sedation level, cannula configuration and type, cannulation site and others.[9] Tracheotomy, mobilization, and physiotherapy also showed wide practice variability among responders in the current survey. Contraindications and ECLS withdrawal in COVID-19 are aligned to these in non-COVID cohort especially regarding irreversible brain damage (e. g. bleeding, ischemia). However, the long-term outcomes after ECLS in COVID and the impact of critical illness and the impact of long-COVID are still not known.

Limitations

The findings reflect opinions of a quite large cohort of physicians who used ECLS in COVID-19 patients, but the number of responses was lower compared to the previous EuroELSO survey approved 2 years ago.[3] The survey announcement was broadly open; thus we are not able to provide any response rate because the questionaries were not distributed directly to the centers or individuals. Further, the interpretation of the results regarding countries is not feasible, thus only descriptive characteristics and no generalizability or statistical tests across the countries were performed. Also, a sub analysis regarding European centers compared to non-European is not feasible. The non-European countries distributed over various continents are underrepresented. We also did not ask for outcome data. Hence, we cannot provide any evidence on ECLS-related end points, as overall survival, or ICU discharge. No analyses regarding center characteristics, age groups, patient categories, modes, and no outcome data were recorded thus no complex statistical analyses are available. The reported pediatric data is very limited to be pointless.

Table 5. Contraindications for the use of ECLS in COVID-19 patients.

Statements	*N*	(%)
Contraindications depending on patient's age generally accepted in the ECLS center (N = 69)		
Relative contraindication age above 65 years	34	(49.3)
No specific cutpoint, individual decision based on biological age	17	(24.6)
Absolute contraindication age above 65 years	11	(15.9)
Age is not considered as a contraindication at all	4	(5.8)
Other considerations	3	(4.3)
Contraindications depending on several conditions generally accepted in the ECLS center (N = 69) (multiple answers possible)		
Multi-organ failure inclusive cardiac failure with need for high-dose vasopressors (continous resuscitation dose)	50	(72.5)
Prolonged invasive ventilation for more than 10 days	48	(69.6)
Prolonged respiratory support with non-invasive ventilation or high-flow oxygen for more than 10 days	15	(21.7)
Proven fungal co-infection with aspergillus	11	(15.9)
Renal failure with need for CRRT	6	(8.7)
Single acute renal failure with need for CRRT	2	(2.9)
Other	9	(13.0)

However, it reflects the pandemic reality while mostly adult population was affected.[13,14]

Conclusion

The majority of the COVID-19 patients on ECLS received respiratory support and adult patients dominated. The indications and contraindications are broadly aligned with available guidelines. Most of the centers considered age >65 or biological age as a relative or absolute contraindication for ECLS in COVID-19. ECLS withdrawal criteria in COVID-19 are still difficult to define because the long-term outcomes after ECLS in COVID and the impact of critical illness and the impact of long-COVID are still not known.

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Supplemental Material

Supplemental material for this article is available online.

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GEospatial aNalysis of ExtRacorporeal membrane oxygenATion in Europe (GENERATE)

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Abstract

Introduction: A cross-sectional survey GENERATE (GEospatial aNalysis of ExtRacorporeal membrane oxygenATion in Europe) initiated on behalf of the European chapter of the Extracorporeal Life Support Organization (EuroELSO), aims to provide a systematic, detailed description of contemporary Extracorporeal Life Support (ECLS) provision in Europe, map the spatial distribution of ECLS centers, and the accessibility of ECLS.

Methods: Structured data collection forms were used to create a narrative description of ECLS provision in EuroELSO affiliated countries. This consisted of both center-specific data and relevant national infrastructure. Data was provided by a network of local and national representatives. Spatial accessibility analysis was conducted where appropriate geographical data were available.

Results: 281 centers from 37 countries affiliated to EuroELSO were included in the geospatial analysis and demonstrate heterogeneous patterns of ECLS provision. Accessibility of ECLS services within 1 hour of drive-time is available for 50% of the adult population in 8 of 37 countries (21.6%). This proportion is reached within 2 hours in 21 of 37 countries (56.8%) and within 3 hours in 24 of 37 countries (64.9%). For pediatric centers, accessibility is similar with 9 of 37 countries (24.3%) reached the covering of 50% of the population aged 0–14 within 1 hour and 23 of 37 countries (62.2%) within 2 hours and 3 hours.

Conclusions: ECLS services are accessible in most of the European countries, but their provision differs across the continent. There is still no solid evidence given regarding the optimal ECLS provision model. The spatial disparity in ECLS provision demonstrated in our analysis requires governments, healthcare professionals and policy makers to consider how to develop existing provision to accommodate the anticipated increase in need for time critical access to this advanced support modality.

Keywords

extracorporeal life support, extracorporeal membrane oxygenation, geospatial analysis, regionalization, ECLS, ECMO

Introduction

The scope of extracorporeal life support (ECLS) has expanded significantly in recent decades. Evidence exists for benefit in organ support by ECLS in a wide range of cardiac and pulmonary pathologies, in adults, children and neonates.[1–6] ECLS term is often used interchangeably with extracorporeal membrane oxygenation,

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however the term ECLS signify a broader term for support and is consistent with recommended Extracorporeal Life Support Organisation (ELSO) nomenclature.[7] ECLS use is supported by a growing number of randomised or observational trials based on robust ELSO registry database[8–14] and features in international guidelines.[15–27] ECLS is a complex and resource intensive undertaking and relies upon personnel and technology previously confined in cardiothoracic surgical centers, ubiquitous access is therefore challenging. Healthcare systems have sought to address the challenges of access to ECLS in different ways.[28] Some have introduced national networks with a limited number of designated, retrieval capable, providers [29,30]; in other countries, arrangements have evolved at local and regional levels without particular restrictions or requirements.[31,32] Based on this geographical diversity, it was difficult to understand and assess the actual provision state and regulations throughout Europe either in terms of access or capacity, particularly under pressure during the COVID-19 crisis.[33–35]

The GENERATE (GEospatial aNalysis of ExtRacorporeal membrane oxygenATion in Europe) survey seeks to support such planning and decision-making by providing a systematic, detailed, and quantitative analysis of contemporary ECLS provision and access in Europe. The project aims to map the spatial distribution of ECLS centers in European countries and to provide a comprehensive analysis of the availability of ECLS, for adult and pediatric, cardiac, and respiratory support in Europe.

Methods

Descriptive analysis

A cross-sectional survey was initiated on behalf of EuroELSO, the European chapter of the Extracorporeal Life Support Organization (ELSO), in collaboration with the Institute of Geography at the University of Edinburgh and Paracelsus Medical University Nuremberg, Germany (Suppl. File 1). The research was reviewed and approved by the Ethics Committee of the School of Geosciences, University of Edinburgh (Ref: 2021-516).

ECLS was defined as the provision of oxygen and carbon dioxide exchange through the use of an extracorporeal circuit consisting minimally of a blood pump, artificial lung, and vascular access cannulae, using blood flows sufficient to support oxygenation and concomitantly enhance carbon dioxide removal.[7] A hospital providing ECLS was defined as a hospital which, within the designated time-period, has initiated ECLS on at least one occasion. Centres using ECLS exclusively for perioperative support are not included. To simplify the manuscript phrasing "hospital providing ECLS" is used equivalent with "ECLS center", but the meaning is not equivalent to designated "ELSO center."

Data was collected by means of a structured survey. Survey text was developed by the members of Steering Committee through an interactive approach according to the CHERRIES[36] statement (Suppl. File 2). Survey content is presented in the supplemental material (Suppl. File 3). Participation of centers was voluntary. Only one response was accepted from each center. Duplicates were merged to one response per center and non-eligible datasets were removed before analysis. The online questionnaire was conducted via Netigate Software (2021 ©Netigate Deutschland GmbH, Frankfurt am Main, Germany) from Nov 1st, 2020, until May 31st, 2021. It was distributed via several different methods: email request via personal networks, via the website of the EuroELSO annual conference, the ELSO and EuroELSO newsletters and social media accounts of ELSO and EuroELSO (i.e., Facebook, LinkedIn, Twitter) (Suppl. File 4). In accordance with General Data Protection Regulation, no private or individual respondent data were stored.

Centers were stratified by the following characteristics: adult, pediatric or neonatal; cardiac or respiratory; availability of ECLS retrieval capability. Travel isochrones, which are lines of equal travel time from a given location in our case, an ECLS center, were generated, and superimposed upon regional European maps to illustrate access to ECLS centers for various ages and modalities.

National level, specific information was sought to be delivered by representatives from each country (Suppl. File 5). The requested information included demographics, health insurance systems and reimbursement policies, presence of national networks, involved scientific societies, role of government in designating centers and national policies (Suppl. File 6).

Geospatial analysis

Using the above stratifications, spatial accessibility analysis was conducted where appropriate geographical data were available. After geocoding all ECLS-providing hospitals in geographic information system (GIS) software ArcGIS online,[37] one, two, and three-hour drive-time service areas for each ECLS-providing hospital were generated for each country based on the road networks of the Environmental Systems Research Institute (ESRI) world street maps.[37] Population data for each country were gathered from the 2020 Unconstrained Global Mosaics Population Count data by different age groups with a resolution of 1 km.[38]

Furthermore, zonal statistics of ArcMap were applied to acquire the specific population count as well as to correspondingly assemble the populations of children (age 0–14) and adults (age >14) into drive-time areas of ECLS-providing hospitals at different bands of time. The population proportion was subsequently calculated for each band, which was used to represent the accessibility of ECLS-providing hospitals within each country.

In the final stage of the analysis, we examined the geographical differences using one-way ANOVA in STATA 13 (Stata Corp LLC, Texas, USA). Specifically, the geographical classification of 37 countries was based on the United Nations GeoScheme for Europe,[39] where 37 countries were classified as Eastern Europe, Northern Europe, Southern Europe, and Western Europe. Georgia, Israel, Kazakhstan, and Turkey were classified as EuroELSO chapter affiliated, non-European countries (Suppl. File 7).

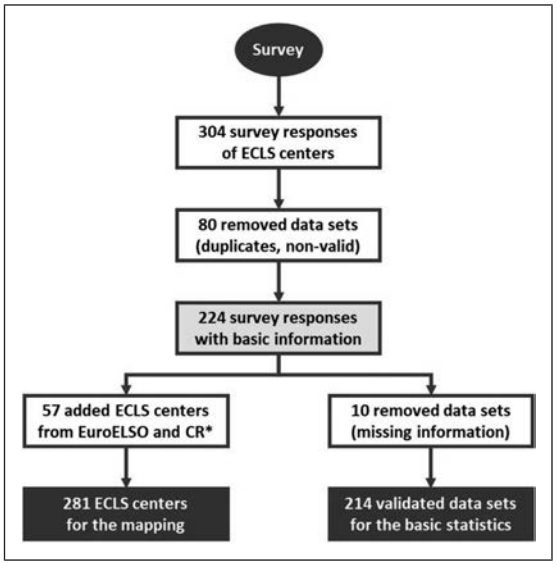

Figure 1. CONSORT flow diagram (GENERATE survey).

Results

Descriptive analysis

The GENERATE survey achieved 304 survey responses from 37 countries affiliated to EuroELSO chapter. Following removal of duplicates and ineligible responses, 214 validated datasets were included in the descriptive and geospatial analysis. A further 57 ELSO registered centers that did not respond to the online survey, were identified in the ELSO center directory as belonging to EuroELSO chapter and included in the geospatial analysis (Figure 1).

Thus, overall, 281 centers from 37 countries affiliated to EuroELSO chapter were included in the geospatial analysis. The number of ECLS centers per capita varied between countries. The mean number of ECLS centers per 1,000,000 citizens is 0.32 center. In 29 countries (78.4%) there are between 0.10 and 1.00 ECLS centers per 1,000,000 citizens. In 4 countries (10.8%) there are less than 0.10 ECLS centers per 1,000,000 citizens and in 4 countries (10.8%) there are more than 1.00 ECLS centers per 1,000,000 citizens. However, there might be different reasons and consequences for a high number of centers per 1,000,000 citizens. Belgium, Estonia, Iceland, and Switzerland, the countries with more than 1.00 centers per 1,000,000 citizens, have a relatively small geographical area in common, but they do not necessarily have a small population size.

The majority of centers - 170 of 214 (79.4%) - provide both cardiac and respiratory support (Table 1). Twenty centers (9.3%) provide solely cardiac and 24 centers (11.2%) solely respiratory support. No center provides both cardiac and respiratory support in Georgia, Hungary, or Slovakia. Data regarding support types is missing for Greece, Latvia, and Serbia.

The analysis indicated that 120 of 214 centers (56.1%) provide retrieval services. In seven countries, no retrieval services were available (Table 1).

The number of centers per 1,000,000 citizens, stratified by adult (15+ years) and pediatric (0–14 years) populations is outlined in Table 2 (Table 2). In total, 86.8% of European centers provide ECLS for adults and 40.9% provide ECLS for children.

A detailed characteristics of country-level ECLS provision and presence of national networks are identified on Table 3 (Table 3).

Geospatial analysis

Table 4 outlines accessibility of ECLS centers in each European country stratified by pediatric and adult centers (with retrieval capabilities) (Table 4). Geographical access to ECLS centers varied greatly across European countries within different drive-time bands, for both children and adults (Figure 2, Suppl. Files 8.1-8.20).

In terms of the accessibility to pediatric centers, Belgium had the highest accessibility followed by Czechia and the Netherlands. Ukraine (2.8%–10.0%) and Kazakhstan (5.6%–11.5%) had the most limited accessibility, 9 out of 37 countries reached a coverage of over 50% of the full population aged 0–14 within 1 h drive-time, whilst 23 out of 37 countries reached the same level of accessibility within 2 h drive-time and 3 h drive-time areas.

Table 1. Basic characteristics of ECLS provision in Europe and provision of 24/7 retrieval services.

Country	ECLS provision per country (total, *N* = 282)					ECLS provision type and retrieval service (survey results, *N* = 215)					
	Number of ECLS centers (*N*, total)	Country population (total)	ECLS centers per 1,000,000 habitants	Number of ELSO centers (*N*, total)	(%)	Number of ECLS centers (*N*, survey)	Type: Cardiac and respiratory	Type: Cardiac	Type: Respiratory	24/7 retrieval service (*N*)	(%)
Austria	9	8,990,000	1.00	4	44%	8	7	1	0	1	13%
Belarus	1	9,980,000	0.10	0	0%	1	1	0	0	0	0%
Belgium	17	11,840,000	1.44	10	59%	13	12	1	0	8	62%
Croatia	4	4,280,000	0.94	0	0%	4	2	1	1	3	75%
Czechia	8	11,090,000	0.72	5	63%	7	7	0	0	3	43%
Denmark	2	5,910,000	0.34	2	100%	2	2	0	0	2	100%
Estonia	2	1,490,000	1.35	0	0%	2	2	0	0	0	0%
Finland	1	5,700,000	0.18	1	100%	1	1	0	0	1	100%
France	12	70,140,000	0.17	7	58%	9	7	1	1	6	67%
Georgia	1	3,920,000	0.25	0	0%	1	0	1	0	0	0%
Germany	40	79,900,000	0.50	29	73%	24	20	1	3	18	75%
Greece	3	10,900,000	0.28	2	67%	0	0	0	0	0	—
Hungary	4	9,870,000	0.41	2	50%	4	0	1	3	1	25%
Iceland	1	340,000	2.92	1	100%	1	1	0	0	0	0%
Ireland	2	4,620,000	0.43	2	100%	1	1	0	0	0	0%
Israel	3	9,070,000	0.33	2	67%	1	1	0	0	1	100%
Italy	34	63,700,000	0.53	21	62%	28	22	1	5	20	71%
Kazakhstan	1	19,010,000	0.05	1	100%	1	1	0	0	1	100%
Latvia	1	2,700,000	0.37	1	100%	0	0	0	0	0	—
Lithuania	2	3,000,000	0.67	0	0%	2	2	0	0	1	50%
Netherlands	14	17,540,000	0.80	14	100%	11	9	0	2	5	45%
North Macedonia	1	2,110,000	0.47	0	0%	1	1	0	0	1	100%
Norway	3	5,190,000	0.58	2	67%	3	3	0	0	2	67%
Poland	11	40,760,000	0.27	5	45%	10	5	1	4	6	60%
Portugal	6	11,250,000	0.53	5	83%	6	6	0	0	4	67%
Romania	3	34,800,000	0.09	0	0%	2	2	0	0	0	0%
Russia	8	153,770,000	0.05	2	25%	7	3	3	1	2	29%
Scotland	4	5,620,000	0.71	4	100%	4	2	1	1	1	25%
Serbia	1	7,190,000	0.14	1	100%	0	0	0	0	0	—
Slovakia	1	5,630,000	0.18	0	0%	1	0	0	1	0	0%
Slovenia	1	2,220,000	0.45	1	100%	1	1	0	0	1	100%
Spain	26	53,390,000	0.49	16	62%	20	18	1	1	11	55%
Sweden	9	10,190,000	0.88	7	78%	5	3	1	1	3	60%
Switzerland	16	8,850,000	1.81	9	56%	12	10	2	0	5	42%
Turkey	8	80,280,000	0.10	4	50%	5	5	0	0	4	80%
Ukraine	1	47,540,000	0.02	0	0%	1	1	0	0	1	100%
UK – England & Wales	21	62,860,000	0.33	21	100%	16	13	3	0	9	56%
Total	**282**	**885,650,000**	0.32	**181**	**64%**	**215**	**171**	**20**	**24**	**121**	**56%**

Table 2. ECLS provision per age group (adults/pediatric).

Country	ECLS provision per country (total, *N* = 282)			ECLS provision (adult 15+ years, *N* = 245)			ECLS provision (neo/ped 0–15 years, *N* = 116)		
	Number of ECLS centers (*N*, total)	Country population (total)	ECLS centers per 1,000,000 (total)	Number of ECLS centers (*N*, 15+ years)	Country population (15+ years)	ECLS centers per 1,000,000 (15+ years)	Number of ECLS centers (*N*, 0–15 years)	Country population (0–15 years)	ECLS centers per 1,000,000 (0–15 years)
Austria	9	8,990,000	1.00	9	7,730,000	1.16	2	1,260,000	1.59
Belarus	1	9,980,000	0.10	1	8,390,000	0.12	0	1,600,000	0.00
Belgium	17	11,840,000	1.44	17	9,860,000	1.72	3	1,980,000	1.52
Croatia	4	4,280,000	0.94	4	3,680,000	1.09	0	600,000	0.00
Czechia	8	11,090,000	0.72	8	9,360,000	0.85	4	1,730,000	2.31
Denmark	2	5,910,000	0.34	2	4,950,000	0.40	1	960,000	1.05
Estonia	2	1,490,000	1.35	2	1,250,000	1.59	0	230,000	0.00
Finland	1	5,700,000	0.18	0	4,800,000	0.00	1	900,000	1.11
France	12	70,140,000	0.17	8	57,850,000	0.14	5	12,280,000	0.41
Georgia	1	3,920,000	0.25	1	3,190,000	0.31	1	740,000	1.36
Germany	40	79,900,000	0.50	39	69,410,000	0.56	7	10,490,000	0.67
Greece	3	10,900,000	0.28	3	9,430,000	0.32	1	1,470,000	0.68
Hungary	4	9,870,000	0.41	3	8,500,000	0.35	2	1,370,000	1.46
Iceland	1	340,000	2.92	1	270,000	3.64	1	70,000	14.65
Ireland	2	4,620,000	0.43	1	4,340,000	0.23	1	270,000	3.64
Israel	3	9,070,000	0.33	3	6,650,000	0.45	1	2,420,000	0.41
Italy	34	63,700,000	0.53	29	55,660,000	0.52	17	8,040,000	2.11
Kazakhstan	1	19,010,000	0.05	1	14,050,000	0.07	1	4,970,000	0.20
Latvia	1	2,700,000	0.37	1	2,300,000	0.43	0	400,000	0.00
Lithuania	2	3,000,000	0.67	2	2,580,000	0.78	0	420,000	0.00
Netherlands	14	17,540,000	0.80	12	14,790,000	0.81	9	2,740,000	3.28
North Macedonia	1	2,110,000	0.47	1	1,770,000	0.57	1	350,000	2.90
Norway	3	5,190,000	0.58	3	4,280,000	0.70	2	910,000	2.19
Poland	11	40,760,000	0.27	10	34,780,000	0.29	3	5,980,000	0.50
Portugal	6	11,250,000	0.53	6	9,860,000	0.61	5	1,390,000	3.59
Romania	3	34,800,000	0.09	2	29,630,000	0.07	1	5,170,000	0.19
Russia	8	153,770,000	0.05	4	128,270,000	0.03	6	25,500,000	0.24
Scotland	4	5,620,000	0.71	3	4,660,000	0.64	1	960,000	1.04
Serbia	1	7,190,000	0.14	1	6,060,000	0.16	0	1,130,000	0.00
Slovakia	1	5,630,000	0.18	1	4,790,000	0.21	0	840,000	0.00
Slovenia	1	2,220,000	0.45	1	1,890,000	0.53	0	330,000	0.00
Spain	26	53,390,000	0.49	25	45,6800,000	0.55	12	7,710,000	1.56
Sweden	9	10,190,000	0.88	9	8,380,000	1.07	2	1,810,000	1.10
Switzerland	16	8,850,000	1.81	13	7,540,000	1.72	5	1,300,000	3.83
Turkey	8	80,280,000	0.10	7	61,230,000	0.11	5	19,050,000	0.26
Ukraine	1	47,540,000	0.02	1	40,470,000	0.02	1	7,070,000	0.14
UK – England & Wales	21	62,860,000	0.33	11	51,940,000	0.21	15	10,920,000	1.37
Total	**282**	**885,650,000**	**0.32**	**245**	**740,280,000**	**0.33**	**116**	**145,370,000**	**0.80**

Table 3. System and Network Information by Country Representatives *RESP – respiratory, CARD – cardiac, ped – pediatric, neo - neonatal.*

Country	Provision and funding types of acute and emergency care		National ECLS network		ECLS retrieval network	
	Provision type	Funding type	Existence of a national ECLS network	ECLS provision type covered by the network	Existence of an ECLS retrieval network	ECLS provision type covered by the network
Belarus	Single provider	Universal/Single payer	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped/neo	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped
Belgium	Multi provider	Universal/Multi payer	No	—	No	—
Croatia	Single provider	Universal/Single payer	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped/neo	Yes (not formally)	RESP: Adult CARD: Adult
Czechia	Single provider	Universal/Multi payer	Yes (not formally)	RESP: Adult/ped/neo CARD: Adult/ped	Yes (not formally)	RESP: Adult/ped/neo CARD: Adult/ped
Estonia	Single provider	Universal/Single payer	Yes (not formally)	RESP: Adult CARD: Adult	No	—
France	Multi provider	Universal/Multi payer	No	—	Yes (not formally)	*N*/A
Georgia	Multi provider	Universal/Multi payer	No	—	No	—
Germany	Multi provider	Universal/Multi payer	Yes (not formally)	RESP: Adult/ped/neo CARD: Adult/ped/neo	No	—
Hungary	Single provider	Universal/Single payer	Yes (not formally)	RESP: Ped CARD: Ped	No	—
Ireland	Single provider	Universal/Single payer	Yes (not formally)	RESP: - CARD: ped/neo	No	—
Israel	Single provider	Universal/Multi payer	Yes (official network)	RESP: Adult/ped/neo CARD: Adult/ped/neo	Yes (official network)	RESP: Adult/ped/neo CARD: Adult/ped/neo
Italy	Single provider	Universal/Single payer	Yes (official network)	RESP: Adult/ped/neo CARD: Adult/ped/neo	Yes (official network)	RESP: Adult/ped/neo CARD: Adult/ped/neo
Netherlands	Multi provider	Universal/Multi payer	Yes (not formally)	RESP: Adult/ped/neo CARD: Adult/ped/neo	No	—
Norway	Single provider	Universal/Single payer	Yes (official network)	RESP: Adult CARD: -	Yes (not formally)	RESP: Adult CARD: -
Poland	Single provider	Universal/Single payer	No	—	No	—
Portugal	Single provider	Universal/Single payer	Yes (official network)	RESP: Adult/ped/neo CARD: Adult/ped/neo	Yes (official network)	RESP: Adult CARD: Adult
Romania	Single provider	Universal/Single payer	No	—	No	—

(continued)

Table 3. (continued)

Country	Provision and funding types of acute and emergency care		National ECLS network		ECLS retrieval network	
	Provision type	Funding type	Existence of a national ECLS network	ECLS provision type covered by the network	Existence of an ECLS retrieval network	ECLS provision type covered by the network
Russia	Single provider	Universal/Single payer	No	—	No	—
Slovakia	Multi provider	Universal/Single payer	No	—	No	—
Slovenia	Single provider	Universal/Single payer	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped
Spain	Single provider	Universal/Single payer	Yes (not formally)	*N*/A	Yes (not formally)	*N*/A
Sweden	Single provider	Universal/Single payer	No	—	Yes (not formally)	*N*/A
Switzerland	Multi provider	Universal/Single payer	Yes (not formally)	RESP: Adult/ped/neo CARD: Adult/ped/neo	Yes (official network)	RESP: Adult/ped/neo CARD: Adult/ped/neo
Turkey	Multi provider	Universal/Single payer	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped/neo	Yes (not formally)	RESP: Adult/ped CARD: Adult/ped/neo
UK – England & Wales	Single provider	Universal/Single payer	Yes (official network)	RESP: Adult/ped/neo CARD: ped/neo	Yes (official network)	RESP: Adult/ped/neo CARD: ped/neo

Table 4. Accessibility of ECLS centers for each European country by adult and pediatric centers.

Country	Provisions of pediatric centers						Provision of adult centers with retrieval service					
	0-1 h		0–2 h		0–3 h		0-1 h		0–2 h		0–3 h	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Austria	656,108	52.19	901,131	71.68	1,082,492	86.10	1,772,627	22.92	5,204,590	67.30	7,157,629	92.55
Belarus	—	—	—	—	—	—	2,202,488	26.27	3,223,640	38.44	4,779,818	57.00
Belgium	1,804,072	91.30	1,975,054	99.96	1,975,923	100.00	9,680,239	98.13	9,861,327	99.97	9,864,682	100.00
Croatia	—	—	—	—	—	—	1,518,851	41.29	2,601,413	70.72	3,246,774	88.26
Czechia	918,962	53.00	1,669,113	96.27	1,733,791	100.00	6,111,621	65.29	9,209,491	98.39	9,360,458	100.00
Denmark	361,227	37.75	488,441	51.04	639,026	66.78	2,953,609	59.64	4,810,130	97.13	4,875,095	98.44
Estonia	—	—	—	—	—	—	—	—	—	—	—	—
Finland	267,987	29.68	478,610	53.01	587,464	65.06	—	—	—	—	—	—
France	3,452,810	28.11	6,198,455	50.46	8,957,485	72.92	19,338,350	33.43	39,382,514	68.07	47,811,072	82.64
Georgia	294,667	40.05	390,092	53.02	450,317	61.20	—	—	—	—	—	
Germany	3,381,541	32.23	6,907,976	65.84	9,036,136	86.13	50,703,309	73.05	67,501,298	97.25	69,139,280	99.61
Greece	192,908	13.16	329,964	22.50	460,586	31.41	—	—	—	—	—	—
Hungary	476,814	34.82	838,700	61.24	1,287,816	94.04	—	—	—	—	—	—
Iceland	51,149	74.91	52,539	76.94	53,873	78.90	—	—	—	—	—	—
Ireland	524,827	43.47	826,084	68.42	1,123,176	93.03	1,810,079	41.68	2,781,915	64.05	3,997,289	92.04
Israel	624,344	25.82	2,109,808	87.24	2,356,441	97.43	1,744,918	26.23	5,883,376	88.43	6,485,305	97.48
Italy	4,206,641	52.32	6,296,903	78.31	7,295,455	90.73	24,006,206	43.13	40,609,953	72.96	52,330,247	94.02
Kazakhstan	279,684	5.63	386,757	7.78	497,415	10.01	747,920	5.33	1,032,545	7.35	1,257,540	8.95
Latvia	—	—	—	—	—	—	—	—	—	—	—	—
Lithuania	—	—	—	—	—	—	1,227,939	47.67	1,947,252	75.60	2,556,394	99.25
Netherlands	2,448,966	89.34	2,727,647	99.50	2,728,153	99.52	13,700,037	92.60	14,719,304	99.49	14,723,751	99.52
North Macedonia	145,761	42.20	218,947	63.39	311,359	90.14	744,900	42.20	1,118,867	63.39	1,591,267	90.15
Norway	320,629	35.11	489,240	53.57	536,877	58.78	1,315,908	30.75	2,055,109	48.03	2,227,675	52.06
Poland	1,391,346	23.26	3,453,670	57.74	5,048,845	84.41	9,739,245	28.00	23,033,698	66.23	30,629,388	88.07
Portugal	150,463	10.79	785,397	56.33	1,220,675	87.55	1,056,716	10.72	5,540,022	56.21	8,636,483	87.62
Romania	683,206	13.22	2,602,628	50.37	3,402,936	65.86	4,343,855	14.66	14,894,613	50.26	19,441,346	65.61
Russia	4,073,881	15.98	5,166,950	20.27	6,326,493	24.81	5,405,162	4.21	6,239,113	4.86	6,593,279	5.14
Scotland	525,442	54.49	781,315	81.02	868,156	90.03	437,321	9.39	1,136,733	24.40	3,913,474	84.00
Serbia	—	—	—	—	—	—	—	—	—	—	—	—
Slovakia	—	—	—	—	—	—	—	—	—	—	—	—
Slovenia	—	—	—	—	—	—	934,885	49.52	1,786,859	94.66	1,884,192	99.81
Spain	2,960,132	38.37	4,541,683	58.88	5,989,827	77.65	22,043,062	48.26	33,865,718	74.14	42,194,446	92.38
Sweden	501,508	27.70	673,160	37.18	818,847	45.22	4,319,586	51.56	6,007,131	71.71	7,176,776	85.67
Switzerland	1,052,364	80.65	1,234,506	94.61	1,292,254	99.04	6,260,558	83.02	7,101,317	94.17	7,468,564	99.04
Turkey	5,165,032	27.12	6,583,292	34.56	7,458,598	39.16	14,634,842	23.90	18,481,793	30.18	22,857,630	37.33
Ukraine	200,837	2.84	413,248	5.85	810,939	11.48	1,025,236	2.53	2,098,429	5.18	3,949,247	9.76
UK – England & Wales	7,781,601	71.26	10,174,928	93.18	10,513,352	96.28	27,389,734	52.73	42,283,722	81.41	48,150,923	92.70

Belgium also had the best access to adult centers with retrieval capabilities followed by the Netherlands and Czechia. Within the 1 h drive-time band, Ukraine was found with the most limited accessibility to adult centers, but it was Russia who has the most limited accessibility to adult centers in 2 h and 3 h drive-time bands. Overall, in eight countries more than 50% of the adult population live within 1 hour drive time of an ECLS centre. This proportion reached 21 countries within 2 h drive-time and 24 countries within 3 h drive-time.

Furthermore, accessibility of ECLS centers differed by geographical classification on statistical testing (Table 5). Countries in Western Europe had higher level of accessibility than countries in other parts of Europe. Furthermore, for pediatric centers, the statistically significant

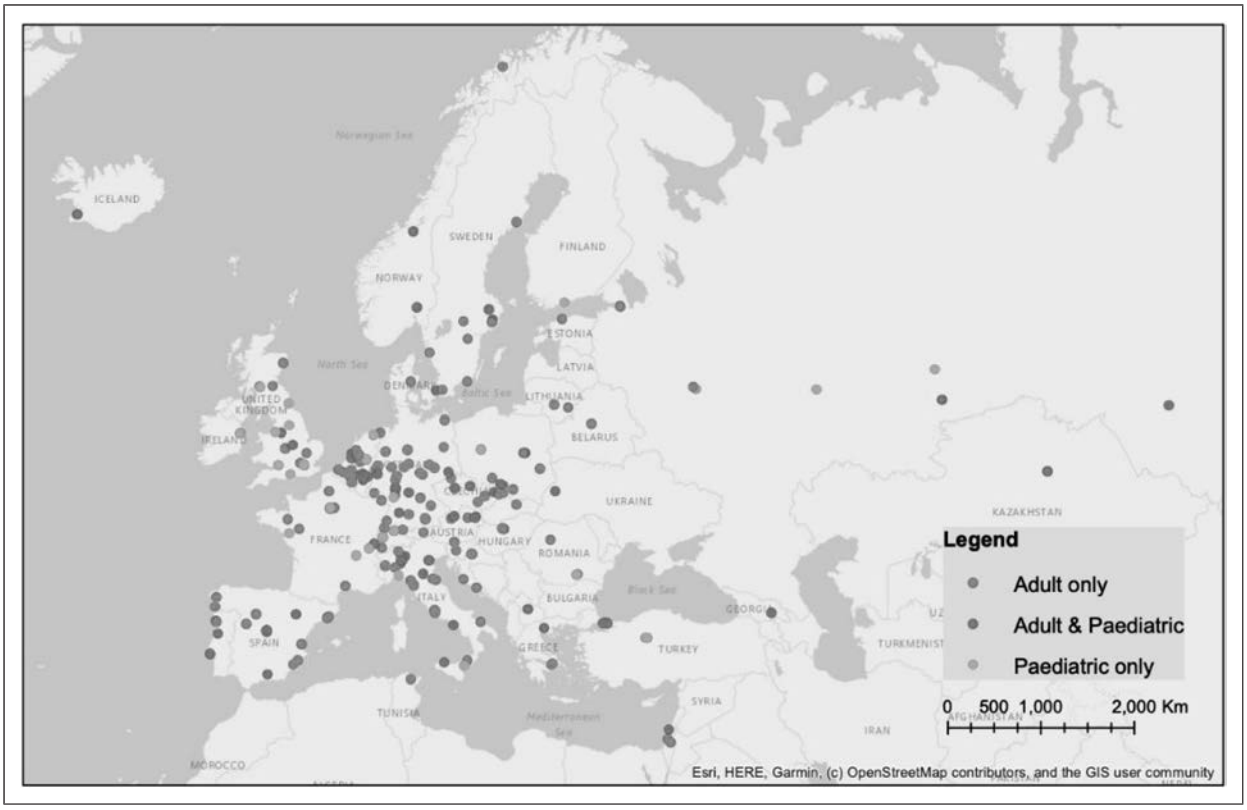

Figure 2. Distribution of ECLS centers across European and EuroELSO affiliated countries.

Table 5. Geographical differences in the accessibility of ECLS centers.

		Pediatric			Adult		
		1 h	**2 h**	**3 h**	**1 h**	**2 h**	**3 h**
Eastern	[1]	1,350,266.67	2,171,117.72	2,713,661.63	8,000,263.15	12,573,983.1	14,961,210.5
	[2]	23.85%	48.62%	63.43%	23.49%	43.90%	54.26%
Northern	[1]	1,596,760.27	2,505,805.34	3,079,711.64	9,386,233.76	14,970,061.4	17,821,333.2
	[2]	46.79%	64.30%	74.26%	41.92%	66.05%	86.31%
Southern	[1]	1,260,608.49	2,170,041.74	2,768,741.01	8,494,194.65	14,007,496.1	16,644,737.8
	[2]	31.37%	55.88%	75.50%	39.19%	72.01%	92.04%
Western	[1]	1,221,055.34	2,020,183.47	2,541,608.4	7,764,775.66	12,461,917.1	14,773,689
	[2]	62.30%	80.34%	90.62%	67.20%	87.71%	95.56%
Non-European	[1]	1,402,443.11	2,257,012.3	2,788,773.15	8,693,497.28	13,459,821.9	16,058,122.4
	[2]	24.65%	45.65%	51.95%	18.48%	41.99%	47.92%
F-values		3.75	1.75	1.54	4.03	2.84	4.01
df		4	4	4	4	4	4
p-values		**0.02***	**0.17**	**0.22**	**0.01***	**0.05***	**0.01***

Note.
[1]The average total population in each drive-time band.
[2]The average proportion of the population that fell within the service area of ECLS-providing hospitals in each drive-time band.

difference was only found within 1 h drive-time (p = 0.02), whilst statistically significant differences were found for each drive-time band for adult centers with retrieval capabilities ($p < 0.05$).

Discussion

The number of patients supported on ECLS is increasing exponentially and the number of ECLS centers have

tripled between 2009 and 2021, particularly in adult population.[40,41] The GENERATE survey offers a detailed description of country-level ECLS provision in countries affiliated to EuroELSO chapter, that gives an understanding of a situation at the beginning of the COVID pandemic. ECLS services were accessible in most of the countries. ECLS service provision differed with respect to cardiac and respiratory support and adult and pediatric centers across the European continent.

ECLS poses a particular challenge for policy makers in the sense that it is a time critical intervention, that requires highly specialised resources. ECLS is often required emergently, particularly in cardiac failure, with an urgency in the need to assess patient suitability and commence ECLS support.[42] Yet the relative infrequency of such cases, and the associated highly specialist resource requirements, make it unfeasible for every hospital to provide ECLS. A balance must therefore be struck between timely access and a degree of centralisation: too many ECLS-providing centers in a country will lead to potential inefficiencies in use of highly specialised resources and dilution of experience; too few ECLS centers, or inappropriate location of centers, and the time to access for many in the population, may also represent a critical aspect to be managed and better programmed. The data from GENERATE illustrates both poles of this challenge.

Some European countries have a relatively large number of centers per capita, with these centers located in areas of high population density. This provides favourable access: almost all the adult population of, for example, Belgium, live within 1 hour of a retrieval capable ECLS center. Yet this arrangement may also lead to a lower case-load per center. GENERATE did not collect case-volume data, however it is reasonable to assume that a higher number of ECLS centers per capita will lead to a lower average case-load per center. The relationship between center volume and outcome is however uncertain.[43–50] Several publications described evidence for improvement in outcomes when patients are managed in high-volume centers, by specialist teams.[31,43–45] This has been demonstrated also for adult and pediatric populations.[44,46,48,49,51] In contrast, other investigators report higher in-hospital mortality in patient transferred to high-volume institutions, this may represent difficulties in controlling for the high-risk nature of patients managed in tertiary units. It has also been suggested that the lower mortality reported by low-volume centers supports the importance of timely access to local ECLS.[43,50–56] Furthermore, volume per se might not be the leading factor; several important factors include training, protocols, team expertise, benchmarking, and maintaining a low threshold for asking for support.[51,53]

Other nations included in GENERATE present a different picture. England and Wales, for example, have a lower-than-average number of centers per capita and therefore likely higher case-load per center. Access is maintained by means of a formal network with retrieval capability. Around half the adult population are located within one hours of a retrieval capable ECLS center and over 80% live within two hours. However, increasing distance from ECLS center has been demonstrated to correlate negatively with referral for specialist care.[57] Furthermore, many case series report the death of patients whilst awaiting retrieval by an ECLS team, illustrating the time critical nature of these transfers.[9,29,58–63] In contrast, other analysed countries have relatively high numbers of ECLS centers, but the timeliness of access is impacted by the retrieval configuration. Scotland, for example, has a higher-than-average number of adult ECLS centers but only 9% and 24% of the adult population are located within 1 and 2 hours of a retrieval service respectively.

The impact of location of retrieval teams is further illustrated by comparing adult and pediatric access. For example, in Germany (Suppl. File 8.3-8.4), the significant differences in the provision of ECLS-providing hospitals for the adult and pediatric populations are because of the limited number of pediatric centers across Germany. Specifically, there are 25 adult centers with retrieval capabilities but only six pediatric centers overall. In the UK, within a 0–1 h time band, the provision of pediatric centers is 71.3%, whilst it is 52.7% for adult centers. There were in total six adult centers with retrieval capabilities and 15 pediatric centers. In addition, there is a concentration of pediatric centers in London (n = 6), which might contribute to greater coverage of the pediatric population considering the high population density in London. In contrast, there are two pediatric centers and three adult centers with retrieval capabilities in Austria. The accessibility of pediatric centers (52.2%) was twice as much as that of adult centers (22.9%) within the 0–1 h time band. This pattern might be explained by the distribution of the pediatric population that one pediatric center is allocated in Vienna.

Establishing networks at a regional level may improve the delivery of emergent interventions such as ECLS to the whole population.[56,64–67] Abrams et al. suggested seamless patient transport and clearly defined pathways for transition to centers of the most complex care with advanced cardiac capabilities.[42] The trends in volume-outcome relationships were described as controversial.[43–50] Moreover, comparable mortality in

low-volume centers might suggest the increased importance of timely access to ECLS.[43,50–56] Thus, referrals and transfer data from networking facilities deserves further investigation. Several publications described evidence for improvement in outcomes when patients are managed in high-volume centers, by specialized caring teams.[31,43–45] This has been demonstrated also for adult and pediatric ECLS support.[44,46,48,49,51] However, volume per se might not be the leading factor; several important factors include training, protocols, team expertise, benchmarking, maintaining a low threshold for asking for support.[51,53,68]

Health systems focus primarily on improving the health of the population and may align resources to assist referring hospitals through regionalization,[45,69–77] and might be better positioned to accomplish this, as efficiency can be increased by sharing resources and capabilities across facilities.[47,55,78–80] The combination of high-volume ECLS center with an effective and appropriately located retrieval service may balance out certain local deficits.[73] The geospatial analysis revealed substantial variation in spatial access to ECLS centers between countries. In general, the availability and allocation of ECLS-providing hospitals, the connectivity of road networks, and the distribution of the adult or pediatric population within each European country may contribute to the significant geographical differences in the accessibility of ECLS-providing hospitals. Greater service areas for each ECLS-providing hospital may be generated in a country with a more connected road network or a country with better road conditions, whereas the connectivity of the road network and road conditions might be further related to the economic performance e. g. gross domestic product (GDP) or the landform (e. g. flat versus mountainous) of the country. However, from the perspective of management, the allocation of ECLS-providing hospitals and the distribution of the adult or pediatric population appears more controversial.

In case of centralization of resources, ECLS services might be provided by fewer centers with retrieval service instead of more centers without retrieval service. However, transport issues may delay the timing of cannulation. Therefore, the option to cannulate and stabilize the patient by the local team and referring to higher level center once transfer avaiable could be considered alternatively. Though, there is still no solid evidence given regarding the optimal ECLS provision model, thus the increase of the number of centers do not improve the outcomes automatically.

However, similar approach GEOS (Geospatial Evaluation of Systems of Trauma Care) was established for Scotland's trauma system as a novel combination of national triage, network analysis, and mathematical optimization of clinical network.[76,77] It shows the increasing potential of geospatial evaluations in planning of distribution of resources and improvement in health care services.

It is important to note that a different approach was taken to the analysis of adult and pediatric patients: we investigated the accessibility of all pediatric centers, regardless of whether they have retrieval capabilities or not, due to the small number of pediatric centers with retrieval services. Adult centers were included in the analysis only if they had retrieval capability whereas all pediatric centers were included, regardless of retrieval capability (Table 4). This decision was taken for several reasons:

The pathologies commonly prompting need for ECLS in adults (e.g. severe respiratory failure from pneumonia, cardiogenic shock from ischaemia, cardiotoxic drug overdose) can present to any acute hospital and will typically be managed in the local intensive care unit. Only a small proportion of those intensive care units will have an ECLS capability and therefore, for the majority of adult patients who progress to require ECLS, a secondary transfer will be required. Establishing patients on ECLS prior to transfer is an accepted standard of care for secondary transfer in adults.

On the other hand, children and neonates with a pathology typically prompting ECLS (e.g. congenital cardiac defect, meconium aspiration syndrome (MAS), persistent pulmonary hypertension of the newborn (PPHN), cardiomyopathy) are far more likely to be managed from the outset in a specialist center with cardiac surgical (and therefore ECLS) capabilities. Even for those children who require secondary transfer to an ECLS center, the need for specialist surgical support for ECLS initiation in children makes remote cannulation and retrieval a far less common occurrence. The availability or otherwise of a pediatric ECLS retrieval service is therefore far less relevant for pediatric services than adults.

The small sample size of pediatric centers in Europe may not be sufficient for the statistical analysis as presented in Table 5. Even so, our findings suggest significant geographical disparities in the accessibility of pediatric centers in Europe and the lack of pediatric services across Europe. We assume the disparities could be intensified after considering the retrieval capabilities of pediatric centers.

Strengths and limitations

GENERATE is the unique analysis about ECLS provision in countries affiliated to EuroELSO. The call for participation was spread widely via networks, social

media and newsletter, data entry was possible during about six months and several reminders were sent additionally. We have sought country representatives through many possible channels, private networks, and connections in order to obtain sufficient information, but recognise that this is not infallible. Thus, missing data in tables represents more a lack of survey response in the country. We cannot confirm with certainty the country missing data represents a true lack of available services and no ECLS centers.

Unfortunately, GENERATE cannot provide exact data comparable to national networks, due to differences in response across all the countries. The survey cannot prove if the redistribution of scarce resources corresponding to the needs of each country's population. Any efforts towards transparency are a prerequisite for underlying governance and accountability structures. However, the aim was also to identify ECLS providing departments beside ELSO designated centers. The survey is based on volunteer participation, which could lead to selection bias and limited completeness of the records.

The overarching purpose of the project is to determine access to ECLS in a timely fashion across Europe. We are aware that in some systems, local teams will initiate ECLS and transport to another center for ongoing management. For the purposes of the analysis, it is the initiation of ECLS that is key with the location of definitive care less relevant. Centers who have initiated ECLS have therefore been included, regardless of the ultimate destination of care. The analysis may also include centers where patients were cannulated and then transported elsewhere to a referral hospital with an ECLS center. Lack of capacity (all devices in use) may also be a reason for such a transfer. This potentially does not reflect ECLS capabilities of that hospital, but rather remote-cannulation and transport capabilities of nearby ECLS centers. These cannulation-only centers have not been identified separately on the maps.

Data about outcomes for individual centers were not collected thus the final conclusion is limited to geospatial and distributive results. Another significant limitation is that it is unknown if the geospatial distribution of diseases, and thus all potential indications for ECLS, and the distance from where patients that might need ECLS come from, are spatially homogeneous, which is an underpinning assumption of the analysis. Moreover, ECLS provision benchmarking depends on more complex and standardized criteria and items, which are recorded longitudinally in ELSO Registry. Our spatial accessibility analysis is based on drive time from residential locations to ECLS centers. Future research may consider use of helicopter in accessing ECLS services which may play a significant role in countries with a large part of mountains and islands. Patients already admitted in hospital may also need to access ECLS thus hospital transferred access is another important element in further research. Further, the delivery of ECLS depends on more than just distance to a capable center – it also requires availability of circuits, trained personnel, ICU beds, etc. Hospital capacities, ICU volume and availability of ECLS devices might be considered for further geospatial analyses as well. Such consideration of hospital capacity relative to population demand while also accounting for travel impedance would give a more complete picture of true access, as distance-only metrics have been shown to underestimate disparities in access to care.

Unfortunately, our analysis needs to be updated due to the changed conditions in Ukraine. Since the beginning of the Russian war against Ukraine, the work of the hospitals, not only those providing ECLS, is significantly affected, and the safe access and health care provision irreversibly changed as medical facilities became a target for the attacks and medical resources were required for injured soldiers and civilians.[81]

Conclusions

GENERATE survey provides a systematic, detailed, and standardized description of contemporary ECLS provision in EuroELSO affiliated countries. The map of spatial distribution of ECLS centers and their accessibility contributes to better understanding of the allocation of ECLS resources. ECLS services are accessible in most countries, but there are substantial differences in provision models between Western, Central and Eastern Europe. There is still no solid evidence given regarding the optimal ECLS provision model. The results of the project may support such planning and decision making by governments, healthcare professionals and policy makers to consider how to develop existing provision to accommodate the anticipated increase in need for time critical access to this advanced support modality.

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Author contributions

SG and JS initiated the project GENERATE on behalf of EuroELSO supported by JB, RL and NB, and mainly developed the survey questionnaire. MF, TS and JS were primarily responsible for the survey data evaluation and the research activities in order to identify missing ECLS centers via ELSO directory and web-based searching machines. CZ and ZF were primarily responsible for the geospatial analysis and all mapping activities due to their geographical background and expertise. SG and NL attended the complete research process as supervisors with their important knowledge about regional setups concerning different structures of ECLS provision and health care systems in Europe. There has been an internal evaluation and review process provided by all authors with discussion in virtual meetings. Discussion and conclusions have been elaborated together and all authors were responsible for writing parts of the manuscript.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Prof. Dr. Lorusso is a consultant for Medtronic, Getinge and LivaNova and medical advisory board member for EUROSETS, all unrelated to this work, all honoraria to the university for research funding. The remaining authors declare that they have no competing interests.

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Ethical approval

Only data regarding the ECLS center, the hospital and institution specific data have been collected. No personal data of the person providing the information about the hospital and ECLS center will be collected, exported, stored, or shared with third parties. The research was reviewed and approved by the Ethics Committee of the School of Geosciences, University of Edinburgh (Ref: 2021-516).

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Supplemental Material

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Perfusion

Pharmacokinetics of cefiderocol during extracorporeal membrane oxygenation: A case report

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Abstract

Patients with extracorporeal membrane oxygenation (ECMO) support do frequently receive broad-spectrum antibiotics, due to the high frequency of infection by multidrug resistant microorganisms. The extracorporeal circuit can alter the pharmacokinetics (PK) of administered drugs, and in the case of antibiotics this may lead to treatment failure. Cefiderocol is a new cephalosporin that exhibits excellent in vitro activity against many multidrug-resistant (MDR) microorganisms, but there is no published data about the modifications of its PK in patients with ECMO support. Herein we report the results of a pharmacokinetic investigation of cefiderocol in a critically ill patient receiving extracorporeal respiratory support.

Keywords

ECMO, extracorporeal membrane oxygenation, pharmacokinetics, cefiderocol, microbial drug resistance

Introduction

Cefiderocol is a siderophore cephalosporin that exhibits excellent *in vitro* activity against many clinically relevant Gram-negative pathogens including multidrug-resistant (MDR) *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, Enterobacteriaceae and *Stenotrophomonas maltophilia* and has been approved for the treatment of adult with severe Gram-negative bacterial infections.[1,2] No data has been published to date about the influence of the extracorporeal membrane oxygenation (ECMO) circuit in the pharmacokinetics (PK) of cefiderocol. The objective of our study was to evaluate the influence of ECMO on the PK of cefiderocol in one critically ill patient receiving extracorporeal support. We obtained sequential arterial blood samples to generate the area under the curve (AUC) and in Cmax and Cmin we further obtained blood samples from pre-oxygenator and post-oxygenator, calculating the extraction ratio across the extracorporeal membrane. We compared our findings with the available data in the literature. The patient gave consent for this publication.

Case report

A 64 years old man with SARS-CoV2 infections was admitted to the Intensive Care Unit (ICU) due acute respiratory failure. On his first day, he needed intubation and invasive mechanical ventilation (IMV) together with sedatives and neuromuscular blockade. Despite these measures, he developed severe hypoxemia, needing prone position for the first 24 h of ICU admission, with partial

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response. On day 16 he developed hypoxemia, refractory to the prone position, so our ECMO retrieval team was activated. Venovenous support was started with a femorojugular (25F/55 cm–17F/15 cm) configuration, and transport was done uneventfully. At our institution, respiratory samples were obtained by a fiberbronchoscopy and empirical treatment was started with meropenem (2 g every 8 h with extended infusion) and linezolid (600 mg every 12 h). With the results of cultures, in which *P. aeruginosa* and *S. maltophilia* were identified, Linezolid was stopped, meropenem was maintained and cotrimoxazole (320 mg every 6 h) was started. After the first results of antibiotic resistance of *P. aeruginosa*, meropenem had to be changed by ceftolozane-tazobactam (2 g every 8 h), but after the extension of the antibiogram, also resistance to ceftolozane-tazobactam and ceftazidime-avibactam were documented. On day 5 of the ECMO run, treatment with cefiderocol (2 g every 8 h, with extended infusion oh 3 h) was started. After 3 days of this treatment start, clinical improvement was evidenced, with compliance increase, possibility of sedatives withdrawn and subtle radiological improvement, together with a decrease of respiratory secretions. No other organ failure was evidenced during the full clinical course. On day 10 of the ECMO run, and day 5 of treatment with cefiderocol, the circuit was changed due to dysfunction. On day 9 of the antibiotic treatment, blood samples were obtained to measure cefiderocol levels (see below). Treatment with cefiderocol was maintained for 14 days. On day 12 of treatment respiratory samples were extracted, being negative for *P. aeruginosa*. The evolution of the patient was good, could be decannulated after 27 days of ECMO support, discharged from our ECMO center after 29 days and discharged home after 80 ICU days and 140 hospital days.

The pharmacokinetic parameters on day 9 of treatment are detailed in Table 1. Extraction ratios through the ECMO oxygenator were very low (<5%), with pre-oxygenator and post-oxygenator concentrations of 66.8 mg/L and 69.2 mg/L respectively in Cmax and 42.8 mg/L and 44.1 mg/L in Cmin. Free Cmin plasma concentrations considering a protein binding of 50% [3] were 20.46 mg/L, and 6.95 mg/mL in lung, considering 34% of lung penetration in hospitalized subjects with bacterial pneumonia [4]. Notably, the AUC of the molecule was markedly higher than the predicted with current available data (AUC 0–8 h of 480.6 mg*h/L) (Figure 1).

Discussion

ECMO is a supportive therapy used in the most severe forms of critically illness. It is not a direct treatment of the disease causing the clinical scenario, making essential to adequately diagnose and effectively treat this underlying condition, frequently related with infectious diseases. Further, nosocomial infections in patients receiving ECMO are frequent complications and have a relevant impact on outcome.[5] The extracorporeal circuit can alter the PK of administered drugs, and in the case of antibiotics this may lead to subtherapeutic blood levels causing irremediable treatment failure.[6,7] Further, infectious diseases caused by multidrug resistant microorganisms (MDR) are becoming more frequent, especially in patients with highly intense therapeutic manoeuvres. New antibiotics covering these microorganisms have been recently developed but there is insufficient data about the effects of ECMO on their PK, making it difficult for the clinicians to titrate the usual doses. To our knowledge, this is the first study showing information about the impact of the ECMO therapy on cefiderocol levels.

Interestingly, we observed plasma levels of the drug well above the median minimum inhibitory concentration (MIC) of *P. aeruginosa* (0.125 mg/L) and free T above MIC during the full dosing interval.

Table 1. Pharmacokinetic parameters of cefiderocol on its day 9 of treatment, in comparison with reference PK parameters of the antibiotic.

	Case	Reference parameters[a]
(C) 0 h (mg/L)	40.92	-
(C) 3 h (mg/L)	103.6	-
(C) 3,25 h (mg/L)	68.19	-
(C) 4 h (mg/L)	67.45	-
(C) 5 h (mg/L)	55.77	-
(C) 6 h (mg/L)	47.63	-
(C) 7 h (mg/L)	40.25	-
(C) 8 h (mg/L)	38.78	-
Cmax (mg/L)	103.6	156
Cmin (mg/L)	38.78	-
tmax (h)	3	1
Kel	0.174	0.255
t ½ (h)	3.8	2.72
AUC 0–8 h (mg[a]h/L)	480.6	366.5
AUC 0-infinity (mg[a]h/L)	823.7	-
CL (L/h)	4.16	5.46
Vd (L)	23.9	-
C extraction ratio Cmin	2.94%	-
C extraction ratio Cmax	3.53%	-

AUC: area under the curve; CL: clearance; Cmax: peak serum levels; Cumin: through levels; [C/T]: concentration of Ceftol; CVVHDF: continuous veno-venous hemodiafiltration; ECMO: extracorporeal membrane oxygenation; Kel: elimination rate constant; tmax: time to peak serum levels; t ½: half life; Vd: volumen of distribution.

[a]Data obtained from Saisho Y, et al. Antimicrob Agents Chemother. 2018; 62 (3): e02163-17.

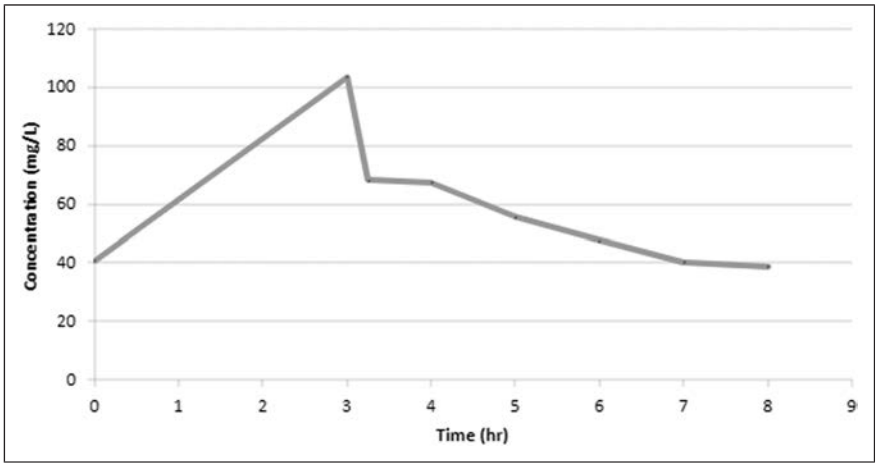

Figure 1. Plasma cefiderocol concentrations over 8 h.

We observed no significant trapping of the molecule in the membrane. Of note, when compared with the PK reference parameters with cefiderocol, the AUC in our patient was notably higher (together with lower peak levels). In a context of little effects of the ECMO system on the molecule, this might be partly due to the use of extended infusion in administering the antibiotic, strategy that would be highly recommended in patients with ECMO support. The pharmacokinetics of beta-lactams are time-dependent, i.e., their clinical efficacy depends on the time that the blood concentration is above the MIC for each sensitive microorganism. Prolonged infusion administration of beta-lactams is superior to short infusion in achieving the therapeutic target, especially in infections caused by Gram-negative bacilli with sensitive but high MICs. Further, the administration of a loading dose allows reaching therapeutic levels rapidly enough.

Also, the real kidney function of this patient might not be perfectly well represented by the values of the laboratory biomarkers (normal levels of creatinine) and some mild degree of renal dysfunction may have contributed to the identified AUC profile. Finally, it should be noted that the available reference PK data of the molecule is drawn from non-critically ill individuals and to infer this information to the patient receiving ECMO support should be associated with important deviations. Regarding the potential toxicity of the drug, being digestive symptoms the most frequent in cefiderocol, in this case no undesirable effect was observed. Nevertheless, a down adjustment of dose may still maintain adequate AUC values while decreasing the associated costs.

Our findings may guide colleagues initiating antimicrobial therapy with cefiderocol in patients receiving ECMO support. They suggest that usual doses delivered with extended infusion may be adequate to reach targeted levels. However, data from only one case may not be definitive and should be extrapolated with caution to other clinical scenarios.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Jordi Riera reports punctual personal fees from Gilead and Werfen Laboratories as Speaker and Medtronic as advisor, all unrelated with the content of the present manuscript. Dr Ricard Ferrer reports personal fees from MSD Laboratory as Advisory Board and Speaker.

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Perfusion

Novel cannulation strategy with a bidirectional cannula for distal limb perfusion during peripheral veno-arterial extracorporeal life support: A preliminary, single-centre study

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Abstract

Introduction: Limb ischemia is a severe complication of peripheral veno-arterial extracorporeal life support (V-A ECLS). Several techniques have been developed to prevent this, but it remains a major and frequent adverse event (incidence: 10–30%). In 2019, a new cannula with bidirectional flow (retrograde towards the heart and antegrade towards the distal limb) has been introduced. A single-centre experience with this cannula in patients undergoing peripheral V-A ECLS is herewith reported.

Methods: This prospective observational study included adults (≥18 years) undergoing V-A ECLS from January 2021 to October 2022 with the use of a bidirectional femoral artery cannula. Primary outcome was limb ischemia requiring intervention during cardio-circulatory support. Secondary outcomes were compartment syndrome, limb amputation, cannulation site bleeding, need for other surgical intervention due to cannula related complications, duplex ultrasound parameters from the femoral vessels, and in-hospital survival.

Results: Twenty-two consecutive patients were included. During extracorporeal life support (ECLS) support, limb ischemia requiring intervention occurred in one patient (4.5%) and no patients developed a compartment syndrome, or required a fasciotomy or amputation. Significant bleeding was reported in two patients (9%) due to slight cannula dislodgement, easily solved with cannula repositioning. In-hospital survival was 63.6%.

Conclusions: The bidirectional cannula is associated with a low risk for limb ischemia-related complications compared to current literature, and apparently represents a safe alternative to dedicated distal perfusion cannula. Further studies are warranted to confirm these preliminary findings.

Keywords

extracorporeal membrane oxygenation, extracorporeal life support, veno-arterial, livanova, bi-flow, bidirectional, cannula

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Introduction

Veno-arterial extracorporeal life support (V-A ECLS) provides life-saving organ support for severe cardiopulmonary failure. Peripheral V-A ECLS with femoral cannulation is the most frequent approach, particularly in post-cardiotomy and acute cardiopulmonary failure. Femoral cannulation is by far the most commonly chosen access in such a V-A ECLS setting, using either open or percutaneous technique for cannula placement. Due to the cannula diameters, required for adequate blood flow and to avoid excessive flow resistance which would cause blood element damage, the distal flow in the cannulated arterial vessel may be compromised to a significant extent, leading to various ischemia-related adverse events. Indeed, the risk for limb ischemia in peripheral V-A ECLS has been described to range between 10 and 30%.[1–6] Severe limb ischemia may necessitate surgical interventions, such as fasciotomy or revascularization, and even lead to limb loss, or contribute to patient death.[4,7–24] Consequently, monitoring and optimization of distal limb perfusion during V-A ECLS is pivotal to prevent sever shortcoming and, most likely, even improve outcomes.[4] In the last decades, several techniques to provide distal limb perfusion and limit or prevent the risk for limb ischemia-related complications have been developed. Nevertheless, such an adverse event remains a critical aspect of peripheral V-A ECLS with femoral vessels cannulation.

Insertion of a distal perfusion cannula (DPC) in the superficial femoral artery (SFA) has been considered the gold standard to provide distal limb perfusion for more than a decade. Other techniques are also available, such as placement of a T-graft in the common femoral artery to supply both retrograde flow towards the heart and antegrade flow towards the limb or a dedicated distal perfusion catheter or cannula.[4] In 2019, a new arterial cannula (Bi-Flow, LivaNova, UK) was introduced in clinical practice which may guarantee flow towards the descending aorta and the distal limb.

Very limited literature is available regarding the experiences with such a cannula in the setting of conventional cardiopulmonary bypass and no experience has been published describing the experiences with this cannula in peripheral V-A ECLS.[25] We hypothesize that the bidirectional arterial cannula is a safe and effective alternative to unidirectional cannulation combined with a DPC during peripheral V-A ECLS. This paper describes the preliminary results of a prospective observational study to explore the clinical outcomes in relation to the limb ischemia-related adverse events of patients undergoing peripheral V-A ECLS with the use of a bidirectional femoral artery cannula.

Methods

This prospective observational study included patients treated with the bidirectional cannula during ECLS support from January 2021 to October 2022 in a university medical centre in the Netherlands. Inclusion criteria were: (1) age ≥18 years; (2) support with V-A, venoveno-arterial (VV-A), or veno-arteriovenous (V-AV) ECLS; and (3) femoral vessel cannulation with a bidirectional cannula. No exclusion criteria were applied. The study followed STROBE guidelines (see Supplements).

Technical methods

In our centre, open cannulation is performed by the cardiothoracic surgeons. Following standard groin incision (uni- or bilateral according to the patient features, surgeon preference or indication for V-A ECLS institution), the common femoral artery is exposed, double purse-string sutures with 5-0 prolene and tourniquets are applied, adequate heparinization administered, and cannula inserted using the modified Seldinger technique, with a pseudo-percutaneous technique (the femoral vessels are exposed with an open approach, but the cannulas are tunneled through separated small incisions distally from the groin vessel exposure, allowing complete closure of the femoral incision).[26] Regarding monitoring of limb perfusion during ECLS support, in addition to usual clinical examination (assessment of the six Ps of acute ischemia: pain, pallor, poikilothermia, pulselessness, paresthesia, and paralysis) and doppler analysis of the posterior tibial and dorsalis pedis arteries, we routinely use bilateral near-infrared spectroscopy (NIRS) to evaluate and compare perfusion of both limbs (significant in case of: NIRS below 40% or a 25% decrease from baseline).

A duplex ultrasound of the SFAs and femoral veins (FVs) is, if logistically possible, performed after ECLS initiation (usually within 24 hours from ECLS initiation). Post-analysis of the duplex measurements is performed according to the consensus statement from the Society for Vascular Medicine and Society for Vascular Ultrasound.[27] For the SFAs, the following parameters were determined during duplex analysis: peak-systolic flow velocity (PSV), end-diastolic flow velocity (EDV), diameter, and flow pattern. For the FVs, the maximum and minimum velocity, vessel diameter, and flow pattern were determined.

Analysis and statistics

Demographic data, baseline characteristics, ECLS and cannula characteristics, and outcome were collected and analyzed. The primary outcome was limb ischemia requiring intervention. Secondary outcome measures were compartment syndrome or fasciotomy, limb

Table 1. Baseline patients' characteristics. Values are reported as count and percentage or mean and standard deviation. For a complete history list, see supplement table 1.

Characteristics	Bidirectional femoral artery cannula
	N = 22
Sex	
Male	16 (72.7%)
Female	6 (27.3%)
Age (years)	59 ± 11
Body mass index (kg/m^2)	27.2 ± 4.5
Body surface area (m^2)	2.02 ± 0.19
Organ failure (at cannulation)	
Cardiac	16 (76.2%)
Cardiac and kidney	3 (14.3%)
Cardiac and pulmonary	2 (9.5%)
History	
Hypertension	11 (50%)
Recent atrial fibrillation (<90 days before presentation)	7 (31.8%)
Myocardial infarction at presentation	6 (27.3%)
Diabetes	5 (22.7%)
Endocarditis	4 (18.2%)
Myocardial infarction (<90 days before presentation)	4 (18.2%)
Indication	
Cardiogenic shock	3 (13.6%)
Post-cardiotomy	8 (36.4%)
Biventricular failure	3 (13.6%)
Left ventricular failure	1 (4.5%)
Right ventricular failure	4 (18.2%)
ECPR	9 (40.9%)
ECPR, cardiogenic shock	7 (31.8%)
ECPR, hypovolemic shock	1 (4.5%)
ECPR, septic shock	1 (4.5%)
Other	2 (9.1%)
Pulmonary embolism	1 (4.5%)
Trauma, hypovolemic shock	1 (4.5%)

amputation, need for other surgical intervention due to cannula related complications, significant bleeding at cannulation site (necessitating transfusion of three or more units of packed red blood cells), duplex ultrasound parameters from the SFAs and FVs, and in-hospital survival.

Continuous variables were reported as mean and standard deviation (±SD) and categorical variables were reported as counts and percentages. IBM SPSS Statistics was used to analyze the data (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp).

Ethical approval

This study received approval from the local ethical committee (2021-2996-A-2). Patient consent was waived due to the inability to give informed consent, the anonymization of data, and the non-invasive nature of the duplex ultrasound.

Results

Baseline and clinical characteristics

In total, twenty-two patients were cannulated with a bidirectional cannula during peripheral V-A ECLS in the study period. Included patients were predominantly male (16 patients, 72.7%), had a mean age of 59 years old, a body mass index of 27.2 kg/m^2, and a body surface area of 2.02 m^2 (Table 1). The majority (16 patients, 76.2%) had mono-organ (cardiac) failure and ECLS was most frequently initiated for extracorporeal cardiopulmonary resuscitation (ECPR) and post-cardiotomy ventricular failure [9 patients (40.9%) and 8 patients

Table 2. Hemodynamic, ventilatory, and extracorporeal life support characteristics at initiation and cannula-related characteristics. Values are reported as count and percentage or mean and standard deviation.

Characteristics	Bidirectional femoral artery cannula
	N = 22
Mode	
V-A	21 (95.5%)
V-AV	1 (4.5%)
VV-A	0 (0%)
Mean ECLS settings (at initiation)	
Blood flow (L/min)	3.5 ± 0.5
Air flow (L/min)	2.8 ± 1
Fraction inspired oxygen (%)	57 ± 14
Arterial blood gas (at initiation)	
pH	7.34 ± 0.11
pCO_2 (kPa)	4.3 ± 0.9
pO_2 (kPa)	15.6 ± 6.2
HCO_3^- (mmol/L)	17 ± 4.2
Norepinephrine (mcg/kg/min) (at initiation)	
0-0.2	5 (22.7%)
0.25–0.5	10 (45.5%)
>0.5	7 (31.8%)
Cannulation mode	
Unilateral	18 (81.8%)
Bilateral	4 (18.2%)
Arterial cannula size	
19 Fr	22 (100%)
Venous cannula size	
21 Fr	0 (0%)
23 Fr	1 (4.5%)
25 Fr	20 (90.9%)
27 Fr	1 (4.5%)
NIRS (%)	
Cannulated limb	59 ± 16
Non-cannulated limb	64 ± 14

ECPR: Extracorporeal cardiopulmonary resuscitation, ECLS: Extracorporeal life support, V-A: Veno-arterial, V-AV: Veno-arteriovenous, VV-A: Veno-veno-arterial.

(36.4%), respectively]. Eight out of nine patients treated with ECPR had an in-hospital cardiac arrest.

Mean ECLS settings at initiation were: blood flow at 3.5 ± 0.5 L/minute, air flow at 2.8 ± 1 L/minute, and a fraction inspired oxygen of 57 ± 14% (Table 1). The mean pH, pCO_2, pO_2 and HCO_3^- were respectively 7.34 ± 0.11, 4.3 ± 0.9 kPa, 15.6 ± 6.2 kPa and 17 ± 4.2 mmol/L. A norepinephrine dose between 0.25 and 0.5 mcg/kg/minute was required in 45.5% at ECLS initiation.

Cannula configuration

Eighteen patients (81.8%) underwent unilateral (arterial and venous cannulation in same groin) and four (18.2%) underwent bilateral (arterial cannulation contralateral to the venous cannula) cannulation (Table 2). Since the bidirectional cannula was only available in a 19 French (Fr) diameter, there was no variation in cannula size. For venous cannulation, 25 Fr cannulas were used in twenty patients (90.9%). Only two patients (9.1%) were cannulated with a 23 or 27 Fr venous cannulas. No major adverse events occurred during cannulation with the bidirectional cannula. Mean NIRS values were 59 ± 16% for the (arterial) cannulated limb and 64 ± 14% for the non (arterial) cannulated side.

Limb ischemia requiring intervention

Table 3 shows the outcome measures of the cohort. Limb ischemia of the cannulated limb during the ECLS

Table 3. Outcome measures of the cohort. Values are reported as count and percentage.

Characteristics	Bidirectional femoral artery cannula
	N = 22
Limb ischemia (at cannulated limb) requiring intervention	
During ECLS run*	1 (4.5%)
After decannulation^	1 (4.5%)
Limb ischemia-related intervention	
Thrombectomy	0 (0%)
Fasciotomy for compartment syndrome	
Yes	0 (0%)
After decannulation^	1 (4.5%)
Amputation^%	1 (4.5%)
Bleeding at cannulation site	
Yes	2 (9.1%)
After decannulation	0 (0%)
Vessel repair	
Yes	0 (0%)
After decannulation	1 (4.5%)
Discharged alive from hospital	
Yes	14 (63.6%)
No	8 (36.4%)

*During ECLS weaning (perfusion flow at 1.5 L/min.); ^More than six hours after decannulation; %Including the same patient as noted requiring fasciotomy after decannulation.
ECLS: Extracorporeal life support.

run requiring intervention occurred in one (4.5%) patient. In this patient, weaning needed to be halted due to occurrence of limb ischemia while decreasing blood flow through the arterial cannula (flow towards the perfusion cannula less than 1.5 L/min). A position-dependent decrease in NIRS value, while manipulating the leg, was noted in one patient but quickly restored after repositioning and did not require further intervention.

Compartment syndrome and amputation

No patient developed a compartment syndrome or required a fasciotomy during ECLS and one (4.5%) patient developed a compartment syndrome seven hours after ECLS removal, required a fasciotomy and in a later stage an amputation (Table 3). Before decannulation, this patient had normal NIRS values (NIRS ≥40% or NIRS values not lower than 25% from baseline). As mentioned earlier, mean NIRS values are reported in Table 2.

Bleeding at cannulation site

Significant bleeding at the cannulation site was reported in two (9%) patients of the cohort. One patient had bleeding at the cannulation site due to incorrect positioning of the elbow of the cannula, immediately solved by repositioning without major intervention.

In-hospital survival

Fourteen (63.6%) patients were discharged alive from the hospital.

Duplex analysis

Duplex measurements were available for eleven patients and shown in Table 4. The mean PSV and EDV for the cannulated SFAs were 44.7 ± 24.5 and 17.1 ± 10.3 cm/s compared to 79.3 ± 19.3 and 8.5 ± 18.9 for the contralateral, non-cannulated SFAs. Mean diameters were, respectively for the cannulated and non-cannulated SFAs, 0.53 ± 0.09 cm and 0.57 ± 0.14. Flow patterns in the cannulated arteries were predominantly classified as monophasic with an intermediate resistive (27.3%), low resistive (27.3%), and minimal phasic (36.4%) flow pattern. The cannulated arteries had more often a multiphasic flow pattern (63.6%).

FV flow velocities were, in the cannulated FVs, between 16.5 ± 5 and 6.4 ± 5.8 cm/s and between 20.2 ± 9.7 and 6.7 ± 3.7 cm/s in the non-cannulated FVs. Flow patterns for cannulated veins were heterogenic and non-cannulated veins (n = 10) showed in 80% respirophasic blood flow patterns (with or without pulsatility).

Discussion

Main findings

To our knowledge, this is the first study reporting experiences and outcomes with the bidirectional femoral artery cannula during peripheral V-A ECLS. In this study we observed no major adverse events during cannulation with the bidirectional cannula while maintaining the capacity to run adequate ECLS blood flows. During duplex analysis a decreased mean PSV in the cannulated SFAs in comparison to the normal values considered for SFA, and a normal mean PSV in the non-cannulated SFAs was observed. Low rates of limb ischemia of the cannulated limb requiring intervention, development of compartment syndrome, need for amputation or thrombectomy, and bleeding at cannulation site were observed compared to the literature.

Adequate distal limb perfusion during peripheral V-A ECLS is important and limb ischemia-related complications have been repetitively correlated to major compromise of patient status during ECLS support and is also linearly associated with patient death.[28–32]

Table 4. Duplex measurements of the superficial femoral artery and femoral vein from the bi-flow group. Measurements of the cannulated and non-cannulated side are displayed. Flow pattern description was based on the consensus statement from the society for vascular medicine (SVM) and the society for vascular ultrasound (SVU).[27]

	Bidirectional cannula (N = 11)	
	Cannulated limb	Non-cannulated limb
Femoral artery		
PSV, mean (cm/s)	44.7 ± 24.5	79.3 ± 19.3
EDV, mean (cm/s)	17.1 ± 10.3	8.5 ± 18.9
Diameter, mean (cm)	0.53 ± 0.09	0.57 ± 0.14
Flow pattern		
Multiphasic	0 (0%)	7 (63.6%)
IABP	0 (0%)	1 (9.1%)
Monophasic		
High resistive	0 (0%)	1 (9.1%)
Intermediate resistive	3 (27.3%)	1 (9.1%)
Low resistive	3 (27.3%)	1 (9.1%)
Minimal phasic	4 (36.4%)	0 (0%)
Plus IABP signal	1 (9.1%)	0 (0%)
Femoral vein		
Maximum velocity, mean (cm/s)	16.5 ± 5	20.2 ± 9.7
Minimum velocity, mean (cm/s)	6.4 ± 5.8	6.7 ± 3.7
Diameter, mean (mm)	0.75 ± 0.13	0.66 ± 0.14
Flow pattern		
Respirophasic	4 (36.4%)	6 (60%)
Respirophasic and pulsatile	2 (18.2%)	2 (20%)
Decreased	0 (0%)	0 (0%)
Pulsatile (cardiac cycle)	2 (18.2%)	2 (20%)
Continuous	3 (27.3%)	0 (0%)

EDV: End-diastolic flow velocity, IABP: Intra-aortic balloon pump, PSV: Peak-systolic flow velocity.

According to current guidelines, a DPC should be considered to reduce the risk of limb ischaemia (Class IIa).[33]

The bidirectional cannula has a bent structure (around 15 degrees angle between the distal and the proximal segments), representing a sort of elbow at the 1/3-2/3 segment of the cannula itself. This 'elbow' contains the additional side hole which guarantees flow towards the distal femoral artery (Figure 1). The cannula is inserted in the common femoral artery and the elbow is positioned just 2-3 cm downstream to the insertion site to guarantee that the retrograde flow jet is not too close to the entry site.[34] The cannula must be positioned with the elbow along the inferior surface of the cannulated artery to guarantee unobstructed flow towards the distal limb. A black marker along the superior cannula surface contributes to a proper cannula position aiming to avoid misplacement of the cannula elbow along the cannulated artery. Purse-string tourniquets ligatures, plus additional three stay-sutures (one at the skin entrance, and other two more distally) are used to secure the cannula to the skin and avoid major cannula dislodgement or rotation.[34] Safety blockers (Figure 1(d)) are also provided with the cannula insertion kit, which might further help to maintain cannula position and avoid dislocation or rotation.

The cannula is designed to maintain a perfusion flow from 2 to 4 L/min or higher and an adequate distal flow as described in the information for use.

The bidirectional cannula may also be positioned percutaneously, taking care to advance the cannula again 2-3 cm more proximally once the cannula placement itself has provided a feeling of abolished resistance to the advancement (which usually is associated with the cannula elbow passage inside the arterial hole). The subsequent steps, including skin sutures and blockers device, follow the same details, excluding the use of purse strings and tourniquets.[34] Decannulation may be achieved with an open technique, with percutaneous closure devices or with manual compression (the latter is not recommended).[26,34]

Based on our preliminary experience, the bidirectional cannula had low rates of limb ischemia requiring intervention (4.5%), development of compartment

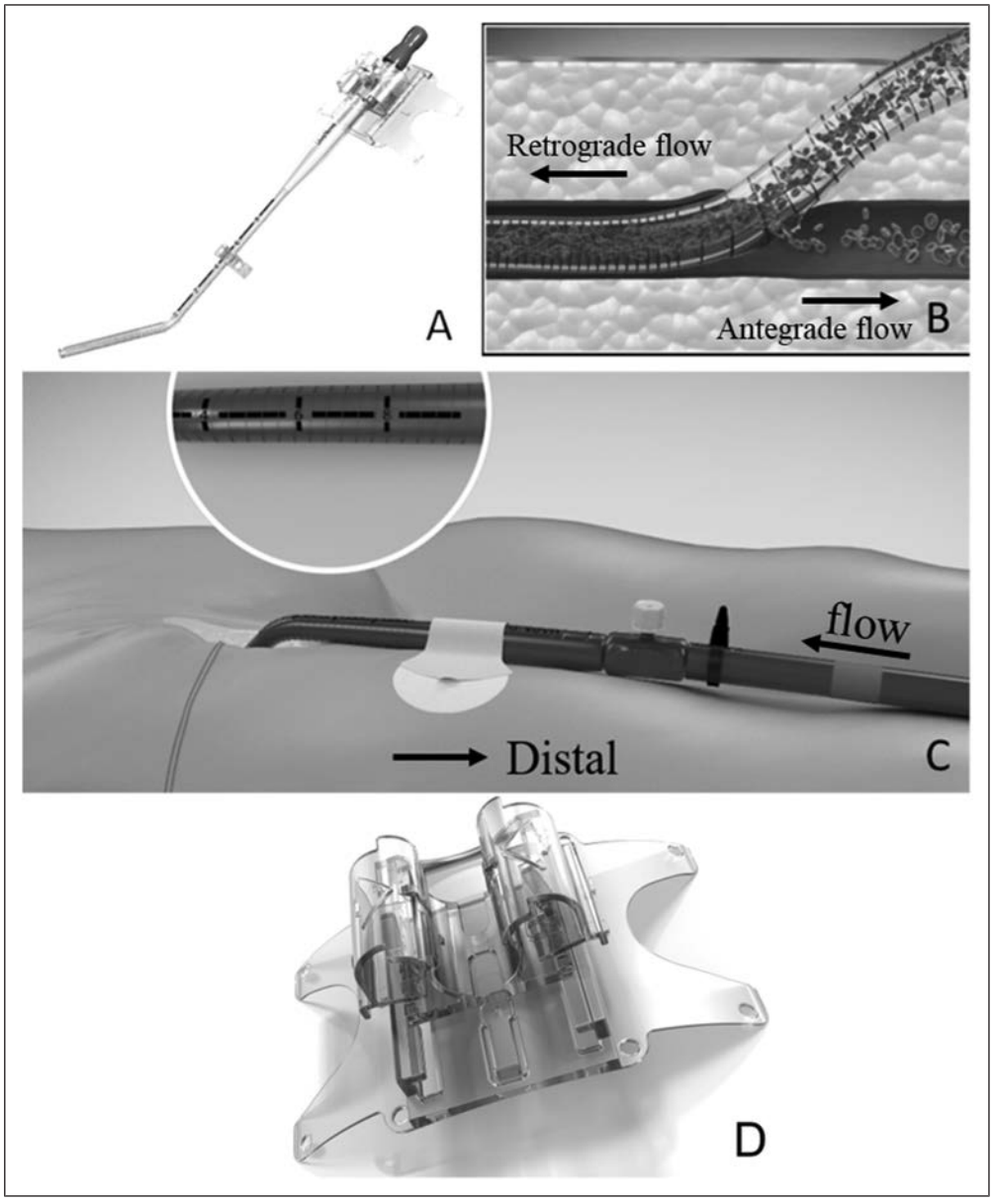

Figure 1. Schematic drawing of the bidirectional cannula used. Panel (a) shows the cannula, panel (b) gives a more detailed view of the proximal patient and distal limb blood flow, and panel (c) shows the marking on top on the cannula (used for correct positioning) and the fixation method advised by the manufacturer. Panel (d) shows the fixation device. By courtesy of LivaNova, UK.

syndrome (0%), need for amputation (0%), and need for thrombectomy (0%) during peripheral V-A ECLS support when comparing to previous studies, addressing limb ischemia-related complications. Indeed, previous studies, in which conventional methods to guarantee cannulated limb perfusion have been applied, rates ranging from 2.2 to 34.6% of limb ischemia episodes requiring an intervention (1.4–10% for compartment syndrome/fasciotomy, 0.7–2.3% for amputation, and 3–4% for thrombectomy) have been reported.[4,9–24] The incidence of cannulation-site bleeding in our study cohort was relatively low (9.1%) and easily managed with minimal cannula repositioning, compared to most published studies reporting bleeding complications at the cannulation site ranging from 8 to 25%.[35–40] We observed no major adverse events during cannulation, but caution should be taken when positioning the cannula and fixating it in its required position to avoid any cannula-related bleeding, malfunction, or dislocation. Indeed, the fixation procedure of this type of arterial cannula presents more stringent features compared to a conventional arterial cannula due to the

risk of possible displacement of the elbow-located hole, thereby causing extravascular bleeding. In case of an apparent hematoma at the cannulation site, the action to be taken is to revise the cannula position in the femoral entry site. In case of limited dislodgement with signs of bleeding from that site, either advancing of the cannula slightly further into the femoral artery or, in case of bleeding around the cannula entry, adding additional purse-string sutures, usually with Teflon felt, are recommended.

Although the design of the cannula avoids the need of an extra DPC, less control can be applied over the blood flow towards the cannulated limb. Such a limitation has been observed during the weaning phase via a decrease in NIRS values if too low flow in the perfusion cannula (and therefore also through the elbow-located hole) is provided. As reported in this study, the weaning of one patient was limited due to the occurrence of limb ischemia when decreasing blood flow immediately solved with an increase of the perfusion flow using an arteriovenous shunt in the ECLS circuit while performing the weaning process.[41] Although relatively rare, this needs to be considered when weaning a patient.

Furthermore, the lack of a dedicated small DPC (usually 6–8 Fr) and related circuit leads to a lower risk of thrombosis and related distal embolization. Thrombosis and related distal embolization may also occur in the vascular segment between the main perfusion cannula and the DPC entry site, risk which is obviously avoided by using the bidirectional cannula.

NIRS monitoring is recommended, and placement of an additional DPC might be a bail-out strategy in case of limb ischemia. Studies investigating the distal limb perfusion at various flows during ECLS are needed to gather insight into the effectiveness of the bidirectional cannula. The combination of ECLS flow, patient anatomy and patient hemodynamics determines the distal limb perfusion which might thus not always be guaranteed.

Another limitation of the bidirectional cannula, besides the limited control over distal limb flow, can be the availability of only one size (19 Fr). Based on our experience and ECLS setup, a maximal blood flow of 4.0–4.5 L/minute is achievable. These blood flows are adequate for most patients but not all. If higher flows are expected, the current Bi-Flow cannula size might be a limiting factor during the ECLS run in patients with large body mass index or patients in need of very high flows (i.e., in septic shock), although this aspect must be confirmed and additionally investigated.

Duplex analysis of the non-cannulated arteries was in line with previous studies reporting normal PSV (normal values of the SFA: 73–90 cm/s) and predominantly multiphasic flow patterns; indicating absence of severe proximal arterial stenosis and an efficient pulse pressure transmission.[42–44] Arterial femoral flow in peripheral V-A ECLS patients can thus be assumed within normal range.

The mean PSV (44.7 ± 24.5 cm/s) in cannulated SFAs was decreased compared to the normal values mentioned above. These values are in line with our previous study reporting PSVs in cannulated SFAs (42.4 ± 19.4 cm/s).[45] It should be noted that the referring study also included bidirectional cannulas and can thus not be used to compare duplex measurements of arteries cannulated with bidirectional or unidirectional strategies. Unfortunately, literature on duplex parameters in cannulated femoral vessels is limited and, therefore, no reference or any further comments can be made in this respect.[45]

When analysing arterial flow patterns of cannulated limbs, a shift towards more resistive flow patterns was seen in the patients with a bidirectional cannula. As described in our previous article about duplex analysis in peripheral V-A ECLS patients, more resistive flow patterns indicate a higher pulse pressure and less obstruction at the proximal part of the arterial tree.[42–45]

Limitations and strengths of the study

This is the first study reporting clinical experiences and outcomes of the bidirectional cannula during peripheral V-A ECLS. Although the cohort can be considered small and no control group was included, and are thus limitations of this study, the bidirectional cannula has been clinically available since a relative short period and reporting preliminary outcomes of this cannula's use is relevant for ECLS clinicians to optimize cannulation strategy decision making. In the future, a large cohort, also with comparative statistics, will be warranted and could contribute to determining the actual safety, efficacy, and role of such a new cannula in the strategy for distal limb perfusion in peripheral V-A ECLS.

The prospective character of this study, and consecutive patient selection, made it less susceptible to selection bias. Also, few as possible exclusion criteria were used to limit bias. Duplex analysis was, if available, done by an experienced vascular ultrasound technician, which increased the reliability and validity of the measurements. In this study, cannulation was done surgically by the cardiothoracic surgeon. Therefore, this study might not be representative for centres performing percutaneous cannulation, although the bidirectional cannula might be implemented also percutaneously. Also, in other centres, patient populations might differ from that included in this study. This thus limits the external validity and generalisability of the study's findings. Additionally, as mentioned earlier in the discussion, the study was limited by the

inherent limitations of the cannula, namely lack of control over distal limb perfusion and limited cannula size availability.

Conclusion

Novel distal limb perfusion techniques during ECLS are clinically relevant due to the important consequences of limb ischemia-related complications. Based on this study, use of the new bidirectional femoral artery cannula was associated with a low rate of limb ischemia-related adverse events, absence of major adverse events and a maintained capacity to run adequate ECLS blood flows. It may therefore represent a safe and effective alternative to unidirectional cannulation combined with an additional DPC.

Declaration of conflicting interests

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Supplemental Material

Supplemental material for this article is available online.

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Addressing inadequate blood flow during normothermic regional perfusion for in-situ donation after circulatory death grafts preservation

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Abstract

Donation after circulatory death (DCD) has emerged as attainable strategy to tackle the issue of organ shortage, expanding the donor pool. The DCD concept has been applied to the multiple declinations of circulatory arrest, as per the Modified Maastricht Classification. Notwithstanding, whichever the scenario, DCD donors experience a variable warm ischemia time whose correlation with graft dysfunction is ascertained. This applies to both "controlled" (cDCD) donors (i.e., the timespan from the withdrawal of life-sustaining therapies to the onset of in-situ perfusion), and "uncontrolled" DCD (uDCD) (i.e., the low-flow period during cardiopulmonary resuscitation – CPR). This sums up to the no-flow time from cardiac arrest to the start of CPR for uDCD donors, and to the no-touch period for both uDCDs and cDCDs. Static and hypothermic storage may not be appropriate for DCD grafts. In order to overcome this ischemic insult, extracorporeal membrane oxygenation devices are adopted to guarantee the in-situ grafts preservation by means of techniques such as the normothermic regional perfusion (NRP) which consists in a selective abdominal perfusion obtained via the endovascular or surgical occlusion of the thoracic aorta. The maintenance of an adequate pump flood throughout NRP is therefore a sine qua non to accomplish the DCD donation. The issue of insufficient pump flow during NRP is prevalent and clinically significant but its management remains technically challenging and not standardized. Hereby we propose a systematic algorithmic approach to address this relevant occurrence.

Keywords

perfusion, donation after circulatory death, extracorporeal membrane oxygenation, normothermic regional perfusion, flow inadequacy

Introduction

Donation after circulatory death (DCD) has emerged in the late nineties as attainable strategy to tackle the infamous issue of organ shortage, de facto expanding the donor pool.[1] The DCD concept has been applied to the multiple declinations of circulatory arrest, as per the Modified Maastricht Classification.[2] Notwithstanding, whichever the scenario, DCD relies on extracorporeal circulation technologies since donors experience a variable warm ischemia time (WIT), that is consistently associated with graft dysfunction.[3,4] This applies to both "controlled" DCD (cDCD) donors (i.e., timespan from the withdrawal of life-sustaining therapies to perfusion onset), and "uncontrolled" ones (uDCD) (i.e., low-flow

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period during cardiopulmonary resuscitation). This sums up to the "no-touch period" for both uDCDs and cDCDs, and to the no-flow time from cardiac arrest to the start of CPR for uDCD donors (Figure 1). Hence, the conventional methods for organ preservation such as static and hypothermic storage may not be appropriate for DCD grafts. In order to overcome the ischemic insult, extracorporeal membrane oxygenation (ECMO) devices are adopted to guarantee the in-situ grafts preservation. Among the existing perfusion techniques, normothermic regional perfusion (NRP) consists in a selective perfusion of the abdomen obtained occluding the thoracic aorta either internally (i.e., endovascular balloon occlusion of the aorta – EBOA) or externally (i.e., surgical cross-clamping). The maintenance of adequate pump flow throughout NRP is a *sine qua non* to accomplish the DCD donation.

The issue of insufficient pump flow during NRP is prevalent and clinically significant. However, its management remains technically challenging, not standardized, and do not necessarily resemble that of conventional venoarterial ECMO. Hereby we propose a systematic algorithmic approach to address this relevant occurrence (Figure 2).

Culprit ascertainment

Insufficient pump flow during NRP can be detected extemporaneously by visual-checking the ECMO console or by setting a low-flow alarm. A delayed and

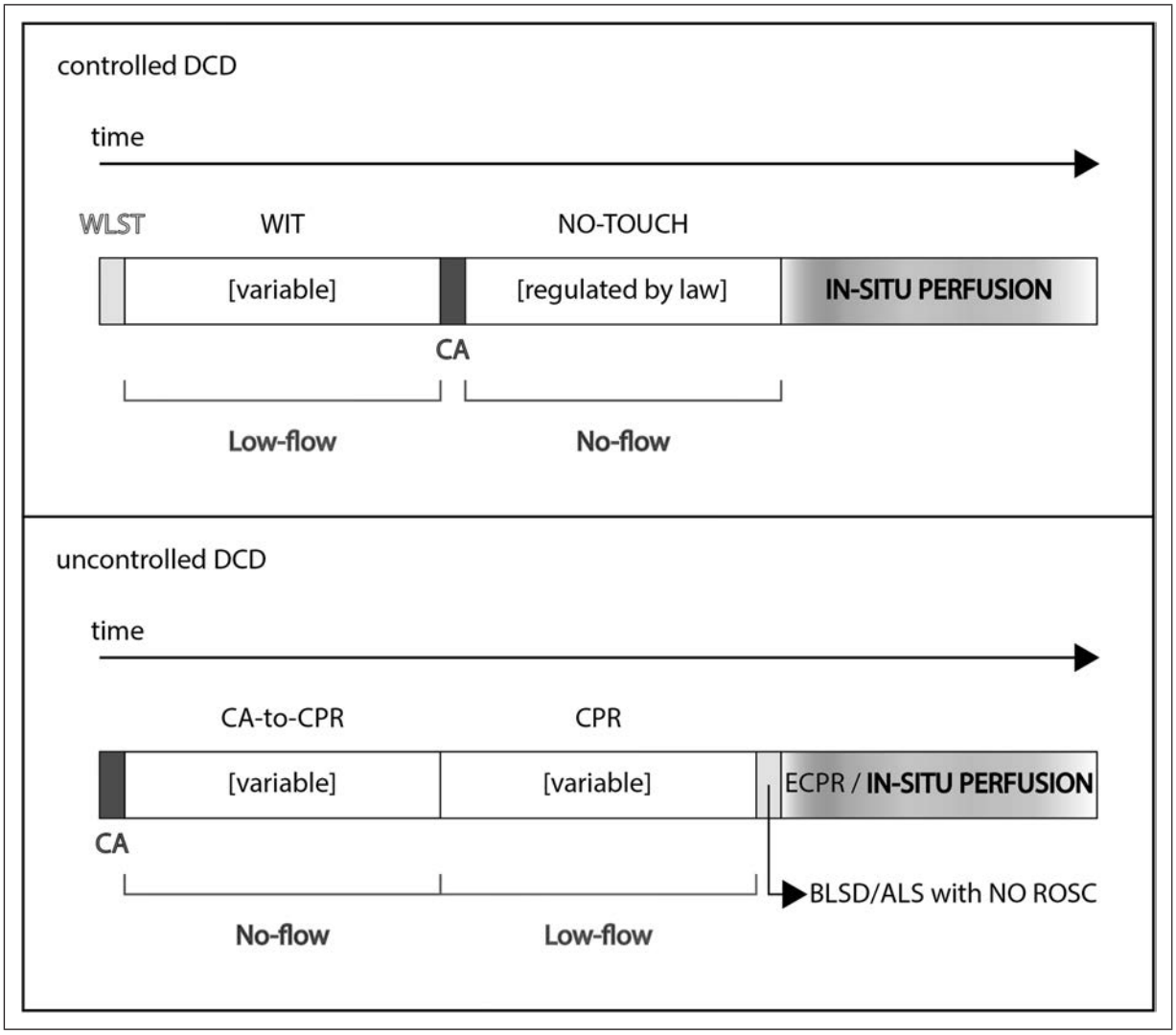

Figure 1. Controlled and uncontrolled DCD timelines, low- and no-flow periods. ALS: advanced life support; BLSD: basic life support and defibrillation; CA: cardiac arrest; CRP: cardiopulmonary resuscitation; ECPR: extracorporeal cardiopulmonary resuscitation; ROSC: return of spontaneous circulation; WIT: warm ischemia time; WLST: withdrawal of life sustaining therapy.

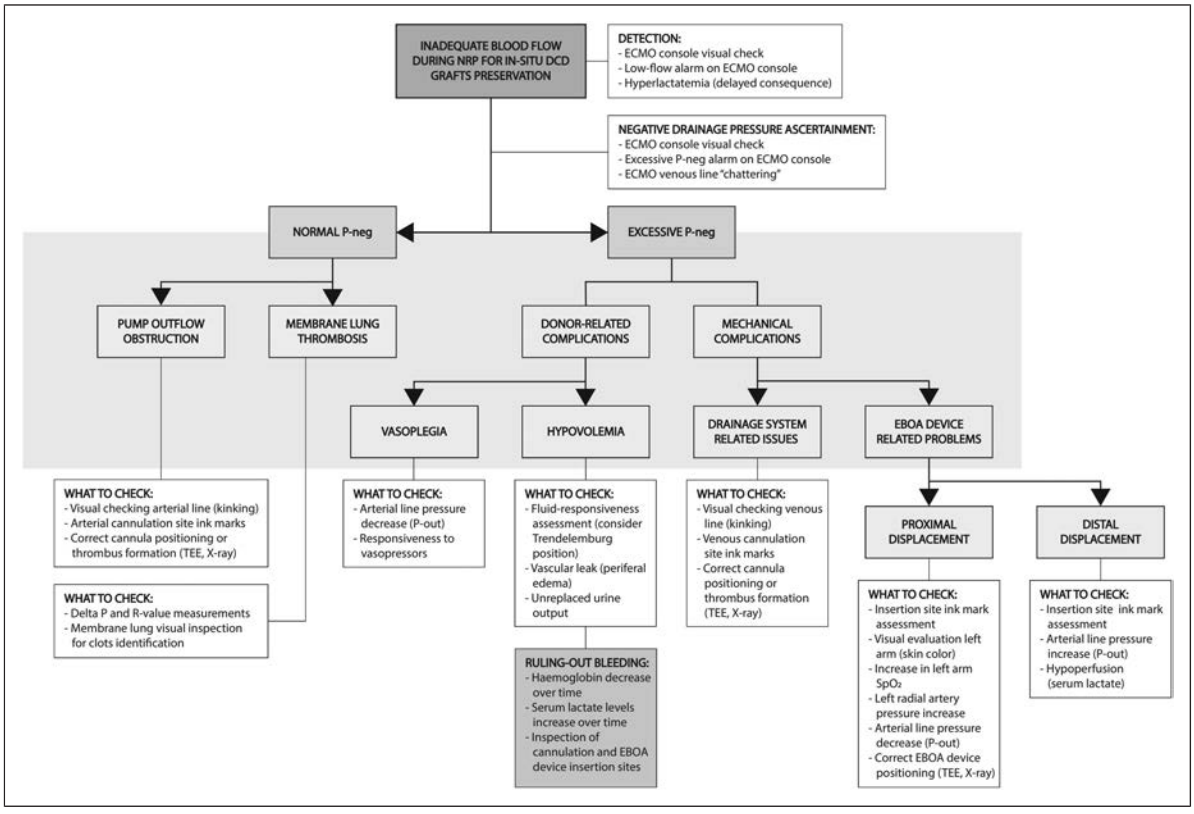

Figure 2. Algorithmic approach to address the issue of inadequate blood flow during NRP for in-situ DCD grafts preservation. Yellow rectangle: plausible causes of NRP flow insufficiency.

indirect detection is also a contingency: an increasing serum lactate concentration over-time is indeed a clear sign of hypoperfusion. However, being lactate an end product of glycolysis under conditions of total or partial anaerobia (i.e., formed from pyruvate mediated by lactate dehydrogenase), the ischemic damage preexist the increase in lactate concentration, making this delayed detection very undesirable.

Drainage insufficiency and pump outflow-related issues are two sides of the same coin that is the inadequacy of pump flood, possibly precipitating towards suboptimal in-situ organ preservation, and graft dysfunction. Clinicians must discern between these two main scenarios in order to further gather the underlying causative factor (or the combination of causes), and address it. In this sense, a drainage pressure-directed ascertainment may immediately rule out either an outflow-related complication or a drainage problem (i.e., characterized by variable degrees of excessively negative drainage pressure). All the more so since an excessively negative pressure is undemanding to be identified by just visual-checking the ECMO console, by setting an appropriate alarm, or simply noticing a movement of the tubing: a phenomenon variably termed "chatter," "chugging", or "kicking." Furthermore, this phenomenon is clinically relevant per se, given the renowned association between excessive negative pressure and entities like cavitation and hemolysis.[5]

Insufficient venous return

A reduced pump preload can result from either donor-related or mechanical, device-related, causes.

Donor-related drainage issues

Two are the major donor-related concerns: vasoplegia and hypovolemia. Vasoplegia increases vasculature capacitance, thus redistributing circulating volume, and reducing venous drainage. This phenomenon is usually difficult to identify while using closed systems like ECMO, whereas its occurrence cannot pass unnoticed when using an open system like conventional cardiopulmonary bypass, in cardiac surgery setting (i.e., lowering of blood level in the reservoir). Vasoplegia commonly occur during NRP, and can be tackled resorting to alpha-adrenergic pharmacologic agents (i.e., noradrenaline). Indeed, a low arterial line pressure

(P-out) results from vasoplegia. Second and more important is the phenomenon of hypovolemia that implicates fluid extravasation, bleeding complications, or unreplaced urine output. While vasoplegia treatment is somehow straightforward, the management of hypovolemia depends on its cause. Bleeding must be immediately ruled out and resolved, as it impose an unpredictable and possibly catastrophic ischemic injury due to its synergistic effect that lowers both NRP flow and oxygen delivery, and that may manifest only after reperfusion in the recipient. Bleeding is commonly due to problems with femoral cannulation or with the external cross-clamp of the Aorta, ergo these sites must be promptly and carefully checked. This point represents a substantial distinction between NRP and ECMO, since cross-clamp is inherent of in situ abdominal perfusion procedures. Finally, internal bleeding can be difficult to detect, thus a thorough monitoring of hemoglobin levels is mandatory during NRP.

The issues of unreplaced urine output and fluid leakage share a common treatment that trivially consists in volume replacement: definitely not a trivial point to be discussed, especially in the scenario of a DCD procedure. These two occurrences differ qualitatively and quantitatively, *ergo* their clinical weights are different. In fact, the urine output must be monitored and replaced as appropriate (even if it normally constitutes scarce amounts during NRP) whereas fluid leakage is a very consistent drawback of DCD in-situ organ preservation. Perhaps, choosing a more oncotic fluid (i.e., albumin or colloids) may better contrast the hydrostatic pressure that, together with the impaired endothelium secondary to the death-related processes and the superimposed inflammatory stress from the extracorporeal device, concurs to the overt vascular hyperpermeability. However, controversies about the use of colloid solutions especially with regards to their effect on kidney function well depicts the lack of evidenced-based consensus.[6,7] Finally, clinicians should cautiously monitor for signs of cutaneous edema (i.e., "pitting") which can direct the diagnostic process.

Device-related drainage issues

The device-related occurrences that can negatively impact the pump preload concern the drainage system (i.e., venous cannula and venous line), and the EBOA device, if used. Both these complications are highly frequent; thus, clinicians must be aware of some banal expedients that may allow to rapidly identify and resolve complications. Aside of the capacitance of the vasculature, it is likely that mechanical factors limit the venous return: for instance, kinking of the venous line must be prevented by carefully supervising the tubing, especially while mobilizing the donor during NRP. This complication is as frequent as opportunely straightforward to be managed by manipulating the drainage line. Venous return is also dependent on the position of the cannula, that can also result inadequate (mostly after mobilization the donor). Marking the correct position of the cannula with a line on the skin is extremely useful to adjust the cannula insertion depth quickly and effectively, particularly when conventional tools are not promptly available (i.e., during transport). However, transesophageal echography (TEE) and X-ray assessments unquestionably represent the gold standard to analyze and eventually correct the positioning of cannulas, all the more so since these imaging techniques also allows the evaluation of possible obstructions of cannulas and tubing (i.e., clots).

Furthermore, TEE and X-ray assessments guarantee the correct positioning of the EBOA device. In fact, while surgical – external – cross-clamping of the thoracic Aorta determines a firm occlusion of the vessel, the EBOA device is very likely to experience inadequate movements throughout NRP, especially while mobilizing the donor – as for both cannulas and lines. Securing the EBOA device on the skin and marking its correct position (as for the venous cannula) may help to rapidly address this problem. Other expedients to recognize an EBOA malposition exist: the detection of increased (or increasing) left radial artery pressure or an increased oxygen saturation disclose the proximal migration of the device up to the left subclavian artery, whereas a distal migration is more elusory to be detected. In this sense, a rise of the arterial line pressure (P-out) may throw particular suspicion on this occurrence. Moreover, a delayed and indirect EBOA malposition detection via an increased serum lactate concentration is possible but undesirable, as previously debated.

Pump outflow-related issues

Aside of the pump preload, a reduced NRP flow can also result from a problem localized after the pump itself. This group of complications is not characterized by an excessively negative drainage pressure. The increase in arterial line pressure (P-out) could be seen instead, or better yet, a specific alarm can be set. For instance, the arterial line can get easily kinked if not adequately supervised, with high-risk scenarios being the mobilization of the donor and transport. Similarly to the kinking of the venous line, this occurrence should be prevented, and can be identified and fixed in

the same manner. An augmented P-out can also manifest in case of arterial cannula malposition or thrombus obstruction, both these conditions must be immediately evaluated by resorting to the same techniques above discussed (i.e., ink marker, ultrasonography, and X-ray), and opportunely resolved.

Another factor that can decrease NRP flow is the thrombosis of the membrane lung (ML). ML clotting is indeed a terrific complication that, just like uncontrolled bleeding, exerts a synergistic action decreasing both NRP flow and oxygen delivery. For this reason, anticoagulation protocols are universally adopted. The continuous monitoring of the "*delta-P*" (i.e., the difference between the pressure measured before the ML, and the one measured after the ML) and the "*R value*" (i.e., that indexes the *delta-P* for the pump flow), is a valuable strategy attaining to prevent this occurrence, or at least to early recognized it. A visual inspection of the ML by using a light source can also allow the detection of clots albeit this finding could be tardive.

Conclusions

With the increase of DCD donations worldwide, it is predictable that the resort to extracorporeal technologies will expand. Considering the marginality of DCD grafts, it is mandatory to guarantee a reliable in-situ preservation (i.e., perfusion and oxygenation). Complex and inherent technical issues (different from VA ECMO) are likely to negatively impact grafts' quality thus lead to dysfunction in the recipient. It is essential to adopt a systematic approach for the management of inadequate blood flow during NRP for in-situ DCD grafts preservation in order to improve patient outcomes.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Prof. Lorusso is a consultant for Medtronic and LivaNova and is on the medical advisory board for Eroses (all honoraria are paid at the University). No other authors report conflicts of interest.

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The ProtekDuo dual-lumen cannula for temporary acute mechanical circulatory support in right heart failure: A systematic review

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Abstract

Introduction: Acute right ventricular failure (aRVF) is associated with high mortality and morbidity. Mechanical circulatory support (MCS) may be considered as an advanced treatment option. The ProtekDuo is a cannula that can be used to provide acute right ventricular support as part of a temporary percutaneous (tp) right ventricular assist device (RVAD) system. The primary objective of this systematic review is to describe patient survival and complications when the ProtekDuo cannula was used as part of an tpRVAD system.

Methods: MEDLINE, Embase, and Scopus were searched from database inception to August 26, 2022. Reference sections of studies were reviewed to screen for database omissions.

Results: Seven studies with 127 patients were eligible for inclusion. The studies included patients with aRVF from a variety of causes. Mean duration of support was between 10 and 58 days in five studies. Patient survival to discharge was between 60% and 85.2% in two studies. Four authors reported 30-day survival between 60% and 85.2%. Devicerelated and non-device related complications were low.

Conclusions: Patients treated with RVAD using the ProtekDuo cannula have comparable survival rates and complications to other tpRVAD systems. Several advantages exist compared to other RVAD systems.

Keywords

ProtekDuo, right ventricular failure, right ventricular assist device, right ventricular assist device, mechanical circulatory support

Introduction

Right ventricular failure (RVF) can occur acutely or persist as chronic disease in association with several conditions which include the common pathophysiologies of RV volume and/or pressure overload.[1–3] The aRVF syndrome occurs when systemic congestion in combination with reduced cardiac output results in organ dysfunction or failure and is associated with a high in-hospital mortality rate that is independent of the primary reason for RVF.[1–7] Management of aRVF begins with invasive or non-invasive interventions to address the underlying condition (e.g., coronary artery revascularization) and pharmacological intervention including diuretics, inhaled pulmonary vasodilators for reduction of RV afterload, and vasopressors and inotropes if indicated to maintain blood pressure and cardiac output. When conventional management fails,

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escalation to mechanical circulatory support (MCS) in the form of extracorporeal membrane oxygenation (ECMO) or right ventricular assist device (RVAD) may be considered.[1–3] RVADs can be inserted surgically via sternotomy or thoracotomy, or percutaneously through access of a large central vein.[8,9] The ProtekDuo® cannula (LivaNova PLC, London, UK) is a percutaneous, single-site, dual-lumen cannula that can be combined with a centrifugal extracorporeal circulatory support pump to create a temporary percutaneous (tp) RVAD system.

The ProtekDuo is inserted into the right internal jugular vein (RIJV) and advanced through the right heart into the main pulmonary artery (PA). When properly positioned, the cannula's proximal side holes lie in the right atrium (RA) and the distal side holes lie in the main PA between the pulmonic valve and bifurcation of the left and right PA. In its normal configuration, and when connected to an extracorporeal pump, the RV is directly bypassed as venous blood is drained from the RA and returned to the main PA. Depending on cannula size and pump speed, blood flow between four and five liters per minute (LPM) may be achieved, making the ProtekDuo cannula an effective RVAD. The wire-reinforced cannula comes in two sizes, 29- and 31-French (Fr), and can be used in conjunction with most commercially available centrifugal extracorporeal circulatory support pumps using standard 3/8-inch blood circuit tubing.

The ProtekDuo has a particular advantage over other tpRVADs in that it is placed at a single site in the upper body versus the groin, enabling the patient to freely use the lower extremities to mobilize.[5,10–12] Additionally, in cases of aRVF and concomitant respiratory failure, a membrane oxygenator can be spliced into the extracorporeal circuit, thus allowing the ProtekDuo cannula to serve as a conduit for dual lumen (dl) venopulmonary (V-P) ECMO or oxygenated RVAD (oxyRVAD) with minimal to no recirculation and potentially earlier extubation of the patient.[13–15] Once pulmonary recovery is achieved, the oxygenator can be easily removed, and RV support continued if needed. The ability to provide respiratory support is a clear advantage of the ProtekDuo when compared to other tpRVADs, which if used, may require exposing the patient to an additional procedure or surgery if severe respiratory failure ensues.

Compared to surgical RVADs, the ProtekDuo cannula affords the advantage of expeditious placement of RV support thus avoiding potential delays that may be associated with the prospect of surgical operation or re-operation.[16] Use of a ProtekDuo as a tpRVAD may also minimize the number of required sternotomies and associated cardiopulmonary bypass, procedural complications, bleeding and need for blood transfusions, and infection.[9,16,17] In our own experience, use of a ProtekDuo cannula for perioperative aRVF has allowed for effective RV decompression and primary, as opposed to delayed, sternal closure.

In this work, we are focused on investigating the ProtekDuo as an RVAD. Therefore, we aimed to conduct a systematic review of the literature to determine the current evidence for its function as tpRVAD measured by survival and complication rates.

Materials and methods

Design

This review was registered with INPLASY (INPLASY202290026) and was conducted in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement to ensure clarity and transparency.[18] We used the PICOS approach (Participants, Intervention, Comparison, Outcome and Study Design) to frame the research question and guide selection of clinical studies following our systematic search as recently described (Table 1).[19]

Search

For the systematic literature search, we queried MEDLINE, Embase, and Scopus databases from inception through August 26, 2022 using the following keywords and their variations: "ProtekDuo," "right ventricular assist device," and "ventricular assist device." We assessed all relevant studies and their reference lists to identify articles for inclusion. We excluded any animal or pediatric studies (<18 years) as well as studies not published in the English language. In the case of publications with overlapping data, we included the largest or most contemporary study. The literature was screened for any publication on the ProtekDuo, and a redundancy check was performed. All authors participated in the study selection and determination of eligibility for inclusion in this systematic review. Discordances were addressed by consensus. Clinical guidelines, reviews, book chapters, editorials, letters to the editor, and conference abstracts were excluded as displayed in Figure 1. All case reports relevant to the subject, however, were reviewed and contextually integrated in the discussion of this systematic review.

Data Analysis

We identified a total of 262 publications, of which 147 were found in EMBASE, 24 in Medline, and 91 in

Table 1. "PICOS" approach for the selection of studies in the systematic search process.

PICOS	
Participants	Patients with right ventricular failure
Intervention	Right ventricular assist device with ProtekDuo cannula
Comparison	Control group if available
Outcomes	Effectiveness of treatment in terms of survival rate and complications
Study design	Prospective and retrospective cohort studies, case series >5 patients

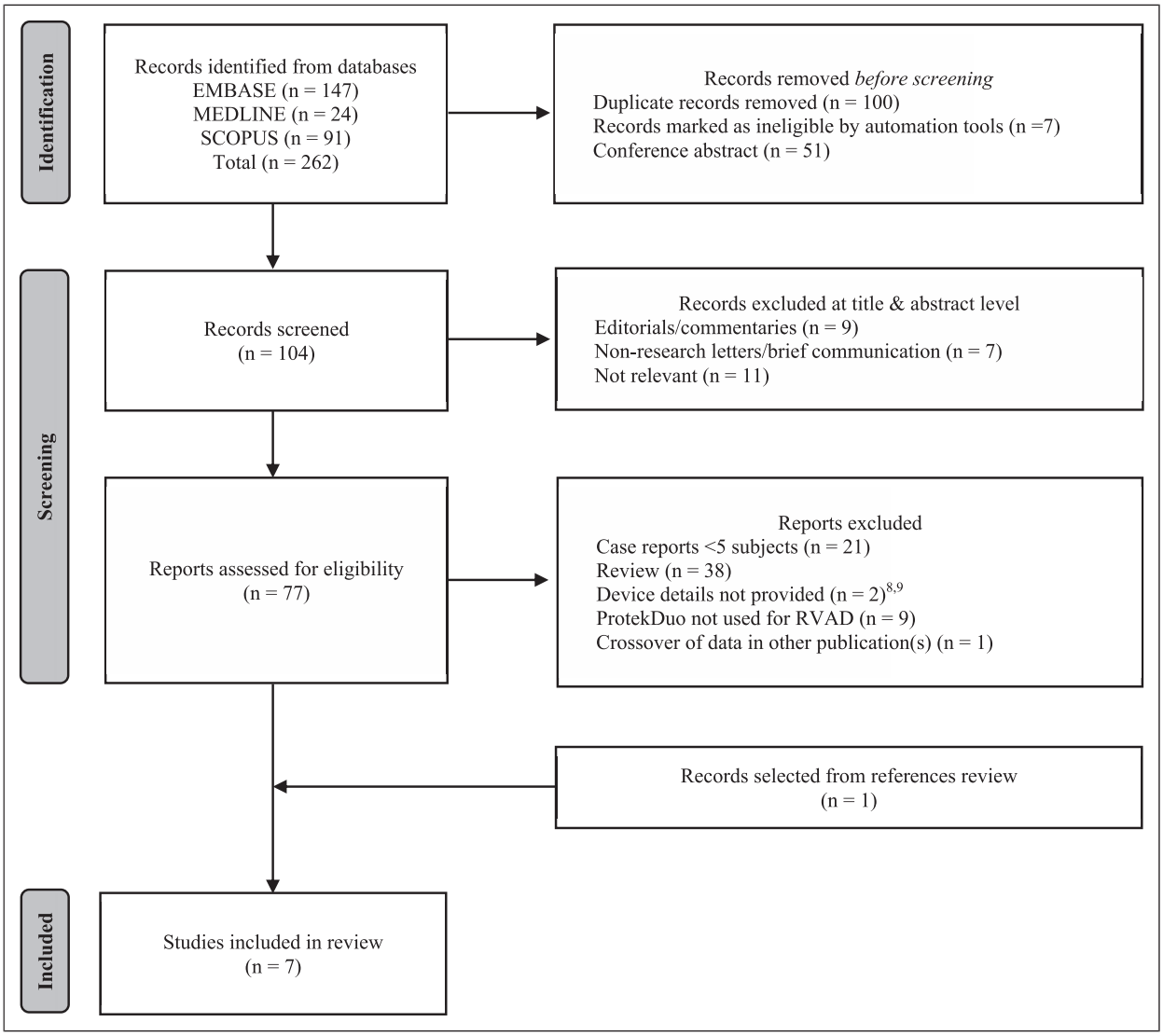

Figure 1. Flow diagram of the systematic search.

Scopus. Prior to screening, 100 duplicates, 51 conference abstracts, and 12 publications marked ineligible by automation tools were discarded, leaving 104 publications for further screening. At the title and abstract level, 11 publications were excluded for being irrelevant to the subject as were nine editorials and seven non-research letters or brief communications, leaving 77 publications to assess for eligibility. Further exclusion criteria at the full text level removed 21 case reports with less than five subjects, 38 reviews, two studies in which outcomes for patients with RVAD using ProtekDuo were co-analyzed with other percutaneous RVADs[9] or configurations,[8]

nine studies in which the ProtekDuo was used for a purpose other than RVAD, and one study with data in another publication. One additional publication was included for analysis after being identified in review of reference lists. In total, seven publications were identified as eligible for this review (Figure 1).

Results

Six retrospective cohort studies[4,6,10–12,20] and one case series[5] with a total of 127 patients were included in this review. Six studies[4,6,10–12,20] were from single centers whereas one study collected data from two centers.[5] Two studies enrolled patients with aRVF that occurred during or after durable LVAD implantation,[4,12] one study enrolled patients with aRVF after myocardial infarction,[10] and four studies enrolled patients with aRVF from different etiologies.[5,6,11,20]

Appraisal of study quality was conducted using the Oxford Centre for Evidence-Based medicine Levels of Evidence.[21] None of the studies had control groups or measured outcomes in a blinded fashion. In most studies selected for review, the authors did not clearly define comparison groups, and only two authors clearly identified primary and secondary outcomes of interest. There was little consistency between studies in the duration of survival and complications reported.

Duration of support with ProtekDuo was between a mean of 10 and 58 days in five studies reporting mean,[4–6,10,11] and between a median of 10 and 11 days in the two studies reporting median.[12,20] The authors of one publication reported survival to weaning of ProtekDuo of 88.9%.[12] The authors of three studies reported survival to discharge between 67.5% and 85.2%.[6,10,12] Four authors reported 30-days survival between 60% and 85.2%.[4,10–12] Six studies reported device-related and/or non-device-related complications.[4–6,10–12] See Table 2.

Discussion

Survival

Studies of RVADs in patients with aRVF have typically demonstrated improved survival with MCS especially when placed early following onset of aRVF.[1,9,12] Salna and coauthors retrospectively analyzed a cohort of 27 patients who developed aRVF after durable LVAD and were supported with RVAD using the ProtekDuo cannula. In their study, they reported 88.9% survival to RVAD weaning, 85.2% survival both to discharge and at 30-days, and 81.5% 1-year survival.[12] In their retrospective study of 10 patients with aRVF secondary to myocardial infarction, Kremer et al.[10] reported survival of 60% at both 30-days and 1-year.[10] Oliveros and colleagues, in their retrospective cohort study of 11 patients with aRVF from various causes, reported 81.8% 30-days and 63.6% 180-days survival.[11] Schmack and coauthors, in their retrospective cohort of 11 patients with ProtekDuo implantation for aRVF at the time of durable LVAD implantation, 72.7% 30-days survival, and 63.6% 60- and 180-days survival.[4] Ravichandran and colleagues reported a 58.8% survival rate over an unspecified period of time in their series of 17 patients with aRVF from multiple causes including post-durable LVAD, post-heart transplant, post-temporary LVAD, and other causes.[5] Lim et al. retrospectively analyzed a cohort of 11 patients with aRVF secondary to multiple causes including post-durable LVAD, post-heart transplant, and end-stage heart failure with a reported survival rate at 90-days of 43%.[20] Badu and coauthors retrospectively analyzed a cohort of 40 patients with aRVF grouped by primary cause: post-cardiotomy, cardiogenic shock (either coronary ischemia or decompensated heart failure), and respiratory failure with RV dysfunction. The authors reported survival to discharge of 68% in all groups. When survival to discharge was stratified by indication for RVAD, patients in the cardiotomy group had an 89% survival, patients with cardiogenic shock had a 42% survival, and patients with respiratory failure had a 60% survival.[6]

The reporting of different survival endpoints makes comparison between the analyzed cohorts more difficult. Similar values are observed in 30-days survival reported in studies included in our review compared to 30-days survival reported for other tpRVADs.[22,23] Unfortunately, survival to discharge was not reported in all included studies in our review.

Complications and adverse events

Six of the seven studies in our review reported complications and adverse effects. Regarding device-related complications, two studies reported cannula migration in a total of five patients and thrombosis at the cannula site in two patients.[6,12] Other device-related complications include moderate to severe tricuspid regurgitation created by the cannula,[12] vascular injury in one patient and bleeding from cannula site in two patients,[5] and superior vena cava syndrome in three patients.[6] A total of two studies explicitly reported having no device-related complications.[4,10] No studies reported clinically significant recirculation-based complications or extent of recirculation (Table 2).

Five studies in our review reported non-device related complications. Two studies reported renal failure requiring

Table 2. Survival and complications in studies of ProtekDuo as RVAD.

First author, year, study design, oxford grade	*n*	Survival *n* (%)							Complications *n*(%)	
		Weaning	Discharge	30-days	60-days	90-days	180-days	1-year	Device-related	Non-device-related
Kremer, 2020 retrospective cohort 4	*n* = 10	—	6 (60.0)	6 (60.0)	—	—	—	6 (60.0)	Reported none	AKI requiring HD: 8 (80.0) Post-operative bleeding: 4 (40.0) Hemorrhagic stroke: 1 (10.0) Organ ischemia: 1 (10.0) Infection/sepsis: 4 (40.0)
Oliveros, 2021 retrospective cohort 4	*n* = 11	—	—	9 (81.8)	—	—	7 (63.6)	—	Did not report	AKI requiring HD: 5 (45.4) GI bleeding: 5 (45.4) HIT: 6 (54.5) Stroke: 2 (18.2) Sepsis: 7 (63.6)
Salna, 2020 retrospective cohort 4	*n* = 27	24 (88.9)	23 (85.2)	23 (85.2)	—	—	—	22 (81.5)	Mod-severe TR: 8 (36.4)[a] Cannula migration: 2 (7.4) Device thrombosis: 1 (3.7)	Hemolysis: 4 (14.8) Conversion to surgical RVAD: 3 (11.1)
Schmack, 2019 retrospective cohort 4	*n* = 11		—	8 (72.7)	7 (63.6)	—	7 (63.6)	—	Reported none	Hemorrhagic stroke: 1 (9.0)
Ravichandran, 2018 case series 4	*n* = 17	—	—	—	—	—	—	—	Vessel injury: 1 (5.9) Bleeding from cannula site: 2 (11.8)	GI bleeding: 1 (5.9%) Hemorrhagic stroke: 2 (11.8)
Lim, 2020 retrospective cohort 4	*n* = 11	—	—	—	—	4 (36.4)	—	—	Did not report	Did not report
Badu, 2020, retrospective cohort 2b	*n* = 40	—	All patients: 27 (67.5) Cardiotomy: 16 (88.9) Cardiogenic shock: 5 (41.7) Respiratory failure: 6 (60.0)	—	—	—	—	—	Cannula migration: 3 (7.5) SVC syndrome: 3 (7.5) RIJV thrombus: 1 (2.5)	Did not report

AKI = acute kidney injury, HD = hemodialysis, GI = gastrointestinal, HIT = heparin-induced thrombocytopenia, TR = tricuspid regurgitation, RVAD = right ventricular assist device, SVC = superior vena cava, RIJ = right internal jugular vein.

[a]22 pts had echocardiogram.

Table 3. Additional outcomes in studies of ProtekDuo as RVAD.

First author	Cause of RVF	Patients included	Weaned *n* (%)	Duration of support (days)		ICU LOS (days)		Hosp LOS (days)		Additional outcomes
				Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Kremer	Acute MI	Acute NSTEMI: 5 Acute STEMI 5	4 (40.0)	10.0 (7.4)		15.8 (11.6)				RV recovery: 4 Required permanent RVAD: 2 Death: 4 (after explantation: 1, hemorrhagic stroke: 1, MOF and biV failure: 2)
Oliveros	Various etiologies	Post-partum cardiomyopathy with biV failure and simultaneous V-A ECMO: 1 Post-lung resection: 4 Massive PE after systemic thrombolytics later converted to central V-V ECMO: 1 Post-LVAD: 1 Acute MI: 1 Post-MV replacement: 1 ARDS with MOF and cardiac arrest: 2	6 (54.5)	58 (47)				103 (67)		
Salna	Post- LVAD	All post-LVAD			11 (7–16)		36 (22–48)		48 (34–81)	Procedural success: 27 Conversion to surgical RVAD: 3
Schmack	Post-LVAD	All post-LVAD	10 (90.9)	16.8 (9.5)		23.8 (16.5)				Patient requiring oxygenator: 1
Ravichandran	Various etiologies	Post-LVAD: 12 Post-OHT: 2 RV failure: 2 TandemHeart LVAD + Protek duo: 1	4 (23.5)	10.5 (6.5)						Conversion to surgical or durable RVAD: 6

(continued)

Table 3. (continued)

First author	Cause of RVF	Patients included	Weaned *n* (%)	Duration of support (days)		ICU LOS (days)		Hosp LOS (days)		Additional outcomes
				Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Lim	Various etiologies	Post-LVAD: 7 Post-OHT: 2 End-stage heart failure with impella support: 2			10					RVAD resulted in significant reduction in CVP and increase in MAP 3 hours post-cannula insertion No significant change in vasopressors/ inotropes 3 hours post-cannula insertion
Badu	Various etiologies	Post-cardiotomy: 18 Cardiogenic shock: 12 Respiratory failure: 10	All patients: 29 (72.5) Post-cardiotomy: 17 (94.4) Cardiogenic shock: 5 (41.7) Resp failure: 7 (70.0)	All patients: 13.8 (7) Post-cardiotomy: 15.8 (7) Cardiogenic shock: 10.6 (5.5) Resp failure: 11.1 (7.1)						Of 29 pts weaned, complete RV recovery: 22, required ECMO: 3, OHT: 2, death after weaning: 2

MI = myocardial infarction, NSTEMI = non-ST segment elevation myocardial infarction, STEMI = ST segment elevation myocardial infarction, RVAD = right ventricular assist device, biV = biventricular, V-A ECMO = venoarterial extracorporeal membrane oxygenation, PE = pulmonary embolism, V-V ECMO = venovenous extracorporeal membrane oxygenation, LVAD = left ventricular assist device, MV = mitral valve, ARDS = acute respiratory distress syndrome, MOF = multiorgan failure, OHT = orthotopic heart transplant, RV = right ventricle, CVP = central venous pressure, MAP = mean arterial pressure, resp = respiratory.

hemodialysis in 13 patients.[10,11] Three studies reported hemorrhagic stroke in four patients[4,5,10] and one study reported ischemic stroke in two patients.[11] Other non-device related complications include bleeding in six patients in three studies [5,10,11] and sepsis in 11 patients in two studies.[10,11] (Table 2).

Overall, the ProtekDuo has a favorable safety profile even when compared to other currently available tpRVAD systems.[22,23] The ProtekDuo, because of its larger size compared to another device, might be expected to have more device-related complications, but this concern is not supported in the studies selected for this review. The ProtekDuo, like all tpRVADs, is subject to migration and device malposition, but the occurrence of this complication did not seem to be frequent in the included studies; moreover, the problem is likely dependent on a number of variables such as method of securing the cannula and patient movement, among others, which were not extensively discussed in the selected studies. It is noted that hemolysis was not reported as a device-related complication in the studies included in our review, though this should be interpreted cautiously as hemolysis may occur at higher flow or suboptimal position of the ProtekDuo cannula. Nonetheless, hemolysis, when significant, is associated with organ dysfunction and increased mortality[24,25] and its significance in patients with tpRVADs should not be underestimated.

Additional reported outcomes

The authors of five studies reported successful weaning from RVAD using ProtekDuo between 23.5% and 90.9% to complete RV recovery, conversion to ECMO or durable RVAD, or heart transplant.[4–6,10,11] The authors of three studies reported intensive care unit length of stay, which in two studies was between a mean of 15.8 ± 11.6[10] and 23.8 ± 16.5 days[4] and a median of 36 [IQR 22–48] days in a single study.[12] Hospital length of stay was reported in two studies and was a mean of 103 ± 67 days[11] and a median of 48 [IQR 34–81] days.[12] Vasopressor and inotrope requirements were reported by the authors in three studies included in our review, two of which reported reduction in doses after ProtekDuo insertion[6,12] and one that reported no significant change in dose.[20] Conversion to surgical RVAD was reported by the authors in three studies in a total of 11 patients for reasons such as persistent hemolysis (not related to ProtekDuo performance) and inability to tolerate weaning from ProtekDuo, though duration of ProtekDuo support before conversion was not reported.[5,10,12] See Table 3 for summary of additional outcomes.

Conclusion

Acute right ventricular failure, independent of primary cause, remains a significant concern in terms of morbidity and mortality. Unfortunately, the ability to accurately predict which patients will experience aRVF, especially those undergoing cardiac surgery, remains limited. When aRVF occurs, the primary goals of treatment should be to quickly implement measures that allow for the highest chance of RV recovery by offloading volume and pressure while maintaining adequate end-organ perfusion. As technology for MCS has progressed, more options for providing temporary support for the right heart have become available, allowing clinicians to be less dependent on potentially harmful medications or invasive measures. The ProtekDuo cannula is one such device that has advantages over others including patient mobility and the ability to provide respiratory support.

The studies included in our review, while informative, face challenges that may limit the application of their results. The most common and significant limitations are that the included studies were single center, retrospective cohort studies with small sample sizes and no control groups. As a result, their generalizability is limited and they are not adequately powered for their reported outcomes, thus making the results hypothesis-generating at most. Additionally, they are at risk from confounding and multiple types of bias. In our opinion, we did not feel that the data was of sufficiently high quality to perform meta-analysis. Instead, we conducted a systematic review alone with the intention of highlighting the current research of the ProtekDuo cannula as a tpRVAD for aRVF. What is clear is that the use of temporary percutaneous devices is likely to increase, and thus, adequately powered prospective studies are needed to answer questions of device superiority and safety in patients with differing etiologies of aRVF.

Declaration Conflicts of Interest

Prof. Dr. Lorusso is a consultant for Medtronic, Getinge and LivaNova and medical advisory board member for EUROSETS, all unrelated to this work; all honoraria to the university for research funding.

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Clinical decision support for ExtraCorporeal Membrane Oxygenation: Will we fly by wire?

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Abstract

Prognostic modelling techniques have rapidly evolved over the past decade and may greatly benefit patients supported with ExtraCorporeal Membrane Oxygenation (ECMO). Epidemiological and computational physiological approaches aim to provide more accurate predictive assessments of ECMO-related risks and benefits. Implementation of these approaches may produce predictive tools that can improve complex clinical decisions surrounding ECMO allocation and management. This Review describes current applications of prognostic models and elaborates on upcoming directions for their clinical applicability in decision support tools directed at improved allocation and management of ECMO patients. The discussion of these new developments in the field will culminate in a futuristic perspective leaving ourselves and the readers wondering whether we may "*fly ECMO by wire*" someday.

Keywords

Extracorporeal membrane oxygenation, extracorporeal life support, ECLS, digital twin, epidemiological- and computational modeling, prognostic models, fly by wire systems

Introduction

In patients receiving ExtraCorporeal Membrane Oxygenation (ECMO) support for severe cardiogenic shock and/or respiratory failure, personalized management could reduce complication rates and improve survival and quality of life.[1,2] Personalization of treatment already occurs with the decision to start or withhold ECMO support and the tailoring of cannulation strategy.[3,4] During ECMO support, patient-specific risks and benefits are accounted for in the personalization of management, such as anticoagulation strategies (weighing risk of bleeding vs. thrombosis) or the necessity to introduce a left ventricular unloading techniques (weighing risk of left ventricular overload vs. risk of vascular damage as a consequence of introduction of a second device).

(Real-time) prognostic models could provide decision support and improve tailoring of ECMO therapy by combining pieces of data that hold predictive information and which would, in their combination, exceed the abilities of physicians to interpret. The rapid digitalization of healthcare has opened up possibilities for models and tools to become more sophisticated and automatically fed with continuously updated data throughout a clinical course.[5]

In this scoping Review, we discuss the potential role of prognostic models for decision support regarding optimal allocation of ECMO and its management. We describe relevant epidemiologic prognostic models and

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computational physiological models (also being referred to as a "Digital Twin") to provide a generic overview of currently available prognostic models in different domains. Finally, we venture on how these model approaches could be integrated in one comprehensive system, potentially allowing us to "*fly ECMO by wire*" in a nearby future.

The relevance of- and rising need for- prognostic models

An accurate assessment of (treatment-related) risks in the setting of ECMO is notoriously difficult given the complexity of the clinical situation, the large heterogeneity between patients and the fact that interventions often carry a "*double edged sword*" effect where different risks exist in each approach.[6] For example, determining the optimal anticoagulation strategy after a severe bleeding complication in a patient supported with veno-arterial (V-A) ECMO after placement of a mechanical mitral valve prosthesis is challenging and heavily relies on accurate assessments of risks for bleeding and valve thrombosis. Decisions to tailor mechanical support and associated treatments in the setting of ECMO are nowadays commonly based on doctors' experience and reasoning, sometimes supported by relatively simple protocolized schemes which provide stratified risks for individual patients.[7,8] Long-standing experience and high degree of expertise are the only tools available now for accurate assessments of risk and benefit for ECMO-related decision making.

Prognostic models could support personalized risk assessments for ECMO-supported patients.[9] These prognostic models are tools that can compute a predicted risk for a particular event (e.g., death, or bleeding) based on patient- and disease-related characteristics.[10] Prognostic models can be simple or more complex, depending on their input and content. Simple prediction formulas have been particularly useful in times when a doctor was required to calculate these scores in their head. Recent and rapid advancements in computing power as well as the availability of digital electronic patient records (EPR) have however mitigated these limitations and opened up the way to more complex algorithms and artificial intelligence (AI) techniques with potentially better predictive performance.[11] Models that perform sufficiently well could be used as clinical decision support tools.[12,13]

Areas of application of decision support in ECMO care

Prognostic models may provide decision support in several areas of ECMO care. These areas cover decisions about the optimum allocation of ECMO support and a multitude of aspects surrounding ECMO management. Below, we elaborate on these areas and reflect on some currently available tools and models.

Optimal allocation of ECMO

From both a patient- and socio-economical perspective, it is essential to reserve ECMO specifically for those patients who are expected to benefit most.[14] That is because of the large impact of ECMO support for patients and the rapidly increasing health care costs and growing shortages in staffing and equipment. Decisions regarding optimum allocation may be improved by knowledge about a patients' prognosis and the expected effect of ECMO support.

We recently summarized all existing prognostic models in the setting of ECMO and identified a total of 58 models that were specifically designed to predict mortality based on variables collected shortly before or after initiation of ECMO.[15] Discriminative performance of frequently externally validated models[7,8] (Table 1) was moderate on average but highly variable across different external validation cohorts. Most importantly, all models were based on cohorts in which ECMO had already been initiated. This conditionality prevents these models from describing prognosis of patients in whom ECMO is considered and also to assess the incremental value of ECMO on outcomes in these individuals. This implies that there is currently no evidence-based prediction tool available to inform the decision on ECMO initiation based on patient prognosis. Existing prognostic models likely approximate patient prognosis at best.

Optimal allocation of ECPR

The identification of patients who would benefit from ECMO support in the setting of cardiac arrest (so called "Extracorporeal CardioPulmonary Resuscitation (ECPR)) is considered a separate challenge because of two reasons. Firstly, a patients' prognosis seems more importantly determined by neurological status mandating different sets of predictors than in other ECMO supported patients. It is because of this very reason that the Survival After Veno-Arterial ECMO (SAVE) score[7] did not include patients after cardiac arrest. Secondly, the setting where a decision regarding ECPR is being made is typically subject to considerable time pressure and discomfort. Success of prognostic models is therefore also largely influenced by simplicity and the availability of measurements in such circumstances.

Table 1. Selection of predictive models for several clinical outcomes in ECMO patients.

Predicted outcome	Score	ECMO type	Setting	Number of patients	Number of centers	Cohort enrollment	Outcome frequency n (%)	Predictors in final model	Internal validation: c-statistic (95% CI)	Internal validation: O:E ratio (95%CI)	External validation: c-statistic (95%CI)	External validation: O:E ratio (95%CI)
Mortality/ Survival to discharge	SAVE[7]	V-A	Cardiogenic shock excluding ECPR	3846	NA	2003–2013	1601 (42)	Age; weight; myocarditis; refractory VF/VT; post heart or lung transplantation; congenital heart disease; other diagnoses; liver failure; central nervous dysfunction; renal failure; chronic renal failure; duration of intubation; peak inspiratory pressure; cardiac arrest; diastolic blood pressure; pulse pressure; bicarbonate	0.68 (0.66–0.69)	0.99	0.70 (0.64 – 0.75) in pooled analysis[15]	1.17 (0.94 – 1.46) in pooled analysis[15]
Mortality/ Survival to discharge	RESP[8]	V-V	Respiratory failure	2355	NA	2002–2012	1338 (57)	Age; immunocompromised status; mechanical ventilation days; acute respiratory failure diagnosis group; CNS dysfunction; acute non pulmonary-associated infection; neuromuscular blocking agents; nitric oxide use; bicarbonate infusion; cardiac arrest; PaCO2; peak inspiratory pressure	0.73 (0.71 – 0.75).	NA	0.66 (0.59 – 0.73) in pooled analysis[15]	0.9[16]
Unsuccessful weaning	Shao et al.[17]	V-A	ECMO after CABG	166	1	2004–2017	60 (36)	Pre-existing hypertension; serum creatinine; serum lactate; platelet count	0.81 (0.75–0.88)	NA	NA	NA

(continued)

Table 1. (continued)

Predicted outcome	Score	ECMO type	Setting	Number of patients	Number of centers	Cohort enrollment	Outcome frequency n (%)	Predictors in final model	Internal validation: c-statistic (95% CI)	Internal validation: O:E ratio (95%CI)	External validation: c-statistic (95%CI)	External validation: O:E ratio (95%CI)
Neurologic function 6 months after discharge	Siao et al.[18]	V-A	ECPR	112	1	2012–2017	29 (26)	Low-flow time; cardiac arrest location; and initial cardiac arrest rhythm	NA	NA	NA	NA
Survival at 1 year after durable MCS implantation after ECMO	Saeed et al.[19]	V-A	Cardiogenic shock	529	11	2010–2018	249 (47)	Age; gender; BMI >30; previous cardiac surgery; lactate; MELD XI score; history of atrial fibrillation	0.71	NA	NA	NA
Nosocomial infection on VA ECMO	Li et al.[20]	V-A	ECMO after cardiac surgery	503	1	2011–2020	213 (42)	Age; duration of mechanical ventilation; white blood cell count; ECMO site	0.73 (0.64–0.82)	NA	NA	NA
Major bleeding according to the ELSO guidelines*, excluding surgical bleeding	Lonergan et al.[21]	V-A and V-V	ECMO	112	1	2010–2013	53 (47)	Hypertension; ECMO type; age	0.66	NA	NA	NA

BMI = Body Mass Index; CABG = Coronary Artery Bypass Grafting; CNS = Central Nervous System; ECPR = Extracorporeal CardioPulmonary Resuscitation; NA = Not Applicable; V-A = Veno-Arterial; VF = Ventricular Fibrillation; VT = Ventricular Tachycardia; V-V = Veno-Venous.

*Bleeding that required surgical exploration or bleeding that required immediate transfusion of at least two units of packed RBCs because of a sudden fall in hemoglobin of 2 g/dL with new hemodynamic instability or ongoing visible blood loss.[22]

Until now, several prediction tools have been developed specifically for the setting of ECPR,[18,23–26] with varying predictive performance in external validation cohorts.[27,28] Decisions to apply ECPR are currently made on typical prognostic signs which are also used in patients with cardiac arrest treated with conventional methods. These include having had a witnessed arrest, shockable rhythm and end tidal CO2 concentration above a certain threshold.[29] However, these measures taken during resuscitation do not only focus on neurological recovery but also aim to assess the chance of return to spontaneous circulation. As restoration of circulation is however guaranteed with ECPR, these predictors may not provide optimum support for the selection of ECPR candidates. In the future, it is likely that neurological measures during resuscitation such as direct pupillometry, near-infrared spectroscopy or a form of electroencephalogram will provide improved predictive performance aiding in the selection of patients for ECPR.

Cessation of ECMO for reasons of futility

Prognostic models may also be utilized to (repeatedly) quantify a patients' prognosis during ECMO support.[30] These estimations could help to assess chances of survival after a number of ECMO support days have passed during which adverse events could have occurred. Continuation of support would for example be pointless if a patients' prognosis would have become futile at some point in time. Currently, no such dynamic prediction models exist that could aid in the decision to withdraw ECMO for reasons of futility because nearly all models predict mortality or survival at a fixed time point shortly after initiation of ECMO support.[30,31]

Weaning from V-A ECMO

Between 30 and 70% of patients can ultimately not be weaned from V-A ECMO.[32] Prognostic information about chances for weaning failure can contribute to planning of care and prevent wastes of resources and time. For such purpose, one model was designed to predict chances for weaning failure in patients who underwent coronary artery bypass grafting (CABG).[17] This model however only incorporated baseline variables and has to our knowledge not been externally validated (Table 1).

Clinical routine is largely based on prognostic factor studies for weaning success during ECMO support and during a weaning trial. Variables acquired during a weaning trial include persistence of hemodynamic stability, aortic time-velocity integral (VTI) > 10 cm, left ventricular ejection fraction > 20 – 25%, and lateral mitral annulus peak systolic velocity ≥6 cm/s,[33–35] however these largely explorative studies did not develop prognostic models that were evaluated for their performance.

Some patients who cannot be weaned from ECMO support are candidates for LVAD implantation or heart transplantation. The scarcity of donor organs, poor overall posttransplant survival for these 'bridge to LVAD/heart transplant' patients and high costs typically justify a certain expectation for survival in these patients.[36] A large international multicenter registry predicted one-year survival after implantation of a durable mechanical circulatory system (MCS) after ECMO, based on model incorporating age, sex, lactate and MELD score on day of MCS implantation, a history of atrial fibrillation, necessity for redo surgery, and body mass index above 30 kg/m^2 [19,37] (Table 1). And while this model has to our knowledge not been externally validated, it would also only be able to predict outcomes in patients who already received an LVAD from the setting of ECMO support.

ECMO management

During ECMO support, many decisions regarding management of treatment have to be taken on a daily basis. These decisions pertain to a multitude of considerations where risks and benefits must be weighted and physicians could benefit from prognostic models and decision support tools. Below we describe three of these considerations.

Thrombotic and bleeding complications. Thrombotic and bleeding complications are among the most frequently encountered events during ECMO support and strongly associate with increased mortality and length of intensive care stay.[38,39] For estimating bleeding risk in ECMO recipients specifically, one study derived a prognostic score based on hypertension, age greater than 65, and ECMO type (V-V or V-A) in a single-center cohort[21] (Table 1). The model showed slightly better internal predictive performance than external predictive performance of the HAS-BLED score.[21] To our knowledge, this model has not been externally validated in other ECMO recipients.

Left ventricular unloading. An increase in left ventricular afterload due to the added flow and pressure by the extracorporeal blood flow of V-A ECMO may exacerbate ventriculo-arterial decoupling and eventually contribute to the development of pulmonary edema, aortic- and intracavitary thrombosis, and significantly

impair cardiac recovery.[40,41] These negative sequelae imposed by V-A ECMO can be mitigated or even reversed by means of different interventions which include a reduction of ECMO flow, condensation of intravascular volume, and the initiation of inotropic medication or concomitant mechanical left ventricular unloading through intra-aortic balloon pump or a trans-aortic microaxial blood pump.[40] A recent expert review[42] recommended a stepwise approach where interventions targeting left ventricular unloading would be escalated on basis of a multimodal assessment of cardiac function and overload. Beyond this first step towards patient tailored left ventricular unloading, to our knowledge, no dedicated studies have examined personalized approaches in observational- or trial-data. These studies, and especially those in upcoming randomized clinical trial data, are eagerly awaited.

Infectious complications. Infections are commonly observed during ECMO support and have been associated with adverse outcomes.[43,44] Recognizing infectious episodes is typically challenging in ECMO patients due to masking of inherent signs, such as fever, through permanent heat loss by the extracorporeal circuit.[20] Proper identification of patients that are (highly) susceptible to acquiring infections during ECMO could lead to timely (antibiotic) interventions, thereby possibly decreasing morbidity. A nomogram predicting probability of nosocomial infections in patients receiving V-A ECMO after cardiac surgery was developed and incorporated age, white blood cell (WBC) count, ECMO site (ICU or non-ICU), and mechanical ventilation duration into the model[20] (Table 1). External validation has yet to be performed.

Limitations of currently available models

Currently available prognostic models seem to fall short from several perspectives. First, not all relevant clinical outcomes are addressed by existing prognostic models. Prognostic models including short-term endpoints – such as events of bleeding and thrombosis, weaning success, necessity for LVAD implantation, and serum levels of antibiotics – are sparse and insufficiently externally validated. With regards to longer term end points, one could advocate that neuropsychological wellbeing and quality of life are also important outcomes to model as some survivors may suffer from a low quality of life and even find their lives not worth living.[45] Additionally, the lack of real-time continuous decision support hampers use of prognostic models during the course of ECMO.

Secondly, currently available models often seem misaligned with their intended use in clinical practice.[46] An illustrative example is found in the section covering the allocation of ECMO. Many studies in ECMO recipients wrongly claim that their prediction tool would qualify to assist in the allocation of ECMO to those who would benefit best. Nevertheless, as previously pointed out,[7] such question can only be answered in a source population which also comprises individuals who eventually did not receive ECMO support.

Thirdly, from a technical point of view, many published studies included relatively small numbers of patients and events per included predictor.[47] Models are thus prone for overfitting and incorrect predictions.[48] Finally, and maybe most importantly, most developed models have never been externally validated.

Important statistical considerations and modern techniques

Moving the field of prognostic modelling for ECMO treatment decisions forward starts with external validation of existing models.[49,50,51] This applies to both statistical regression models and AI algorithms alike. One could argue that reliable predictions in patients that were not used for development of the model are all that matters, irrespective of the methods used to derive a model.[52,53] Time and effort should be dedicated to carefully set up external validation studies with appropriate data and statistical analyses.[46] Collected data needs to accurately reflect the population of interest at the intended moment of making the prediction. In addition, measurement procedures of the outcome and predictors should correspond to the derivation data set, including the moment at which they are measured.[51,54,55] The statistical analysis plan should describe how missing data are handled (which requires different considerations in prediction research compared to etiologic or therapeutic research)[56,57] and how predictive performance in terms of model discrimination and calibration is assessed.[58,52,59]

One opportunity for validation studies is to combine data sets from multiple studies to assess the external predictive performance of a range of prognostic models more thoroughly. In such studies, researchers can assess the predictive performance of multiple models across ECMO centers and subgroups of ECMO patients. If a prognostic model has poor predictive performance in new data, it does not imply that the model should simply be discarded. Rather, it can be assessed if- and

how- intercept-updating or tailoring strategies (such as recalibration) can improve performance.[60–63]

Prognostic models currently available in the literature are insufficient to provide full decision support as they do not cover all decisions related to ECMO initiation and management. Development of new models for specific medical decisions can be considered for future research. For instance, to decide whether to initiate ECMO weaning versus continuing ECMO, a physician may want to consult a prognostic model several times during ECMO treatment of a single patient. This requires a dynamic prediction modelling technique in which predictions are updated given the history of ECMO up to that point in time, such as a landmarking approach[31] or joint modelling.[30] Still, methods to assess predictive performance of dynamic prediction models have yet to be developed.

When the intended use of a prognostic model is to inform decisions regarding initiation or management of ECMO, we are typically interested in the treatment-naïve prediction of the outcome. For instance, in a patient who is difficult to wean from V-A ECMO support, it could be of interest to know the potential benefit of LVAD implantation in terms of mortality risk reduction. For such purpose, a prognostic model needs to be able to calculate the mortality risk if an LVAD is not implanted – a scenario that would be counterfactual for patients who actually received an LVAD implantation. When the decision is informed based on a prediction that does not take LVAD implantation into account, high-risk patients are likely to be indicated at low risk of mortality, as their prediction is reflective of interventions made to lower the risk of similar patients under current LVAD assignment policies.[64,65] Developing a prognostic model that can predict treatment-naïve outcome risks requires counterfactual reasoning and corresponding statistical approaches.[64,66,67]

Making so-called "*counterfactual predictions*"[68,69] seems attractive, but the complexity of developing such models should not be underestimated, especially the specification of the counterfactual prediction target and the assessment of identifiability. Assessing predictive performance of counterfactual prognostic models is difficult as currently no consensus exists on how to assess predictive performance for counterfactual predictions.[64] Moreover, not all treatment decisions require counterfactual predictions. For instance, because ECMO is often initiated as a live-saving support, a treatment-naïve risk of mortality is not always informative. Rather, a prognostic model that predicts risk of mortality under current ECMO assignment policy can be of support in making the decision to initiate ECMO or not. Such a model can be developed using factual predictions only (i.e., without counterfactual prediction). In such a study, details about the current ECMO assignment patterns are necessary to assess applicability of the model in particular clinical settings.

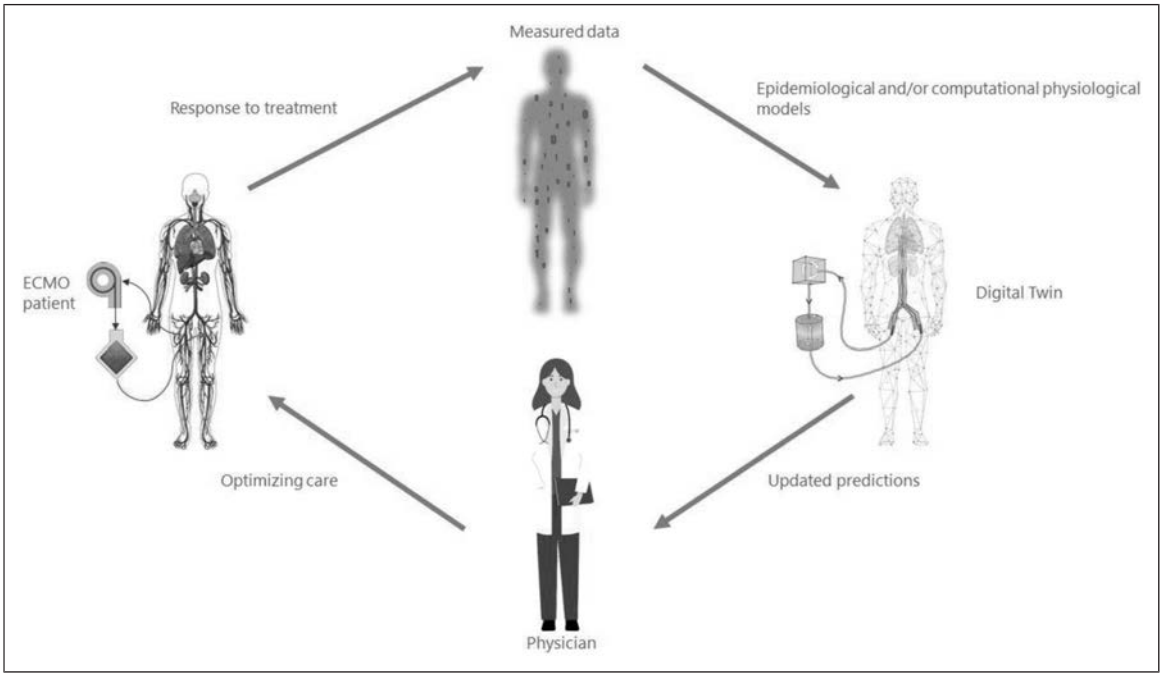

Figure 1. A digital twin in a healthcare environment.

Simulating treatment response through a "Digital Twin"

In recent years, attention is given to so called "Digital Twins", that may serve to optimize clinical management and workflow in healthcare to improve patient's outcome in complex and critical clinical scenarios. In general terms, a Digital Twin is a computational representation of a physical system, used to predict and optimize its behavior in a real-time setting.[70] A Digital Twin could provide insight into a patient's expected outcome under the possible counterfactual scenarios of a treatment decision using simulations. At present, there are no Digital Twins specifically for ECMO, but several attempts are ongoing to develop Digital Twins for ICU in general, they are discussed briefly in this paragraph.

Ideally, the Digital Twin reads data from a patient and from the medical devices connected, and processes this information with the support of a mathematical model to reproduce and make predictions on a patients' status, and finally informs physicians about the optimal care accordingly (Figure 1).[71] This type of Digital Twin is expected to act at bedside level and to simulate patient's status and the main interaction with one or multiple therapies dynamically in (quasi) real time.

A Digital Twin is not one (novel) technique but can be based on (deterministic) physiological models or on statistical models ranging from simple regression to more complex AI techniques, such as neural networks, or a combination of the two. The deterministic physiological models can reach different levels of complexity, depending on the number of organs or anatomical sites represented and the details implemented.[40,72] The level of complexity to embed in a Digital Twin is a non-trivial choice: on one hand sophisticated models can be informative and useful to investigate pathophysiology and unravel patient-device interaction; on the other hand the large amount of variables to be tuned requires more clinical data to be inserted manually by the clinician or retrieved automatically from the monitoring systems, thus hindering their application at bedside.[73] In the case of ECMO, a possible Digital Twin is composed of a deterministic physiological model of cardiac and vascular functions and of the ECMO pressures and flow. Such a model would retrieve hemodynamic data from the ICU monitor and offer a replica to be used for example to test different ECMO speeds on patient's hemodynamics. Then a titration of ECMO therapy would be operated accordingly, in an automatic or semiautomatic manner, depending on the level of supervision of the clinician in the process. If the output of the Digital Twin goes beyond the prediction of the mere hemodynamics, then data-driven (AI) models can be added in combination. These models can convey a more holistic description of patients, although they lack in

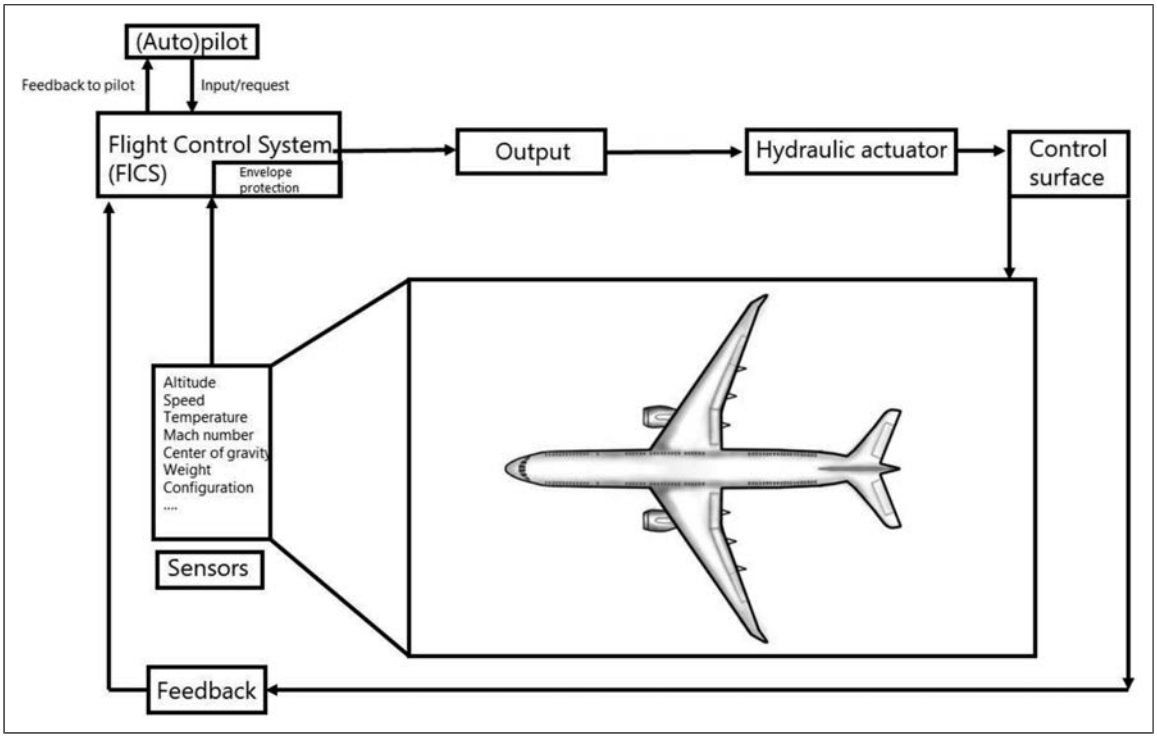

Figure 2. Simplified example of a flight control system.

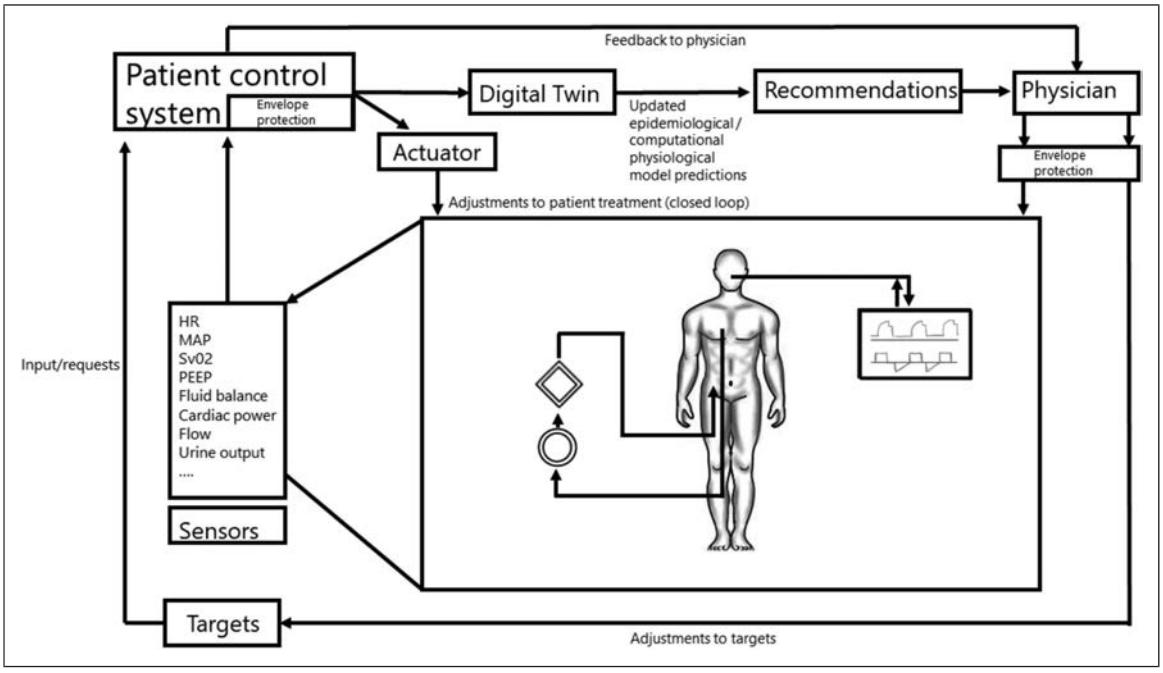

Figure 3. A hypothetical patient control system for an intensive care patient supported with ECMO.

representing cause-effect mechanisms of patient-device interaction.[74]

It goes without saying that as a Digital Twin is based upon modelling techniques, the limitations mentioned beforehand for prognostic models apply also here, plus other challenges specific for deterministic models (e.g. thorough verification, validation and uncertainty quantification of model parameters). As such, the process of upgrading a computational model to a Digital Twin applicable to the clinical environment is a non-trivial task.

In addition to therapy optimization, Digital Twins can help improving ICU processes and their strategic management by incorporating administrative data and tracking the location of medical personnel and equipment over time.[75] This type of Digital Twin could improve medical workflow and in turn patient outcomes. Furthermore, Digital Twins could be used for training purposes in healthcare staff working with ECMO via high-fidelity simulation. Still, major challenges hamper its full implementation in healthcare. It is not trivial to schematize and numerically model clinical decision making (especially when it involves multiple clinical specialists). It is difficult to standardize healthcare processes and workflows due to the large variability in structures and resources among different clinical centers; clinical data lacks integration and is poorly accessible due to safety and privacy issues.[76] Besides that, it should be taken into account that all clinical data is prone to measurement error and measured values do not always represent the actual status of a patient (i.e., when continuously measuring blood gas within the ECMO circuit, the measured values could be different from those within the patient). Furthermore, the prognostic and therapeutic problems that Digital Twins aim to address have so far remained unsolved in research and some modesty in expectations therefore seems appropriate.

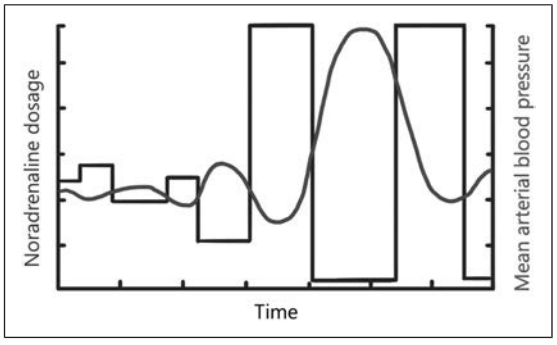

Figure 4. Overcorrection of noradrenaline dosages resulting in undesired fluctuations in mean arterial blood pressure.

Regardless of the modelling technique used, a patient Digital Twin, ascribable to clinical use, is considered as a full-fledged medical device and needs to comply with regulatory requirements depending on its intended use and purpose.[77,78] This aspect becomes more crucial if we envision a Digital Twin

not only as a support to clinical decision, but also as a tool fully integrated in the clinical workflow that automatically titrates a therapy (e.g., ECMO flow level, dose of drug infusion, mechanical ventilation settings) in closed loop fashion without clinical staff supervision.

Overall, the use of Digital Twins in ECMO and more general in the ICU is still in its infancy, but if the listed hurdles are overcome Digital Twins could aid in more personalized treatments.

Flying ECMO by wire

Current developments led us to speculate about a future where we would possibly fly ECMO "*by wire*". The fly-by-wire concept is naturally adopted from the world of aviation but has the potential to significantly stimulate and inspire our visions on future intensive care support tools. Below we have allowed ourselves to elaborate on this concept, applying some of the known concepts from aviation to the context of ECMO care but purposely leaving out some important ethical and legal considerations.

"*Flying ECMO by wire*" would imply that certain adjustments in ECMO settings would be automatically taken care of by digital interfaces and differential equations striving for target values or intended actions as defined by a treating physician. In aviation, a flight control system largely controls a planes' actions by integrating feedback from sensors and input from the pilot, preventing impossible actions from the point of an aircrafts' "physiology". For the setting of intensive care and ECMO, an intelligent "*patient control system*" (PCS) could optimize treatment decisions, for instance using real-time prognostic models or Digital Twin approaches (Figure 2). Minor changes in treatment settings within certain predefined safety boundaries (e.g., increasing ECMO flow) could be directly fed back to the ECMO console or another device. Recommendations for larger adjustments could instead be relayed back to the nurse or physician for supervised adjustments. Sensors registering pressures, flows, temperatures, and blood levels of certain markers (like SvO2) in the ECMO circuit, indwelling catheters, but also other devices such as the ventilator and infusion pumps, could, by cross talk, provide integrated feedback on specific interventions or adjustments which were advised or carried out by the PCS (Figure 3). The underlying Digital Twin model could in turn improve its predictive power by recalibrating based on the integrative feedback. Safety of the PCS could meanwhile be ensured by a variant of "*flight envelope protection*" which would prevent the operator (e.g., physician, nurse) from dangerously handling the ECMO console. An example would be that it would become impossible to reduce FiO2 and/or gas flow on the gas blender below a certain level while supporting a patient with V-A ECMO.

Flying by wire approaches have significantly improved safety, efficiency, economy, and comfort in aviation[79] and could possibly also improve some of these aspects in intensive care medicine. For example, "*pilot-induced oscillation*"[80] describe the development of undesired fluctuations in an aircrafts' altitude or flight path which arise secondary to an increasing series of adjustments in opposite directions by a pilot, each of which is intended to restore a previous input. Such series of overcorrections in opposite directions can also be experienced during ECMO support. For instance, frequent adjustments in noradrenaline dosages (illustrated in Figure 4), sedative medication or even ECMO revolutions per minute can result in large variations in blood pressure, states of arousal, or suction events, respectively. All these events base back on difficulties in assessing patient response rates and delays to the effects of medications. Automation of some of these processes might prevent some of the aforementioned events.

For this potential *fly by wire* future to become reality, some important considerations need mentioning. Translating predictions or physiological input from prognostic models or Digital Twins into treatment decisions requires setting a threshold value for physiological parameter(s) and for risk prognostications. Research should be conducted to find accurate thresholds.[81] To inform automated management of ECMO with prognostic information, the development, evaluation and implementation of dynamic prediction models needs to be further studied.[62] Methods need to be developed to evaluate dynamic predictive performance and to update implemented models, as well as software to integrate a prognostic model or Digital Twin in routine care. There is also a need to consider which data are required to develop prognostic tools that can support ECMO decisions. For example, a variable that would indicate that a patient could be eligible for ECMO is necessary for a prognostic model used in ECMO allocation but is not (readily) available in EPRs. A large proportion of the required data for predictions is currently unavailable or unstandardized in different EPRs, requiring extensive efforts to standardize terminologies and definitions before use in prognostic models.[82]

Conclusion

Currently available prognostic models for ECMO recipients are limited in their clinical value, amongst other reasons because of their fixed design, only incorporating variables at one moment in time. Prognostic modelling techniques have developed to the point where they have the potential to incorporate high-dimensional and time-varying data from ECMO supported patients to aid clinical decision making regarding both allocation and management of ECMO. From this perspective, dynamic prediction modelling, incorporating counterfactual reasoning, and Digital Twin approaches seem promising for evaluating and simulating treatment responses providing decision support for physicians at the bedside. These developments lead us to speculate about a future where we could fly ECMO by wire. Before we could use such techniques, many important hurdles regarding logistical, technical, medical-ethical, and legal aspects have to be overcome.

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Adult - Cardiac failure

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The ProtekDuo for acute right heart failure in thyrotoxicosis

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Objectives: A 25-year-old female patient with history of diffuse toxic goiter and non-adherence to antithyroid medication presented with acute symptoms of thyrotoxicosis, cardiogenic shock and acute respiratory failure. The echocardiogram demonstrated a severely enlarged right ventricle with severely reduced function. She was intubated and pulmonary embolism was excluded by computed tomography pulmonary angiography. Labs were obtained and remarkable for thyroid stimulating hormone <0.01 micro IU/mL (Ref 0.4-5.5 micro IU/mL), free thyroxine 2.3 ng/dL (Ref range 0.8-1.8 ng/dL), T3 resin uptake 49% (Ref range 22-25%), total thyroxine 5.0 mcg/dL (Ref range 5.1-11.9 mcg/dL). This patient showed the very rare diagnosis of acute right ventricular failure secondary to thyrotoxicosis and required high doses of inotropes and vasopressors.

Methods: We placed a ProtekDuo cannula with ECMO circuit in venopulmonary configuration in the cardiac catheter laboratory for the ability to extubate the patient as soon as possible. A post cannulation echocardiogram demonstrated good right heart decompression and inotropes and vasopressors could be weaned.

Results: The patient was treated with methimazole 40mg daily for 10 days. Free thyroxine level decreased to <0.3ng/dL Methimazole was resumed 11 days later at a dose of 20mg daily due to rising free thyroxine level with peak of 6.5 ng/dL; she was treated with that dose for 12 days and the dose was reduced to 10mg daily. The patient was supported with ProtekDuo for seven days. The oxygenator could be removed after three days, leaving the cannula for four days as right ventricular assist device. After nine days in the ICU, and 26 days of total hospital stay, the patient was fully recovered and discharged home.

Conclusions: To the best of our knowledge, this is the first case in which the ProtekDuo has been used for isolated right ventricular failure secondary to thyrotoxicosis. It serves to significantly reduce inotropes and vasopressors and represents an excellent alternative to venoarterial ECMO in this setting. It serves as bridge to recovery, since the right heart showed good function after the management of the thyrotoxicosis.

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Characteristics and predictors of mortality among acutely poisoned adults in the US receiving veno-arterial extracorporeal membrane oxygen support: A retrospective study from 2003-2019

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Objectives: Describe the clinical characteristics of VA-ECMO recipients for poisoning in the US and identify predictors of mortality.

Methods: We conducted a retrospective study using the Extracorporeal Life Support Organization's ECMO registry. Adult patients who received VA-ECMO for poisoning in the US were identified using the International Classification of Disease codes for Poisoning

Table 1

	Variable	Non-survivors	Survivors	p-value
Pre-ECMO	Hypotension*,N(%)	11(68.8)	18(51.4%)	0.393
	pH	7.07(6.96,7.28)	7.22(7.16,7.27)	0.024
	HCO_3(mmol/L)	14(12,18)	20(15.2,22.8)	0.015
	Lactic Acid (mmol/L)	9.4(6.6,14.5)	6.5(3.4,9.4)	0.05
24-Hours Post-ECMO	Hypotension*,N(%)	7(43.8)	12(34.3)	0.736
	pH	7.36(7.28,7.45)	7.44(7.39,7.47)	0.007
	HCO3 (mmol/L)	22.9(20.1,24.4)	25(23,28)	0.008
	Lactic Acid (mmol/L)	9.5(4.6,14.1)	2.2(1.3,3.2)	0.002

* SBP<90mmHg or MAP<65mmHg

from 01/01/2003 to 30/11/2019. Two study investigators reviewed cases to verify inclusion. Demographic and clinical characteristics between survivors and non-survivors were compared.

Results: We identified 88 cases. Median age was 38.7 years, 47.7% were female. The most common exposure was cardiovascular agents (31.8%) and the most common intention of intoxication was self-harm/suicide (29.5%). 47 cases (53.4%) experienced cardiac arrest prior to cannulation, and 17.0% received extracorporeal cardiopulmonary resuscitation (ECPR). 53 cases (60.2%) survived to hospital discharge. Pre-ECMO pharmacologic interventions and time to ECMO cannulation were similar between survivors and non-survivors. Clinical parameters for pre- and post-ECMO are summarized in Table 1. VA-ECMO support improved metabolic and hemodynamic parameters in both survivors and non-survivors. Non-survivors experienced lower pH and HCO3, and elevated lactic acid levels prior to VA-ECMO. Persistent acidemia, metabolic acidosis, and lactic acidosis 24-hours post VA-ECMO were associated with mortality.

Conclusions: Overall survival to discharge was 60.2%. Acidemia, metabolic acidosis, and elevated lactate levels before and 24-hours after VA-ECMO cannulation were associated with mortality.

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V-AV ECMO for venous air embolism with cardiopulmonary failure

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Objectives: Venous air embolism (VAE) carries a mortality rate of 48 - 80%. It can occur when gas is introduced into venous circulation leading to potentially life-threatening complications, such as acute cardiopulmonary failure. We present a case of VAE following routine removal of a central venous catheter (CVC) used for plasma exchange (PLEX) to treat newly diagnosed neuromyelitis optica (NMO). VAE led to capillary leak syndrome (CLS) with severe non-cardiogenic pulmonary edema and acute right ventricular (RV) failure ultimately requiring a hybrid extracorporeal membrane oxygenation (ECMO) configuration for circulatory and respiratory support.

Methods: Chart review and literature search were performed.

Results: A 22 year old female was initially admitted for acute, painful right-sided blurry vision and diagnosed with NMO. She received both high-dose steroids and PLEX therapy. Shortly after CVC removal she developed tachycardia and hypoxia associated with chest pain, shortness of breath, agitation and diaphoresis. Chest computed tomography angiogram revealed right subsegmental pulmonary emboli, diffuse pulmonary edema and RV strain. Hemodynamic deterioration followed, prompting transfer to the cardiothoracic intensive care unit. Bedside ultrasound showed echogenic turbulence within the RV and inferior vena cava consistent with venous air (Figure 1). Hyperbaric oxygen therapy was deferred given progressive cardiogenic shock despite vasopressors and inotropes. While preparing for ECMO initiation, she suffered a brief cardiac arrest. She was cannulated for V-A ECMO. On ECMO day 2, she remained in refractory hypoxemic respiratory failure necessitating conversion to V-AV ECMO hybrid configuration for full cardiopulmonary support. The patient was decannulated on ECMO day 6 with complete recovery of RV function and discharged 9 days later neurologically intact.

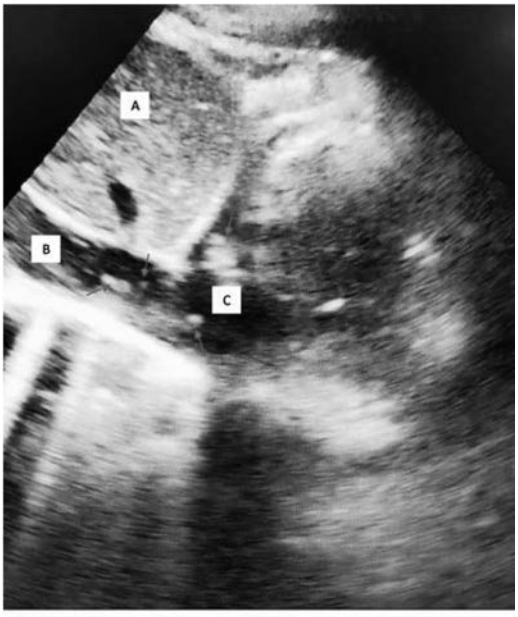

Figure 1. Point-of-care ultrasound echocardiogram with subxiphoid view. The liver (A), IVC (B) and inferior cavoatrial junction (C) are seen. Air bubbles are noted within the IVC and inferior cavoatrial junction (red arrows).

Conclusions: When standard management techniques for air entrainment and non-cardiogenic pulmonary edema fail, extracorporeal life support should be considered in the critically ill patient. ECMO therapy for VAE and CLS is described in other published case reports; typically, V-V or V-A ECMO alone is sufficient. Our case may be the first to report successful use of a hybrid ECMO strategy in this clinical scenario.

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The safety of discontinuing heparin in patients with venoarterial ECMO

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Objectives: The necessity of continuous heparin infusion during maintenance of venoarterial ECMO is well documented. However, there are situations where prohibitive risk of bleeding exist. The objective of this study was to assess the safety of heparin-free approach in patients being supported with venoarterial ECMO.

Methods: A total of 90 adult cases involving the insertion and maintenance of venoarterial ECMO by cardiovascular surgeons were included (2018–2021). ECMO sessions with less than 24 hours of support were excluded. The use of bolus heparin injection during insertion, continuous heparin infusion during support, and the duration of heparin free status were reviewed. Patients were divided into two groups; no heparin infusion for ≥ 24 hours during support (heparin (–) group, (n = 66)) and the others (heparin (+) group (n = 24)). Early outcomes including hemorrhagic and thrombotic complications were compared between groups.

Results: The cause of ECMO support was post-cardiotomy shock in 37 patients (41%), and 44 insertions (49%) were performed during E-CPR. Total support duration was not significantly between groups; 118±15 vs 106±22 hours in heparin (–) and (+) groups, respectively (P = 0.734). The reason for not using or intermittently discontinuing heparin during support was bleeding in all patients. In heparin (–) group, the complications included limb amputation (n = 1) or fasciotomy (n = 1) due to ischemia, bleeding from surgical site (n = 2) or cannulation site (n = 2), and pulmonary hemorrhage (n = 1). In heparin (+) group, there were limb amputation due to ischemia (n = 1), and arterial endarterectomy due to thrombosis (n = 1). Overall incidence of hemorrhagic and thrombotic complications were not significantly different between groups; 7/66 (10.6%) vs 2/24 (8.3%) in heparin (–) and (+) groups, respectively (P= 0.751).

Conclusions: No additional thrombotic risk could be found in selective discontinuation of heparin during venoarterial ECMO support. Continuous heparin infusion during ECMO support is necessary by principle, but should also be tailored by clinical scenario.

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Pitfalls of six months mechanical support with VA-ECMO, impella and ECMELLA as a bridge to cardiac transplantation

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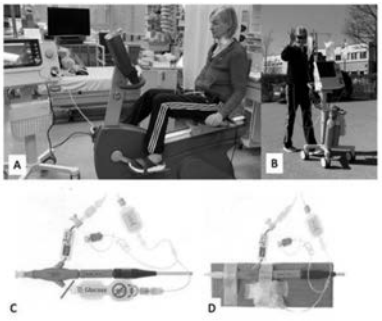
Objectives: To describe the pitfalls of a long-term mechanical circulatory support.

Methods: Case presentation.

Results: A 49 y/o female patient suffering from dilative biventricular cardiomyopathy was placed on femoral VA-ECMO. On day 6 of support, an Impella 5.5 was implanted surgically, and VA-ECMO was weaned over the following two days to facilitate mobilization. Long-term mechanical support was not considered suitable due to an impaired right ventricular function. On day 51 of support, a hazardous purge system alarm occurred signalizing leakage. The only resolution was an

emergency repair. On day 58 of support, an elective exchange of the Impella 5.5 was necessary due to the leackage issue under conscious sedation. During the intervention, her neurologic status suddenly altered. The patient was intubated, and an emergency cranial CT-angiography revealed thrombotic occlusion of a cerebral artery, which was immediately resolved by an interventional thrombectomy. The patient recovered neurologically within a few days. On day 67 of support, the right ventricular function severely deteriorated despite inotropic support. Femoral VA-ECMO was reinstituted in an ECMELLA configuration with a flow of approximately 2 L/min support. On day 113 Impella/46 of ECMELLA support, the purge system pressure increased to 1100mmHg and a semi-successful local lysis was applicated, utilizing r-tPA through the purge system. A suitable organ was found and transplanted on day 185 of Impella support and 118 day of ECMELLA support. The patient was discharged home 4 weeks after the transplantation in a good physical and mental status.



A: Patient practicing bicycle ergometry; **B**: Patient during physiotherapy walking outside;
C: Y-connector of the Impella for connecting the purge cassette with a red line showing the crack; **D**: emergency repair ensuring the purge flow.
Remark: Newer Impella devices have different connectors with less probability of cracking

Conclusions: The Impella support enables long-term support and tremendously facilitates mobilization. The Achilles' heel of the device seems to be the purge system. Close surveillance and strict anticoagulation monitoring are mandatory.

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Postcardiotomy ECLS – worth the effort?

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Objectives: Postcardiotomy extracorporeal life support (ECLS) is increasingly used for multiple reasons, lacking any evidence. As is known, mortality of postcardiotomy-ECLS remains very high up to 76%. We report the corresponding outcomes in a high-volume center.

Methods: A total of 8.757 patients underwent cardiac surgery at our facility in a 5-years period from 2017 to 2021. Of these, 41 (0.47%) were treated for postcardiotomy cardiogenic shock with an ECLS. Pre-, intra- and postoperative data were analyzed. The primary endpoint was hospital survival. The data were analyzed in the context of the overall institution's outcomes. Statistical analysis was done using R software.

Results: Mean age was 63.0 ±8.7 years – significantly younger compared to non-ECLS-patients (69.8 ±0.5 years; p<0.001). Preoperatively, LVEF averaged 50.0 ± 15.5%. ECLS-patients predominantly underwent non-elective surgery – 63.4% (n=26/41). First surgeries comprised 65.8% (n=27/41), the remainder were redos (n=15; 34,2%). The majority of procedures (n=35/41; 83.4%) were combined with aortic valve (n=15/34) or CABG-surgery (n=14/35). Isolated procedures were aortic valve replacement (n=5/6) and CABG (n=1/6). Involvement of the aortic valve was clearly overrepresented in ECLS-patients compared to the non-ECLS-population (48.8% vs. 31.9%; p<0.001). Mean perfusion time was 174.0 ±78.2min, cross clamp time 76.2 ±41.3min, which was significantly longer than in the non-ECLS-population (66.5 ±39.0min and 47.3 ±28.6min, p for both <0.001, respectively). Hospital survival of the ECLS-patients was 12.2% (n=5/41), compared to 96.1% overall survival in the observed period. Life-quality of the survivors at discharge was predominantly poor with 4 out of 5 survivors being discharged to an "Intensive neurologiocal and respiratory rehabilitation"-facility suffering from critical illness polyneuropathy and myopathy and the sequelae of long-time ventilation with tracheostomy. Hence, the rate of survival discharge with an expected good life quality was 2.4% (n=1/41).

Conclusions: Postcardiotomy-ECLS is rare. There was a disproportionately high involvement of aortic valve surgery with assumable intraoperative difficulties. Survival outcomes are poor – in a 5-years period only five patients were momentarily saved from death. The life quality results are extremely poor – only one patient survived with acceptable life quality.

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V-A ECMO as a bridge to surgery in patients with post-infarction mechanical complications: Results from the CAUTION study

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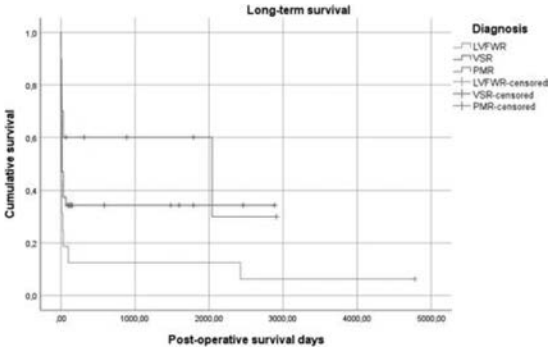
Objectives: Mechanical complications (MCs) are uncommon but often lethal sequelae of acute myocardial infartion (AMI). Prompt diagnosis and management can lead to successful treatment, but severe preoperative conditions may be associated with ominous prognosis. Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) has been proposed as a bridge to surgery in subjects presenting with refractory hemodynamic compromise or cardiac arrest, but available data are limited to case reports. The aim of this study was to assess the outcomes of patients with post-AMI MCs supported preoperatively with V-A ECMO from an international, multicentre, retrospective study including post-discharge follow-up.

Methods: The CAUTION study (Clinicaltrials.gov: NCT03848429) database was queried to identify all adult patients with post-AMI MCs submitted to V-A ECMO support as a bridge to surgery from January 2000 to December 2018. The primary outcome of the study was in-hospital mortality. Post-discharge survival was also assessed at available long-term follow-up.

Results: The patient cohort included 58 subjects (76% males) from 795 patients constituting the CAUTION database. Mean age was 65 ± 9 years. 81% of patients suffered from STEMI before the occurrence of MCs. Ventricular septal rupture was the most common MC (55%; 32/58) encountered. Twenty individuals (34.4%) experienced cardiac arrest at hospital admittance. Preoperative cardiogenic shock was the main indication for V-A ECMO support (52%; 30/58). Concomitant IABP was used in 43% of the patients. Median V-A ECMO duration was 3 days (IQR 1-7). The in-hospital mortality was 60% (35 patients). Multiorgan failure was the leading cause of death (60%; 21/35). Late death occurred in 6 subjects (mean follow-up: 3.2 ± 3.5 years). Kaplan-Meier survival curves are shown in Figure 1.



Conclusions: MCs are one of the leading causes of post-AMI in-hospital death. In this setting, despite V-A ECMO is applied as a bridge to surgery in severely compromised patients (one/third in cardiac arrest), in-hospital survival may reach 40%, with also a rather favorable post-discharge prognosis. Further studies are warranted to further evaluate the actual management and outcome of V-A ECMO in such a context.

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Infections during veno-arterial ECMO support

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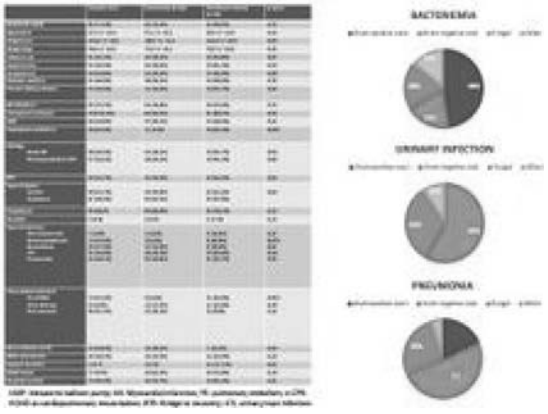
Objectives: Infections remain a significant complication in patients under ECMO support. We aimed to describe the pattern of infections in our veno-arterial (v-a) ECMO patients.

Methods: Retrospective study of all v-a ECMO implants in our center since 2014 (n=115). Demographic

characteristics, clinical characteristics of infections, duration and type of antimicrobial prophylaxis, and prevalence of multidrug resistant (MDR) bacterial colonization were recorded. We classified patients according to their preimplant length of stay (LOS; Community origin if <3 days and health-care related if >3 days). Continuous variables are presented as mean +/- standard deviation (SD) or as median and interquartile range (IQR) as appropriate. Descriptive statistics for categorical variables were reported as frequency and percentage.

Results: One hundred and fifteen patients were included, being 71,3% male. Medium age at implant was 57,45 years (SD 16 years). 82,6% of patients received antimicrobial prophylaxis, all covered gram-negative bacilli and gram-positive cocci including MDR bacteria, without differences related to patients' origin. Gram negative rods were the most common pathogen in urinary infections and pneumonias (58% and 51%, respectively), whereas gram positive cocci were the most common pathogen in bacteriemia (48%). Preimplant infection was more frequent in the health-care related subgroup (4,3% vs 23,9%; p=0,001) as it was cannulation site infection (7,2% vs 28%; p=0,002). The higher percentage of infections happened in both groups after device removal (36,2% vs 50%). There were no differences in survival. Figure 1 summarizes these results.



Conclusions: There were no differences in antibiotic prophylaxis between groups. Most infections occurred once support had been removed. Pre-implant infections were more frequent in the healthcare related group as were cannulation site infections. Further clinical studies are needed to reduce the risk of infection in v-a ECMO patients.

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Introduction and justification of the extracorporeal cardiopulmonary resuscitation beneficence score (EBS)

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Objectives: The collateral benefit of extracorporeal cardiopulmonary resuscitation (ECPR) for organ donation is well described. The Cerebral Performance Category (CPC) scale and modified Rankin Score (mRS) are widely accepted scoring tools used to stratify patients by survival and neurological function. As ECPR becomes more widespread, an objective measure that captures and weights neurologically-intact survival, death with organ donation, and survival with poor neurologic function would be useful.

Methods: We divided ECPR outcomes, determined at time of hospital discharge, into four simplified categories: A) survival with good neurologic function (CPC 1-2, mRS 0-2); B) survival with poor neurologic function (CPC 3-4, mRS 3-4); C) death (CPC 5, mRS 6) with organ donation; D) death without organ donation. Our multidisciplinary panel assigned relative weights to these outcomes with the goal of maximizing benefit to the patient, their family, and society.

Results: Neurologically-intact survival (A) is unequivocally the best outcome of ECPR while survival with poor neurologic function (B) was widely considered to be the worst. Despite improved outcomes for cardiac arrest using ECPR, death without organ donation (D) was considered to be the default/neutral outcome. Death with organ donation (C) was deemed the best alternative to neurologically-intact survival (BATNIS). Thus, our proposed ECPR Beneficence Score (EBS) is as follows: EBS = [5*(#A) + 2*(#C) – 2.5*(#B)] / [A+B+C+D]

Conclusions: Herein we describe a novel ECPR Beneficence Score (EBS). While the ethics of assigning value to simplified outcomes is difficult, the incredible resources necessary for ECPR require

objective measures to capture comprehensive effects and program performance. Importantly, the ultimate goal of ECPR is neurologically-intact survival, not organ donation; hence the newly-proposed term "BATNIS." Absolute modifiers of the EBS variables can be debated at an upcoming ELSO conference. Following consensus, the EBS should be considered for incorporation into the ELSO registry.

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Thrombocytopenia, hemorrhage, and platelet transfusion in VA ECMO: A complicated trinity

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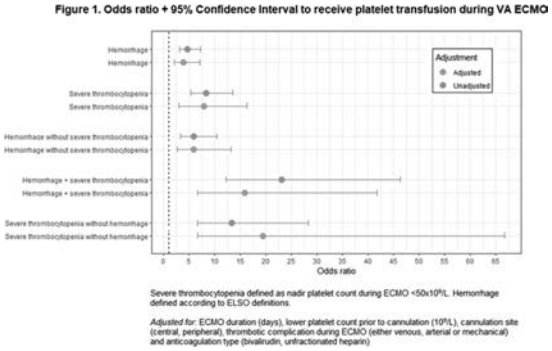
Objectives: To investigate the association between thrombocytopenia, hemorrhage, and platelet transfusion during venoarterial extracorporeal membrane oxygenation (VA ECMO).

Methods: This was a sub-study of a multicenter (n=16) mixed-method study on transfusion practices in patients receiving ECMO in intensive care units (ICUs) worldwide, combing a retrospective cohort with a survey. The survey aimed to make an inventory of local transfusion and anticoagulation thresholds and practices. Data was collected retrospectively from Jan-2018 to Jul-2019 and consisted of patient, ECMO, outcome, and daily transfusion parameters. This sub-study focused on platelets in VA ECMO. Platelet trend and amount of transfusion received were compared using Mann-Whitney U or Chi^2. Univariable logistic regressions and multivariable regressions correcting for predefined variables, were performed to assess the trinity of thrombocytopenia, hemorrhage, and platelet transfusion, shown as odds ratio (OR) with 95% confidence interval (95%CI).

Results:



A total of 226 out of 419 VA ECMO patients received one or more platelet transfusions during ECMO, and 150 suffered a hemorrhagic complication (66%). Seventy-six non-hemorrhagic patients (36%) still received platelet transfusions. Lowest platelet count was $<50 \cdot 10^9$/L in 167 patients (40%), 50-100$\cdot 10^9$/L in 150 patients (36%), and 100-150$\cdot 10^9$/L in 56 patients (13%). In bleeding as well as transfused patients, platelet count was lower before ECMO implementation, showed a larger decrease after cannulation, and remained lower during ECMO. If a patient suffered from both hemorrhage and severe thrombocytopenia ($<50 \cdot 10^9$/L), odds to receive a platelet transfusion was 23.1 (95%CI 12.2-46.3). Figure 1 shows the effects after correcting for predefined variables.

Conclusions: Severe thrombocytopenia and hemorrhage are very important factors for platelet transfusion. Future studies should focus prospectively on prevention of hemorrhage, as well as identifying reasons for platelet transfusion in the absence of bleeding.

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Investigations of differential hypoxemia during venoarterial membrane oxygenation with and without impella support.

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Objectives: Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is used in patients with refractory cardiac or cardio-pulmonary failure. Native ventricular output interacts with VA-ECMO flow and may hinder sufficient oxygenation to the coronary arteries and supraaortic vessels, resulting in differential hypoxemia. VA-ECMO leads to afterload increase and might require additional ventricular unloading, commonly performed with the Impella device. The aim of

the study was to investigate aortic blood flow and oxygenation for various ECMO settings and cannula positions with a numerical model.

Methods: Four different aortic cannula tip positions (ascending aorta, descending aorta, abdominal aorta, and iliac artery) were included in a model of a human aorta. Three degrees of cardiac dysfunction and VA ECMO support (50%, 75% and 90%) with a total blood flow of 6 l/min were investigated. Pulmonary dysfunction was represented with a pO_2 of 70 mmHg. Blood coming from the cannula was assumed to have a pO_2 of 400 mmHg. Additionally, the Impella CP device was implemented under the same support conditions, resulting in 24 scenarios. Blood oxygen saturation at the aortic branches and the pressure acting on the aortic valve were calculated.

Results: Analyzing all scenarios showed that a more proximal tip orientation is necessary to increase oxygen supply to the supraaortic and coronary arteries for 50% and 75% support. During the 90% support scenario, proper oxygenation can be achieved independently of tip position. The simultaneous use of the Impella pump does not strongly affect oxygenation of the supraaortic and coronary arteries. Pressure load on the aortic valve increases with more proximal tip position and is slightly decreased during Impella use.

Conclusions: We present a simulation model for the investigation of hemodynamics and blood oxygenation with various mechanical circulatory support systems. Our results underline the intricate and patient-specific relationship between extracorporeal support, cannula tip orientation and oxygenation capacity. The methodology can be translated to other applications, for instance pulmonary artery flows.

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Implementation of structured eCPR programme to improve outcomes in a specialist hospital in the United Kingdom

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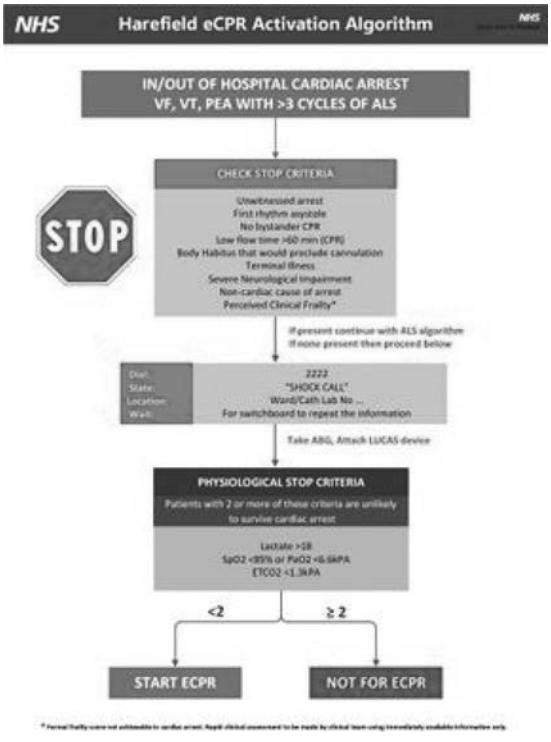
Objectives: With increasing randomised evidence to support the use of extracorporeal cardiopulmonary resuscitation (eCPR) we sought to implement an evidence-based protocol and training programme to improve outcomes.

Methods: A retrospective analysis of our centre's eCPR activity was performed between 1st May 2019 and 1st October 2021 for 6 month survival and functional outcome defined by cerebral performance category (CPC). We also analysed cardiac arrest calls between 1st June 2020 and 1st October 2021 to determine if patients were appropriately considered for eCPR. A multi-disciplinary working group discussed our current practice and evaluated the evidence base for eCPR then utilised a modified delphi method to develop a standard operating procedure best suited to our population base and service. This was designed to be applicable to in and out of hospital cardiac arrests. We developed an extensive training programme and a rapid, systematic screening process of all in and out of hospital cardiac arrests led by our critical care outreach nursing team. We prospectively analysed eCPR cases with the new service from 1st April 2022 to 1stDecember 2022.

Results: The cardiac arrest team was activated 185 times from 1June 2020 to 1October 2021. 14 Patients received eCPR, 6 patients met eCPR criteria but were treated with conventional CPR and all died. Survival to discharge home for eCPR was 21% (3/14 patients). All eCPR survivors at discharge had CPC 1 or higher. The delphi process occurred over a 3-month period with 9 rounds to the final version shown in Figure 1. The training programme was implanted over a further 3 months and the service was launched 1st April 2022. The prospective analysis has shown a survival to discharge home of 83% (5/6 patients). One patient from the survivor group underwent heart transplantation prior to discharge home. All survivors had CPC 1 or higher on discharge.



Conclusions: We demonstrated that in our institution a standard operating procedure, strict adherence to predefined selection criteria, systematic screening and extensive training improved outcomes for eCPR.

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Hypoalbuminemia is associated with increased mortality in patients on Extracorporeal Membrane Oxygenation (ECMO) therapy

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Objectives: Low albumin (< 3.5g/dL) is predictive of mortality in critically ill patients with cardiogenic shock, sepsis, end-stage renal disease, and certain malignancies. The objective of this study was to determine if pre-cannulation albumin is associated with in-hospital mortality in patients supported with veno-arterial extracorporeal membrane oxygenation (V-A ECMO).

Methods: A single-center retrospective cohort study was performed on patients supported with isolated V-A ECMO from 2016-2019. If a patient was re-cannulated, pre-ECMO data was collected prior to the initial run. Patients were stratified into tertiles of pre-ECMO albumin. A multivariable logistic regression adjusting for sex, SAVE score, etiology of cardiogenic shock, renal replacement therapy, and acute liver failure, was used to determine the likelihood of in-hospital mortality based on pre-ECMO albumin.

Results: Of the 219 patients assessed, 197 patients met inclusion criteria. The overall mean pre-ECMO albumin was 2.7 ± 0.7 g/dL. Baseline characteristics are detailed in Table 1. For patients with a pre-ECMO albumin <2.3 g/dL vs. 2.3-2.9 g/dL vs. >2.9 g/dL, the in-hospital mortality was 58.5% vs. 38.5% vs. 22.7%, respectively (p<0.001). In multivariate logistic regression analysis, higher albumin (per 1 g/dL increase) at cannulation was associated with a decreased odds of in-hospital mortality (OR, 0.56; 95% CI, 0.32-0.96). This multivariate model had good discriminatory value (AUROC of 0.8). Patients with a pre-ECMO albumin <2.3 g/dL required significantly more blood transfusions and had a higher incidence of ischemic stroke (both p<0.05).

Table 1. Baseline characteristics of patients on VA-ECMO between 2016-2019.

Variable*	Albumin <2.3 g/dL (n=53)	Albumin 2.3-2.9 g/dL (n=78)	Albumin >2.9 g/dL (n=66)	p value
Age – median (IQR)	59 (48-64)	56 (45-66)	54 (42-59)	0.12
Female – n (%)	19 (35.8)	34 (43.6)	21 (31.8)	0.33
BMI (kg/m^2) – median (IQR)	31.1 (25.4-35.1)	29.6 (24.5-35.9)	29.7 (26.9-36)	0.70
Cause of cardiogenic shock – n (%)				
eCPR	19 (35.8)	25 (32.1)	7 (10.6)	<0.001
Myocardial infarction	8 (15.1)	7 (9)	10 (15.2)	
Pulmonary embolism	5 (9.4)	23 (29.5)	24 (36.4)	
ADHF	1 (1.9)	4 (5.1)	15 (22.7)	
Other†	20 (34.5)	19 (24.4)	10 (15.2)	
Laboratory values at cannulation				
HCT (%) – mean ± SD	28.3 ± 6.7	28.8 ± 5.8	34.6 ± 7.5	<0.001
PLT (K/μL) – median (IQR)	104 (59-176)	142 (86-226)	188 (116-239)	<0.001
AST (units/L) – median (IQR)	235 (111-1023)	212 (76-467)	147 (55-328)	0.16
ALT (units/L) – median (IQR)	99 (56-589)	95 (48-228)	115 (47-305)	0.72
INR – median (IQR)	1.8 (1.6-2.8)	1.7 (1.3-2.2)	1.4 (1.2-1.7)	0.002
SCr (mg/dL) – median (IQR)	1.4 (1-2)	1.3 (1-2.3)	1.5 (1.1-2.2)	0.29
On RRT at cannulation – n (%)	9 (17)	9 (11.5)	10 (15.2)	0.66
ALF at cannulation¥ – n (%)	24 (45.3)	23 (29.5)	11 (16.7)	0.003
SAVE score at cannulation – mean ± SD	-7 ± 7	-6 ± 6	-5 ± 7	0.36
Post-cardiotomy – n (%)	20 (37.7)	25 (32.1)	6 (9.1)	<0.001
Cannulation – n (%)				
Peripheral	43 (81.1)	63 (80.8)	63 (95.4)	0.02
Central	10 (18.9)	15 (19.2)	3 (4.5)	

*Baseline laboratory values were included if they were measured within 6 and 12 hours of cannulation, respectively.
†Other causes of cardiogenic shock included post-transplant primary graft dysfunction, inability to wean from cardiopulmonary
¥Acute liver failure was defined as an INR ≥2.0 or total bilirubin ≥10 mg/dL

Conclusions: Pre-ECMO hypoalbuminemia was associated with an increased odds of in-hospital mortality in patients supported on V-A ECMO. Pre-ECMO albumin may serve as a key prognostic indicator for clinicians who wish to effectively allocate this costly resource.

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Extracorporeal resuscitation for out-of-hospital cardiac arrest: The 12-year experience of an Italian referral center

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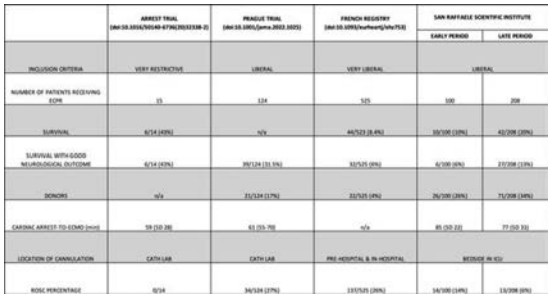
Objectives: Extracorporeal resuscitation (ECPR) for out-of-hospital cardiac arrest (OHCA) is debated, with literature showing contrasting results. We analyzed ECPR data at an Italian referral center with the aim of assessing data, trends and outcomes over time.

Methods: Single center retrospective study including all 308 OHCA adult patients receiving ECPR at IRCCS San Raffaele Scientific Institute (Milan, Italy) from Jan-2009 (start of ECPR program) to Nov-2022. In order to assess changes in outcomes over time, the first 100 treated patients (*early period*: 26/01/2009 – 04/07/2016) were compared with patients treated thereafter (*late period*, n=208, 10/07/2016 – 05/11/2022).

Results: Survival to hospital discharge was 10% (10/100) in the early period and 20% in the late (42/208; p=0.004). Survival with GCS 14-15 was 6% (6/100) in the early

period and 13% (27/208) in the late (p>0.05). ICU survival increased from 12% (12/100) to 21% (44/208; p=0.051). Potential multiorgan donors increased from 26% (26/100) to 34% (71/208, p=0.01). Times of OHCA-to-door, door-to-ECPR, OHCA-to-ECPR decreased respectively from 66±17; 19±13; 85±22 minutes to 59±16, 18±26, 77±31 minutes (respectively p=0.001, p=0.006, p=0.0003). A trend towards decrease in complications was observed (53% to 42%, p=0.06). 65% of patients received IABP on top of VA-ECMO: survival was 22% (45/201). 11% of patients received Impella in adjunct to VA-ECMO: survival was 45% (15/33). VA-ECMO+IABP and VA-ECMO+Impella were associated with survival (p<0.001).

Conclusions: Our study adds new data to current existing literature on ECPR for OHCA (Table 1) and documents improvement in survival and in time to ECPR, complications reduction and increased number of potential multiorgan donors over time; thereby reinforcing the basic role of ECPR. Further studies should focus on identifying predictors of survival with good neurological outcome.



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Findings and clinical implications of an early, standardized whole body CT in eCPR patients

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Objectives: Patients with extracorporeal cardiopulmonary resuscitation (eCPR) should be promptly evaluated for reversible causes of arrest, iatrogenic trauma and therapy limiting conditions with computed tomography (CT). Nevertheless, whole body CT scans are not routinely performed in clinical practice due to a lack of knowledge regarding prevalence of findings and their implications.

Methods: We implemented a standardized, contrast enhanced, whole body CT protocol at our center for all eCPR patients. CT was performed immediately after cannulation/after coronary angiography if a coronary cause was likely. Structured reports were given by the radiologist on duty. The treating clinicians were later interviewed and had to state both the clinical implications (see table) and relevance (1 – not relevant to 5 – critical) of the findings in the report.

Results: 32 patients (56.8 ± 11.2 years, 21% female) were included. In 31 patients, CT led to one or more clinical implications (see table). In total, 346 (10.8 ± 4.4 per patient) findings were documented with the highest counts in the cardiovascular system (n=102, 30%) followed by thorax (n=62, 18%), abdomen (n=58, 17%), musculoskeletal (n=43, 12%), tubes & lines (n=42, 12%) and head & neck (n=39, 11%). Findings were rated as critical in 13% (n=45), highly relevant (15%, n=51), relevant (20%, n=69), slightly relevant (19%, n=64) or irrelevant (34%, n=117).

Table:

Clinical implications per patient following the CT scan	patients, % (n=32)
Monitoring (addition/change)	12 (37)
Follow-up exam	14 (44)
Non-invasive intervention	10 (31)
Minimal-invasive intervention	9 (28)
Surgery	2 (6)
Medication	18 (56)
Decision support	11 (35)
Withdrawal of further therapy	2 (6)
Other	4 (13)

Conclusions: A standardized whole body CT protocol is able to detect relevant findings with clinical implications in the vast majority of eCPR patients.

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Predicting physiologic instability in swine ECMO model using machine learning methods

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Objectives: Extra-corporeal membrane oxygenation (ECMO) requires continuous hemodynamic monitoring to reduce complications arising from changes in patient hemodynamics. We seek to use machine learning methods to predict physiologic status changes earlier in the course of decompensation, which will be critical to intervention decision making.

Methods: Sixteen swine were used in an induced tamponade physiology model. Arterial blood pressure high fidelity waveform (ABP), one-minute trend (HR, ARTS/M/D, CO, SVR, etc.), were collected for each swine using a 15-minutes window that progressed every 5 minutes including Hypotension (SBP≤90mmHg, MAP≤50mmHg), Tachycardia (HR≥120bpm), Bradycardia (HR≤60bpm) and Shock Index=HR/SBP≥1 were calculated every 5 minutes. ABP_VS and 1min_VS based random forest machine learning (RF) models were used to predict the five outcomes. Area under receiver operating characteristic curve (AUC) was used to evaluate predictive power and Delong's method was used to compare AUCs where $p<0.05$ was considered statistically significant.

Results: Sixteen swine were divided into a training group (n=9) and a testing group (n=7). By changing the prediction window dT from Point-Of-Care (POC, dT=0min) to an hour (dT=60mins), we could evaluate the prediction power changes over time. The following are the optimal earlier time and methods for predicting each outcome. Using this method, we could predict episodes of SBP<=90mmHg 20 minutes ahead of time (0.82 AUC - 95% confidence interval - CI:0.77-0.86), MAP<=50mmHG 30 minutes ahead (0.81 AUC - CI: 0.75-0.85), bradycardia 10 minutes ahead (0.82 AUC - CI:0.77-0.86), and SI>=1 30 minutes ahead with (0.81 AUC - CI:0.77-0.88) using 1min_VS based modeling. We could also predict trachycardia 30 minutes ahead (0.89 AUC - CI:0.80-0.94) using the ABP_VS based modeling.

Conclusions: This study showed that physiologic instability during ECMO could be predicted up to 60 minutes ahead of the event. This early-events-detection process could be used to alert care providers to critical physiologic instability and decompensation.

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Mechanical circulatory support to improve end organ function before post-myocardial infarct ventricular septal defect closure

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Objectives: Post-myocardial infarction (MI) ventricular septal defects (VSD) are associated with high rates of mortality with two-week mortality being reported 70-90%. Our preferred treatment strategy for these patients is cardiopulmonary support with mechanical circulatory support (MCS) then proceeding with surgical repair after correction of end-organ perfusion and metabolic derangements. We sought to quantify our surgical outcomes using this treatment algorithm.

Methods: We present a single center case series on patients ≥ 18 years of age who had a post-MI VSD and received MCS for cardiogenic shock before undergoing VSD repair from 2015 to 2022. Survival after Veno-Arterial ECMO (SAVE) score was calculated before initiation of MCS. The highest Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE) II scores were calculated for the 24-hour periods before initiating MCS and surgical repair.

Results: Seven patients were identified. The mean SAVE score was -5.7 (95%CI -9.5 —1.9). Mean time from initiation of support to repair was 16 days (95% CI 10.9–21.4). The mean SOFA score before MCS was 9.4 points (95%CI 6.2–12.7) and before repair was 3.4 points (1.2–5.6) with a mean decrease of 6 points (10.3–1.7, p=0.0139). The mean APACHE II score before cannulation was 18 points (95%CI 9.6–26.4) and before repair was 8.3 points(5.2–11.3) with a mean decrease of 9.7 points (5.0–16.9 p=0.0156). Two patients remained supported post repair for 3 and 4 additional days respectively before weaning support. 5/7(71%) patients survived to discharge of which all five are alive, two at 5 and 6 months respectively and the remaining three at >1yr. No patients had residual VSD on follow-up echocardiogram.

Patient	Age	Gender	BMI	MCS type	Pre-operative days on ECMO	LVEF	SAVE Score	Cause of death	90-day survival
1	61	Female	32.0	Impella + Fem-Fem VA ECMO	8	55	0	NA	Yes
2	64	Male	28.8	Impella + Fem-Fem VA ECMO	11	20	-9	NA	Yes
3	55	Female	35.0	Fem-Fem VA ECMO	14	20	-3	NA	Yes
4	56	Male	25.6	Fem-Fem VA ECMO	22	65	-9	NA	Yes
5	70	Male	27.4	Impella + Fem-Fem VA ECMO	22	65	-11	Stroke	No
6	49	Male	34.3	Impella + Fem-Fem VA ECMO	15	25	-2	Shock	No
7	55	Male	25.6	Tandem Heart	21	65	-6	NA	Yes

Conclusions: Pre-Operative MCS can be utilized to improve end organ function with acceptable short and midterm survival and repair integrity.

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The dynamic role of rehabilitating a patient with biventricular assist device implantation – a case report

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Objectives: Describe a rehabilitation program and report its results focusing on enhancing respiratory function, muscle strength and mobility in a BiVentricular Assist Device (BiVAD) implanted patient.

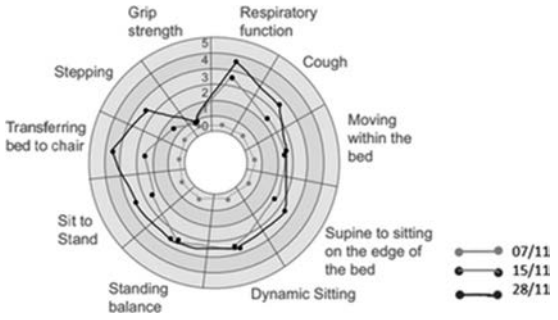
Methods: **Case Presentation:** A 63-year-old man was admitted for BiVAD implantation after a myocardial infarction, and subsequent heart failure. During hospitalization, the patient faced complications that delayed extubation and the smooth progression of rehabilitation. The rehabilitation program focused on three main dimensions: enhancing respiratory function, muscle strength and mobility. The outcomes were evaluated in three stages of the patient's recovery through assessment tools. The respiratory function was evaluated through a Borg modified scale for dyspnea and The Borg Rating of Perceived Exertion; the muscle strength through a Medical Research Council Scale for Muscle Strength and mobility through an Intensive Care Mobility Scale. An overall picture of patient's improvement was obtained through the Chelsea Critical Care Physical Assessment Tool (CPAx).

Results: Table I. Timeline of rehabilitation progression and goals achieved

Rehabilitation Program Goals	Rehabilitation Program Interventions
Airway Clearance Prevent respiratory complications	D1 - Bronchial drainage techniques D1 and on (when needed) – Suction (SOS) D3 and on (when needed) - Cough techniques – Huff D3 and on (when needed) - Forced expiratory technique D9 – Speech Therapy commenced above cuff vocalization to keep tracheostomy cuff inflated.
Prevent complications of bed rest Increase functional mobility Increase in Activity Tolerance Promote Muscular Strength Promote Body Balance	Graded mobilization D5 –SOEOB with nurse on Endotracheal Tube. D9 - Started 2xday sessions. SOOB, transfer to chair in the morning. Pedals in afternoon 10min. D10 – Morning SOEOB with Ao2; 4x STS with Ao2 and transfer to chair. Walked for 22 steps with RF. Afternoon 3x STS. D15 - Transferred to SOEOB with Ao2; STS to RF with Ao1 and Ao1 on frame; Manage to walk 52 steps with 3 resting stops with RF and Ao1 with patient and Ao1 with frame. D16 – First time walking out of the room for a total of 95 steps and 1 stop rest and 4 STS. D18 - Walked out of the room for a total of 160 steps and 1 stop rest. D22 – Walked 40 meters with RF and Ao1 with patient and Ao1 with frame. Only 1 rest and performing a total of 286 steps.

D – Day of rehab session; SOEOB - Sitting On Edge Of Bed; SOOB - Stand Out Of Bed; STS – Sit To Stand-up; Ao2 – Assistance of 2; RF – Rollator frame

Figure I. Evaluation of CPAx on November 7th, 15th and 28th



Conclusions: The patient presented a positive progression in all the evaluated parameters. The rehabilitation program was well-tolerated in this case without significant complications or adverse events.

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ECPella 5.0 - can we further improve outcomes?

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Objectives: ECPella is an established strategy for cardiogenic shock. The additional implantation of Impella leads to a maximization of VA-ECMO effects and to its reduced duration. Impella 5.0/5.5, instead of CP, might further impact. Potential benefits favoring Impella 5.0/5.5 are: shorter duration of inotropic therapy, less device related hemolysis and access site complications; higher dose of unloading and cardiac forward support, resulting in greater myocardial recovery and earlier de-escalation from ECPella to isolated left-sided support. The aim of this study is to report our experience on the use of primary ECPella 5.0 configuration.

Methods: We retrospectively collected data on patients admitted to our unit from January to December 2022 treated with primary ECPella 5.0. Outcomes included Impella explantation, as a result of myocardial recovery, heart replacement therapy or death. Secondary endpoints were: duration and dosage of inotropes, haemolysis, duration of ECLS, access site complications.

Results: 5 male patients (mean age 60-years) received Ecpella 5.0 with surgical transaxillary fluoroscopy/TEE guided implantation. Clinical outcomes are reported (Figure 1): notably all patients were quickly weaned from ECLS (1 to 4 days), but one who underwent emergency HTx on ECPella; no ECMO related complications were observed during support, neither right ventricular failure after its removal; no Impella access related complications were recorded, but one patient had axillary artery thrombosis after removal, which was successfully treated. Mean duration of Impella support in patients who showed native heart recovery was 7 days.

Patient		1	2	3	4	5
MCS duration (days)	*VA-ECMO*	2	3	4	11	1
	Impella	13	3	6	7	7
Impella within 24h		yes	yes	yes	no	yes
IABP pre Impella		yes	yes	yes	yes	no
Inotropic duration hours		422 ~18 days	89 ~4 days	31	15	24
Maximum inotropic score		46	23	4	5	2,5
Bleeding		no	no	no	no	no
LDH peak U/L		3860	2636	3686	4190	1585
Access site complications		no	no	no	no	axillary artery thrombosis
Outcome	*Recovery*			x		x
	HTx				x	
	Death	x	x			

Conclusions: Maximizing Impella support with a surgical axillary pump further expands the concept of ECPella with quick descalation from ECMO. If logistically feasible (timely surgical availability), we endorse this configuration as a further step in the management of cardiogenic shock; notwithstanding, this might also account for reduced costs.

Conflict of interest: FP is consultant for Abiomed.

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V-A ECMO supported high-risk PCI. Case-control study

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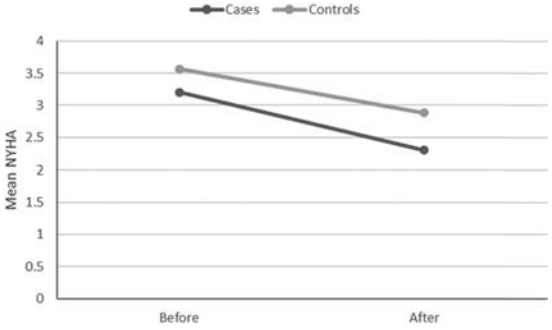
Objectives: The study is designed to assess the outcomes of using V-A ECMO on high-risk PCI procedures.

Methods: A prospective interventional study performed on patients with viable ischemic myocardium who refused CABG, syntax score>22, excluding scarred myocardium. V-A ECMO (Fem-Fem configuration) will be initiated during elective high-risk PCI procedure, compared to patients who underwent high risk PCI refusing ECMO, also excluding patients suffering from acute decompensated heart failure.

Results: A case-control study total of 20 patients were identified, 10 patients underwent high risk PCI on V-A ECMO support, (Control group) 10 patients underwent high risk PCI without V-A ECMO, our study showed a statistically significant higher SYNTAX score in group 1 than in group 2 P value 0.025, no statistically significance difference between number of cases with left main lesions, unprotected LM and MVD between group 1 and group 2, average ECLS duration of 2.5 hours, 6 patients on awake ECMO, statistically non-significant difference between NYHA class between group 1 and group 2 also our study showed no statistically difference between LV EF before and after PCI in both groups, group 1 eight patients had complete revascularization in one session while group 2 only seven patients had complete revascularization, one patient in group 1 had VT while group 2 patient had VF and another one suffered of bradycardia then asystole, group 1 patients all discharged home within one week while group 2 had 2 mortalities during PCI.



Conclusions: ECMO can be successfully used to facilitate elective high-risk PCI minimizing risk of cardiovascular complications.

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DIC score is associated with short-term mortality in patients undergoing VA-ECMO after cardiac surgery

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Objectives: Disseminated intravascular coagulation (DIC) score is associated with short-term mortality in various critical conditions, but has not been studied in postcardiotomy cardiogenic shock (PCS) patients supported with venoarterial extracorporeal membrane oxygenation (VA-ECMO). The objective of this study was to evaluate the relation of DIC score and short-term mortality in VA-ECMO-treated PCS patients.

Methods: VA-ECMO-treated PCS patients at the Beijing Anzhen Hospital between January 2015 and December 2018 were included. Multivariable logistic regression analysis was performed to assess the relationship between DIC score and mortality, and control for potential confounding variables.

Results: Of 222 PCS patients treated with VA-ECMO, 145 (65%) patients could be weaned from VA-ECMO, and median ECMO support duration was 5 (3-6) days. In-hospital mortality was 53%. The median DIC score was 5(4-6). Patients with DIC scores ≥5 (overt DIC) had 64% mortality, compared to 22% for patients with DIC scores <5 ($p < 0.001$). After adjustment for age, sex, ECMO indications, and peak serum lactate, a one-point rise in peak DIC score (OR 2.20, 95% CI 1.64-2.95) or peak DIC score ≥5 during ECMO (OR 4.98, 95% CI 2.42-10.24) was associated with an increased risk of in-hospital mortality (Figure 1). The area under the receiver operating characteristic curve for peak DIC score during ECMO was 0.76 (95% CI, 0.69–0.82), and the combination of peak DIC score and change in DIC score during ECMO improved overall classification.

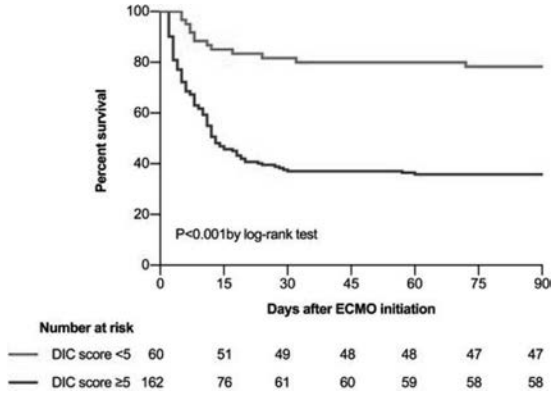

Figure 1

Conclusions: DIC score is associated with short-term mortality in patients undergoing VA-ECMO after cardiac surgery, independent of age, sex, disease characteristics and severity of illness.

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A review of cardiac arrest team activations for patients undergoing mechanical circulatory support

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Objectives: Patients receiving mechanical circulatory support (MCS) can display atypical physiology leading to absence of normally reliable signs of adequate circulation such as a palpable pulse. These changes often necessitate modification of conventional resuscitation strategies in the event of cardiorespiratory collapse. We sought to describe and evaluate our experience with these cases, focusing on whether arrests were device or non-device-related and identifying areas for improvement.

Methods: Over the period 1st January 2020 to 1stAugust 2022, the clinical notes were reviewed of all patients undergoing MCS for whom a cardiac arrest call was activated. The device type, cause of deterioration, treatment and outcome (survival to discharge and Cerebral Performance Category (CPC) at discharge) were recorded.

Results: The cardiac arrest team was activated on 25 occasions for patients receiving MCS in the study period. The devices in use were: Impella CP (n=9), Heartware HVAD (n=8), intra-aortic balloon pump (n=3), Centrimag BiVAD (n=2), HeartMate 3 (n=1), VA ECMO (n=1), and Syncardia total artificial heart (n=1). On five occasions the patient's deterioration was caused by a device issue, including LVAD pump thrombosis (n=2), LVAD acute pump failure (n=2), and Impella CP migration from optimal position (n=1). In the 20 non-device-related cases, reasons for activation included ventricular arrhythmia (n=10), non-arrhythmic deterioration in cardiac function (n=3), acute intracranial event (n=2), temporary cardiac pacing failure (n=1), and hypercapnic respiratory failure (n=1). 6 of the 25 patients (24%) survived to hospital discharge. All had a CPC score of 1/5, apart from one who had a

score of 3/5. The survival to discharge rate in the device-related group was 2/5 (40%), compared to 4/20 (20%) in the non-device-related group. Areas for improvement were identified in five cases, i.e. inaccurate assessment of the presence of an adequate circulation leading to delayed or inappropriate resuscitation.

Conclusions: The assessment of cardiac arrest in patients undergoing MCS can be challenging and such incidents carry a high mortality. Staff training is of paramount importance to ensure these vulnerable patients who undergo complex therapy receive optimal care.

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Lactate levels for prognosticstion of short-term outcomes for patients on Veno-Arterial extracorporela membrane oxygenation therapy (VA-ECMO) for cardiogenic shock: Review article

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Objectives: Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has been increasingly used as a rescue therapy for management of refractory cardiogenic shock (CS). Prediction scores such as SAVE and ENCOURAGE scores offer useful means of identifying patients who will benefit more from VA-ECMO therapy but are quite complex and not readily applicable at the bedside, thus use of biomarkers such as arterial lactate levels which is a validated marker of tissue hypoperfusion serves as a useful tool for prognostication. This review aimed at:* Analysing the accuracy of lactate level in forecasting short-term outcomes of patients on VA-ECMO for cardiogenic shock particularly mortality and early weaning off VA-ECMO. * Identifying factors to enhance effective use of arterial lactate for outcome prognostication.

Methods: Five retrospective observational studies involving 684 patients that investigated use of lactate measurement as a prognostication tool for patients receiving VA-ECMO therapy were identified from databases of CINAHL, MEDLINE, Academic search elite and PubMed. These studies were critically appraised using Step-by-step guide to critiquing quantitative research tool by Coughlan, Cronin and Ryan and the level of evidence assessed using the GRADE recommendations.

Results: The studies were widely heterogenous and did not meet the criteria for evidence upgrade, but the area under the receiver operating characteristic (AUROC) curve from all the studies were closer to 1. All the studies showed a reduction in lactate levels of survivors of cardiogenic shock on VA-ECMO when compared with non-survivors and this was associated with mortality outcome. Lactate clearance (LC) as early as 6 hours post-insertion was noted to be predictive of mortality. The studies reviewed did not investigate association between lactate levels and time of weaning off VA-ECMO, but lactate levels at the point of weaning was a prognostic value for survival post decannulation, and decannulation rate was better in patients with improved lactate levels at 24 hours post device insertion.

Conclusions: Dynamic (trends) lactate measurements offer better prognostication as opposed to static lactate readings and a decrease in baseline lactate level was a strong predictor of mortality.

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Refractory circulatory failure in COVID-19 patients treated with veno-arterial ECMO: A retrospective single-center experience

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Objectives: Data about COVID-19 patients treated with veno-arterial-ECMO (VA-ECMO) is limited. Reported survival rates range from 27.9% to 77.8%, depending on VA-ECMO indication. A subgroup of patients suffers from circulatory failure due to a COVID-19 associated hyperinflammatory state (CovHI). In these patients, differentiation between inflammation and sepsis is difficult but important. In this retrospective case series, differential diagnoses of COVID-19 associated refractory circulatory failure and survival rates in different indications for VA-ECMO are investigated.

Methods: Retrospective analysis of 28 consecutive COVID-19 patients requiring VA-ECMO at the University Hospital Regensburg between March 2020 and May 2022. Specific treatment for COVID-19 was in accordance with respective guidelines. Mycotic infections were either invasive or met current definitions of COVID19-associated-pulmonary aspergillosis.

Results: At VA-ECMO initiation, median age was 57.3 years (IQR: 51.4 – 61.8), SOFA score 16 (IQR: 13 – 17)

and norepinephrine dosing 0.53μg/kg/min (IQR: 0.32 – 0.78). Virus-variants were: 61% wild-type, 14% Alpha, 18% Delta and 7% Omicron. Survival to hospital discharge was 39%. 17 patients were primarily supported with VA-ECMO only (survival 42%), 3 patients were switched from VV to VA-ECMO (survival 0%), and 8 patients were converted from VA to VAV or VV-ECMO (survival 50%). Indications for VA-ECMO support were pulmonary embolism (PE) (n=5, survival 80%), right heart failure due to secondary pulmonary hypertension (n=5, survival 20%), cardiac arrest (n=4, survival 25%), acute left heart failure (ALHF) (n=11, survival 36%) and refractory vasoplegia (n=3, survival 0%). Inflammatory markers at VA-ECMO initiation were higher in patients with ALHF or vasoplegia; in these patients a higher rate of invasive fungal infections (10/14, 71% vs. 4/14, 29%; p=0.023) compared to the other patients was found.

Conclusions: Survival on VA-ECMO in COVID-19 depends on VA-ECMO indication, which should be considered in further studies and clinical decisions making. Circulatory failure due to vasoplegia should be considered very carefully as indication for VA-ECMO. A high rate of mycotic infections mandates an intense microbiological workup of these patients and must be considered as an important differential diagnosis to CovHI.

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Possible positive effect of plasma bilirubin on refractory out-of-hospital cardiac arrest outcome

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Objectives: We evaluated the effect of total bilirubin (TB) levels at admission on neurologic outcome of refractory out-of-hospital cardiac arrest, considering bilirubin to be a potent endogenous antioxidant agent.

Methods: We made a retrospective cohort study of patients with refractory out-of-hospital cardiac arrest from Prague-OHCA trial whose TB levels at admission were obtained. We compared initial TB levels of patients with good 180-days neurologic outcome assessed as cerebral performance category (CPC) 1 or 2 to those with bad neurologic outcome (CPC 3 – 5). We also made a retrospective univariate analysis evaluating the effect of low (<0.3mg/dl and increased (>1 mg/dl) TB levels on patient outcome. Similarly, the analysis of TB levels in subgroup of patients treated with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was performed.

Results: The initial plasma TB levels were obtained in 186 out of 210 (89 %) patients enrolled in Prague-OHCA who reached the hospital. The median level of TB at admission was 0.63 mg/dl (10.7 μmol/l). Patients with CPC 1,2 had significantly higher TB levels in comparison with CPC 3 - 5 patients with median 0.77 (13.15 μmol/l) and 0.57 mg/dl (9.7 μmol/l), respectively; p<0.001. The relative risk (RR) of bad neurologic outcome in group of patients with TB <0.3 mg/dl was 1.61 (95% CI 1.44 - 1.81), whereas in group of those with increased TB levels (>1 mg/dl) the RR of bad outcome was 0.797 (95% CI 0.538 - 1.18). VA-ECMO was implanted in 73 (39.2 %) of cases enrolled in the analysis. Among this subgroup, there was also significant difference between initial TB levels in CPC 1,2 and CPC 3-5 group with median values 0.69 mg/dl (11.85 μmol/l) and 0.53 mg/dl (9.1 μmol/l) with p=0.039.

Conclusions: Patients with refractory out-of-hospital cardiac arrest with good 180-days neurologic outcome present with significantly higher total bilirubin levels at admission. This also applies to those treated with VA-ECMO. Low total bilirubin level at admission significantly increases the relative risk of bad 180-days neurologic outcome.

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Relation between severe shock and vitamin D levels in post-resuscitation survivors requiring extracorporeal membrane oxygenation (ECMO)

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Objectives: Vitamin D deficiency is associated with various cardiovascular diseases, including sudden cardiac arrest (SCA). Severe shock is related to morbidity and mortality in patients resuscitated from SCA. This study investigated the association of vitamin D deficiency with severe shock in post-resuscitation survivors requiring ECMO.

Methods: We enrolled patients who were successfully resuscitated from out-of-hospital cardiac arrest of presumed cardiac cause. The severe shock was defined as hypotension requiring ECMO despite fluid loading and high-dose vasopressor therapy. The vitamin D level was measured as plasma 25(OH)D concentrations and severe vitamin D deficiency was defined as 25(OH) D <10 ng/mL.

Results: A total of 96 patients [67 men (70%), mean age 55.4 ± 15.8 years] were included in this study. The first monitored rhythm was shockable in 59 patients (62%)

and non-shockable rhythm in 37 (38%). Bystander cardiopulmonary resuscitation (CPR) was performed in 78 (81%) and mean arrest time and CPR time were 28.9 ± 17.9 and 26.0 ± 17.2 minutes, respectively. The severe shock was observed in 27 patients (28%). The Mean vitamin D level was 10.0 ± 5.2 ng/mL and severe vitamin D deficiency was diagnosed in 56 patients (58%). Vitamin D level was significantly lower (7.2 ± 4.1 vs. 11.2 ± 5.2 ng/mL, p=0.001) and vitamin D deficiency was observed more frequently (82 vs. 49%, p=0.004) among patients with severe shock. Patients with severe shock were likely to have more left ventricular systolic dysfunction (LVEF <40%, 78 vs. 44%, p=0.002) and to be obese [body mass index (BMI) >24 kg/m^2, 74 vs. 51%, p=0.038]. In multivariate logistic analysis, vitamin D deficiency was the significant independent predictor of severe shock after SCA (OR 4.83, 95% CI 1.56-14.91, p=0.006) with left ventricular systolic dysfunction (OR 4.83, 95% CI 1.66-14.08, p=0.004) after adjusting for confounding variables such as first monitored rhythm, bystander CPR, baseline renal function, and BMI.

Conclusions: Vitamin D deficiency was strongly associated with severe shock in post-resuscitation survivors requiring ECMO.

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Prognostic influence of gender in patients undergoing extracorporeal cardiopulmonary resuscitation

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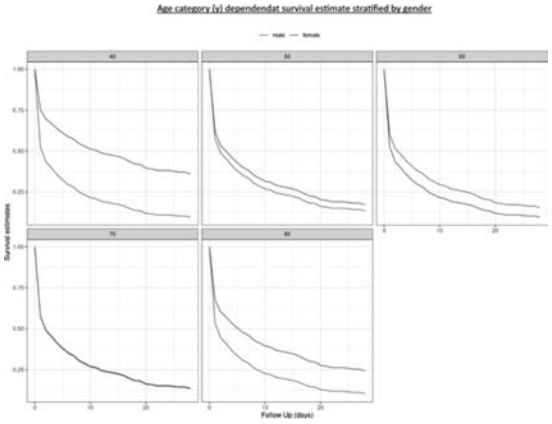
Objectives: Extracorporeal cardiopulmonary resuscitation (eCPR) has prevailed as a therapy in refractory cardiac arrest (CA). In this context, knowledge of outcome-relevant predisposing patient (pt) characteristics is of increasing importance. We evaluated the prognostic influence of demographic characteristics in pts presenting with in- or out of hospital cardiac arrest (IHCA/OHCA) treated with eCPR.

Methods: We retrospectively analysed data of 330 pts treated for IHCA and OHCA using eCPR in our cardiac arrest center from the years 2016 to 2022. Primary outcome was defined as survival of the primary hospital admission with favourable neurological outcome (cerebral performance category [CPC]-score ≤2). Statistical analyses were performed using baseline comparison, survival analysis, as well as univariable and multivariable analysis.

Results: Overall survival was 21%, with favourable neurological outcome in 14% of cases. Multivariable analysis revealed female gender (p=0.004), performance of bystander CPR (p=0.032), pre-interventional use of amiodarone (p<0.001) and a shorter overall CPR duration (p<0.001) to be independent predictors of favourable outcome. In the female subgroup a higher age (p=0.009, figure 1) and body mass index (BMI; p=0.005) were associated with worse outcome. Comparison of female and male pts resulted in less prevalence of pre-existing coronary artery disease (48% vs. 75%, p<0.001) and cardiomyopathy (17% vs. 34%, p=0.01), while prevalence of other cardiovascular risk factors did not differ. Female pts showed a higher prevalence of witnessed collapse (97% vs. 86%; p=0.016) and were more likely to receive bystander CPR (94% vs. 85%; p=0.065).



Conclusions: These findings indicate a significant survival benefit for female patients undergoing eCPR, possibly based on a higher prevalence of witnessed collapse and bystander CPR. Interestingly, the impact of pts age on neurologically favourable outcome was higher in female pts than in male, warranting further investigation.

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VA ECMO for cardiogenic shock complicating acute myocardial infarction: Insights from a French nationwide database

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Objectives: We aimed to analyze the impact of timing of implantation (strategy-outcome relationship) and volume of procedures (volume-outcome relationship) on survival of veno-arterial extracorporeal membrane

oxygenation (VA ECMO) for cardiogenic shock complicating acute myocardial infarction (AMI).

Methods: We conducted an observational retrospective study through two propensity score-based analyses using a nationwide database between January 2013 and December 2019. We classified patients into early implantation (VA ECMO on the day of primary percutaneous coronary intervention [PCI]) and delayed implantation (VA ECMO beyond the day of PCI) groups. We classified patients into low- or high-volume groups based on the median hospital volume.

Results: During the study period 649 VA ECMO were implanted across 20 French hospitals. Mean age was 57.1 ± 10.4 years, 80% were male. Overall, 90-day mortality was 64.3%. Patients in the early implantation group (n=479, 73.8%) did not show a statistical difference in 90-day mortality than in the delayed group (n=170, 26.2%) (HR: 1.18; 95% CI 0.94-1.48; p=0.153). The mean number of VA ECMO implanted during the study period by low-volume centers was 21.3 ± 5.4 as compared to 43.6 ± 11.8 in high-volume centers. There was no significant difference in 90-day mortality between high-volume and low-volume centers (HR: 1.00; 95% CI: 0.82-1.23; p=0.995).

Conclusions: In this real-world nationwide study, we did not find a significant association between early VA ECMO implantation as well as high-volume centers and lower mortality in AMI-related refractory cardiogenic shock.

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The impact of COVID-19 on extracorporeal cardiopulmonary resuscitation (ECPR) for out-of-hospital cardiac arrest (OHCA): A single centre study

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Objectives: The COVID-19 pandemic has been affecting everything including ECMO service. At the moment we have to equip PPE before ECPR and we thought it may influence on time to establish veno-arterial ECMO and patient outcomes.

Methods: We compared OHCA-patients who underwent ECPR in our hospital before (January 2015 - March 2020) and after (April 2020 - December 2022) the Government of Japan declared a state of emergency in relation to COVID-19.

Results: There were 32 and 9 patients in the pre- and post-COVID-19 pandemic sample. Of these, 9 (28.1%) vs. 5 (55.6%) survived extracorporeal life support (ECLS), p=0.23, and 4 (12.5%) vs. 2 (22.2%) had good neurologic outcomes (cerebral performance category 1–2) after ECLS. Seven (21.9%) vs. 1 (12.5%) were discharged or transferred alive from the hospital (one patient of the post-COVID-19 cohort has been still hospitalised for rehabilitation), p>0.99. Mean values of low-flow time were respectively 67.3 minutes (SD 18.3) and 55.6 minutes (SD 17.1), p=0.091, and median values of time to establish ECMO from admission were respectively 32.5 minutes (IQR 15.8) and 26.0 minutes (IQR 4.0), p=0.23.

Conclusions: There were no differences in time-to-ECMO or outcomes in patients who underwent ECPR for refractory OHCA before and after the COVID-19 pandemic.

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ECMO code in Castilla y León: Single-center experience with primary ECMO transportation and "mobile ECMO" team built by two phisicians

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Objectives: Interhospital trasfer of patients suffering by refractory cardiogenic shock is challenging and still asociated with poor clinical outcomes. We present our initial experience with primary vaECMO ground transportation by the team, built by two phisicians.

Methods: From March 2019 untill June 2022, the "mobile ECMO" team has been activated on a total of 40 occasions, transferring for case evaluation in 16 of them, and performing vaECMO implantation in 15 patients. 13/15 (86.6%) were men, with a median age of 60 years-old (range 28-66). The most frequent indication was cardiogenic shock secondary to acute myocardial infarction (5 patients, 33.3%), and septic/toxic cardiomyopathy (5 patients, 33.3%). Prior to ECMO insertion, all patients were sedated and mechanically ventilated, with a median ionotropic score of 192 units (range 15-510), median SOFA score of 10 (range 7-17), and blood lactate of 8.5 mmol/l (range 3-16). 9/15 (60%) were supported with an intraaortic balloon pump.

Results: ECMO insertion was performed bedside in 10 patients. Cannulation was percutaneous in 12/15

patients, whereas 3/15 required surgical cut-down for arterial cannula placement. Distal leg perfusion line was inserted before transfer in 12/15 cases. The median distance traveled was 95 km (range 5-128 km). None of the patients had transport associated complications nor morbidity. Clinical stabilization was achieved in 12/15 (80%) patients. Major causes of death were multiorgan failure and stroke. One patient presented non-recoverable left ventricule function, and was successfully bridged to heart transplantation. ECMO was weaned from 9/15 (60%) of the patients after a median duration support of 7 days (range 1-19 days). 8/15 (53%) were discharged home and are still alive.

Conclusions: Primary ground ECMO transportation for patients with refractory cardiogenic shock is related to improved outcomes and provide a reasonable survival opportunity. The initial experience with a compact mobile ECMO team formed by two physicians provide safe implantation and a free of complications transport to an ECMO center.

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Fulminant myocarditis following SARS-CoV-2 mRNA vaccination rescued with venoarterial ECMO: A report of two cases

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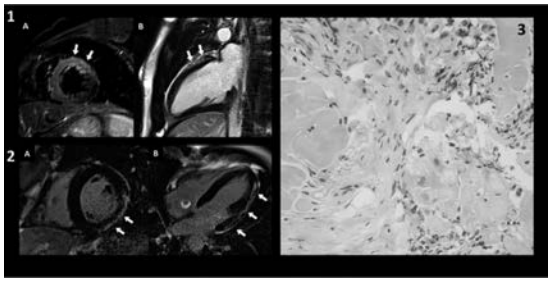
Objectives: Cases of fulminant myocarditis after mRNA COVID-19 vaccination have been reported. The most severe may need venoarterial extracorporeal membrane oxygenation (V-A ECMO) support. Here we report two cases successfully rescued with V-A ECMO.

Methods: We included all the cases supported with V-A ECMO for refractory cardiogenic shock due to myocarditis secondary to a mRNA SARS-COV2 vaccine in the high-volume adult ECMO Program in Vall Hebron University Hospital since January 2020.

Results: We identified two cases (table). One of them was admitted for out-of-hospital cardiac arrest. In both, a peripheral V-A ECMO was implanted in the cath lab. An intra-aortic balloon pump was needed in one case for left ventricle unloading. Support could be successfully withdrawn in a mean of five days. No major bleeding or thrombosis complications occurred. Definite microscopic diagnosis could be reached in one case (Image, 3). Treatment was the same, using 1000mg of methylprednisolone/day for 3 days. A cardiac magnetic resonance 10 days after admission showed a significant improvement in systolic function and diffuse oedema and subepicardial contrast intake in different segments (Image, 1-2). Both patients were discharged fully recovered.

	Case 1	Case 2
Gender; age (years)	Male; 43	Male; 22
Vaccine type; dose and days since vaccination	BNT 162b2; first dose; 8	BNT 162b2; second dose; 14
Vasoactive drugs dose and lactate levels before cannulation	Noradrenaline 0.4 mcg/kg/min and dobutamine 4 mcg/kg/min Lactate 9.3 mmol/L	Noradrenaline 1 mcg/kg/min and dobutamine 4 mcg/kg/min Lactate 5 mmol/L
Type of cannulation and configuration	Percutaneous femoro-femoral 25F/55 cm right femoral drainage cannula 17F/15 cm right femoral return cannula Reperfusion cannula 8F	Percutaneous femoro-femoral 25F/55 cm left femoral drainage cannula 17F/15 cm right femoral return cannula Reperfusion cannula 8F
Endomyocardial biopsy	Non conclusive	Lymphoplasmacytic infiltration with eosinophils, interstitial oedema, and mild cardiomyocyte necrosis
Cardiac Magnetic Resonance	Subepicardial antero-lateral and infero-lateral late gadolinium enhancement from base to apex	Diffuse edema and a subepicardial basal anterior contrast uptake
LVEF at admission and discharge	15%; 67%	10%; 50%



Conclusions: V-A ECMO should be established in cases of COVID-19 vaccine-associated myocarditis with refractory cardiogenic shock during the acute phase.

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Contrast enhancement in the pulmonary arteries and systemic arterial circulation in computed tomography in VA-ECMO patients

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Objectives: Contrast-enhanced computed tomography (CE-CT) scans after implementation of femoro-femoral Venoarterial Extracorporeal Membrane Oxygenation (VA-ECMO) following cardiac arrest are of utmost diagnostic relevance. In this setting, siphoning, mixing, and dilution effects of contrast agent and non-contrasted blood often lead to inhomogeneous vessel contrast and impair exam quality. An ECMO-flow reduction has been proposed to overcome this issue but is not sufficiently proofed yet. In this study, we evaluated CT contrast enhancement of the pulmonary arteries and aorta in VA-ECMO patients with reduced ECMO flow-rate.

Methods: We included patients with VA-ECMO due to cardiac arrest, who were subsequently examined with a standardised whole-body CE-CT protocol. Patients were excluded if a reduction in ECMO blood flow-rate of 25-50% during the scan was not feasible (e.g., hemodynamic reason, undercut of the minimum flow-rate of 1.5 litres per minute). Patients or their legal representatives were asked for written informed consent after neurological recovery. The study team assessed contrast enhancement by measuring Hounsfield-Units (HU) in a standardised Region Of Interest (ROI) in the pulmonary trunk, pulmonary arteries (PA), the ascending and descending aorta, the infrarenal aorta and the carotids. A qualitative assessment of vessel opacification was performed using a 5-point Likert scale. Results are presented with mean and standard deviation averaging geminate structures (carotids, pulmonary arteries).

Results: Data analysis is still in progress at the time of abstract submission. The results will be presented in full at the congress if the abstract is accepted.

Conclusions: In this study, ECMO blood flow-rate reduction during the CT scan resulted in sufficient simultaneous contrast enhancement of both the pulmonary and systemic arterial circulation. Therefore, this CT protocol allows for the evaluation of pulmonary embolism and aortic pathologies within one scan.

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Management of harlequin syndrome in veno-arterial extracorporeal membrane oxygenation

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Objectives: Patients with cardiac and pulmonary dysfunction who are supported on femoral veno-arterial membrane oxygenation (VA-ECMO) may experience differential hypoxia to their upper body (Harlequin syndrome) as poorly oxygenated blood is ejected from the left ventricle. The purpose of this study was to evaluate our institutional experience in managing this complication.

Methods: Single center retrospective cohort study was performed on patients who experienced Harlequin syndrome while supported on femoral VA-ECMO from 2016-2021. Harlequin syndrome was defined as a right radial PaO2 < 80mmHg, and an upper body oxygen saturation < 90% during ECMO support. Patients were grouped as those who underwent ECMO revision (conversion to veno-venous or veno-arterio-venous, or repositioning of cannula) and those who were managed with physiologic interventions alone, and outcomes were examined. Physiologic interventions were defined as (1) respiratory (increased ventilatory support, therapeutic bronchoscopy), or (2) reduction in native cardiac output (decreasing inotropy, volume removal, increasing ECMO flow).

Results:

Table 1.

	Overall (N= 44)	ECMO revision (n = 11)	No ECMO revision (n = 33)	p-value
Age (y)	56 (IQR 48-62)	53 (IQR 43-67)	56 (IQR 49-62)	0.75
Sex (Female)	15 (34%)	5 (11%)	10 (23%)	0.47
Lowest PaO2 (mm Hg)	53 (IQR 48-60)	50 (IQR 47-61)	54 (IQR 48-59)	0.60
ECMO Duration (d)	8.5 (IQR 4.7-16)	7 (IQR 3.5-17.5)	9 (IQR 5-16)	0.74
Respiratory intervention	25 (56%)	6 (54.5%)	19 (58%)	0.10
Reduction in native cardiac output	29 (66%)	4 (36.4%)	25 (76%)	0.05
Time to resolution (hours)	4.5 (IQR 1.4-7.8)	7.7 (IQR 2.7-12.4)	3.5 (IQR 1.4-6.7)	0.23
Neurological injury	14 (32%)	3 (27%)	9 (27%)	1
Survival to decannulation	18 (41%)	8 (73%)	23 (70%)	1

482 patients supported with femoral VA-ECMO, 44 (9%) experienced Harlequin syndrome. 11 (25%) were managed with ECMO revision +/- physiologic interventions, and 33 (75%) were managed with physiologic

interventions alone. The time until resolution of Harlequin syndrome for patients who had an ECMO revision compared to those who did not was a median of 7.7 hours (IQR 2.7 - 12.4) versus 3.5 hours (IQR 1.4-6.7) (p = 0.23), respectively. Patients who underwent ECMO revision had a similar incidence of neurologic injury (27% vs 27%, p=1) and survival-to-decannulation (73% vs 70%, p=1) when compared to those who did not.

Conclusions: Harlequin syndrome can be a morbid complication associated with femoral VA-ECMO. The majority of patients can be managed with physiologic interventions alone, and these strategies should be attempted prior to ECMO revision.

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Implementation of a multi-disciplinary response team for initiation of extracorporeal cardiopulmonary resuscitation (ECPR) in patients presenting after out of hospital cardiac arrest (OHCA)

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Objectives: This study will examine the effects of the implementation of a formalized multi-disciplinary ECPR Team on OHCA patients.

Methods: This is a single-center, retrospective study examining the effects of the implementation of a formalized ECPR Team on outcomes for patients receiving ECPR in the ED. The data was collected from May 2013 to November 2022. We included all adult ECPR patients successfully cannulated in the ED both before and after implementation of the ECPR Team. Exclusion criteria are age <18 years, trauma activation or presumed non-cardiac cause of arrest. The primary outcome is discharge alive from the hospital.

Results:

Year	Total OHCA Transported to ED	ECPR	ECPR Survival
2013	29	1	1
2014	70	6	1
2015	68	2	0
2016	83	1	0
2017	83	2	0
2018	121	9	4
2019	123	15	7
2020	115	3	2
2021	126	8	4
2022	90	13	6

Between May 2013 to November 2022 there were 900 OHCA patients that were treated in the ED and 60 ECPR patients were cannulated. Survival to hospital discharge pre and post-implementation of the ECPR Team was 23.1% (3/13) and 46.8% (22/47) respectively with a P value of 0.125. The post implementation survival rate of 46.8% remained consistent across the years except for 2020 when the program was put on hold. Secondary outcomes are pending.

Conclusions: ECPR remains a promising intervention for neuro-intact survival however it is resource intensive with unproven benefits. We describe the impact of the implementation of a multidisciplinary ECPR Team for OHCA at a urban academic center. Survival to hospital discharge improved from 23 to 46% after implementation, although this value was not statistically significant due to the relatively small number of cases pre ECPR Team. This trend towards improvement in survival is multi-factorial including extensive diagnostic and treatment protocols. The limitations of this study include its retrospective, single-center design, and small number of pre-intervention patients. We believe that this study shows the benefit of a ECPR Team for OHCA patients.

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Spinal cord infarction in patients supported with extracorporeal membrane oxygenation: A review of incidence, risk factors and outcomes

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Objectives: Spinal cord infarction (SCI) in patients requiring extracorporeal membrane oxygenation (ECMO) for cardiogenic shock is an uncommon complication with only a few case reports detailing its incidence. SCI carries with it a high risk of long-term morbidity in the event of hospital survival. This review aims to investigate the incidence, risk factors and outcomes of patients with SCI following ECMO.

Methods: A systematic review of the literature was conducted through PubMed and EMBASE through December 2022. Articles reporting on spinal cord infarction in patients supported with ECMO were included. Appraisal of studies for inclusion and data extraction were performed independently by two reviewers. Meta-analysis was not feasible due to the small number of studies available.

Results: Seven studies with a total of 19 patients (9 female, 10 male) were reviewed. The mean age was 49.4±17.2 years old. The most common indication for ECMO was acute cardiovascular failure (n=12, 63%) followed by primary graft failure following cardiac transplantation (n=5, 26%). All patients were supported on veno-arterial ECMO (VA-ECMO) with one

patient converted to veno-pulmonary artery ECMO for right heart support. The average duration of ECMO was 12.2±11.3 days. Five patients (31%) had concomitant intra-aortic balloon pump (IABP) therapy and four patients (25%) had concomitant renal replacement therapy. Average time to evidence of neurological deficit was 11.6±6.8 days, with radiological diagnosis delayed to an average of 34.7±24.5 days. The thoracic spinal cord was the most common level of spinal cord infarction (n=15, 79%). Incidence of paraplegia was 84% (n=16) with neurological recovery in only 16% of cases (n=3). Hospital survival was 31% (n=6).

Conclusions: Spinal cord infarction is a rare but devastating complication of ECMO. We have noted in our institution that patients who have been on VA-ECMO and IABP may be at a higher risk of SCI and this is reflected in this review. However, there is a paucity of data on this dire complication, and we have demonstrated that more long-term and international data is required.

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Radiofrequency catheter ablation with ECMO support in electrical storm patients: Single center results

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Objectives: Electrical storm (ES), defined as three or more repetitive episodes of sustained ventricular tachycardia or fibrillation within 24-h, is a life-threatening medical emergency that requires immediate diagnosis and treatment. Radiofrequency catheter ablation (RFCA) is an effective treatment modality for refractory VT and ES episodes. In this case series, we aimed to present the results of patients diagnosed with malignant arrhythmia and RFCA with ECMO support.

Methods: The study included five patients whose ES was treated with RFCA under mechanical support (VA-ECMO) in our clinic in 2022.

Results: The mean age of patients was 63.4±3.9 years, and BMI was 28.58±2.3 kg/m^2. While 4 patients had ES due to ischemic origin, 1 patient had non-ischemic ES, and their PAINESD scores were 19.8±4.6 (14-28)(min.-max.). Four of patients were discharged from the hospital. Surgical sympathectomy was performed in 2 patients after RFCA with ECMO.

Conclusions: Radiofrequency catheter ablation (RFCA) has an important role in the treatment of patients with structural heart disease presenting with recurrent ventricular tachycardia (VT). In high-risk patients for whom preprocedural hemodynamic optimization is not possible, placement of extracorporeal mechanical assist devices should be considered to prevent periprocedural acute heart failure and potentially reduce mortality. Baratto et al. shows that implanted preemptive ECMO in 59 of 64 patients who underwent RFCA for unstable VT, while the remaining five patients used salvage ECMO for acute heart failure during the procedure. Procedure was completed without any problem in 92% of the patients, they reported that 88% overall survival was detected in their 21-month follow-up. We implanted preemptive ECMO in 5 of our patients who underwent RFCA. While 4 of our patients were discharged, 1 patient died on the 1st day after the procedure. In conclusion, in high-risk patients, prophylactic implantation of an extracorporeal mechanical device should be considered to reduce the risk of acute heart failure and adverse post-procedure outcomes.

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Evaluation of an e-learning module on extra-corporeal life-support in cardiac arrest for emergency healthcare professionals in a hospital setting

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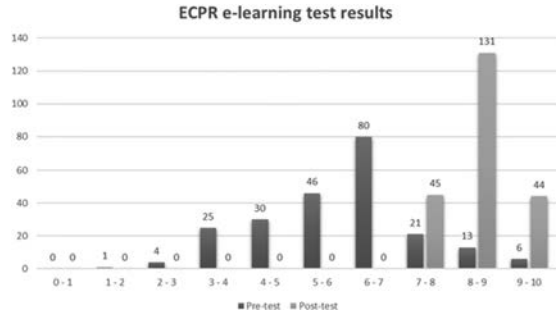
Objectives: ECPR practice for refractory cardiac arrest is increasing worldwide and many hospitals are planning to offer this complex and resource-demanding service. The use of e-learning modules as a method for training healthcare professionals (HCP) has gained increasing attention in recent years due to their flexibility and convenience. In this study, we sought to evaluate the effectiveness of an e-learning module on extra-corporeal cardiopulmonary resuscitation (ECPR) for 260 HCP working in the emergency setting of a hub hospital that is starting an ECPR program.

Methods: The e-learning module consisted of 15 video lessons for a total amount of 8 hours in length. Quizzes supplemented lectures to assess learning progress. The module was designed to be self-paced, allowing participants to complete the course over two months. To evaluate the effectiveness, we administered a

multiple-choice questions test covering the critical concepts taught in the module. Participants compiled a pre-test of 12 questions and post-test of 36 questions, randomly extracted from a larger pool of 70 questions. Each participant had five attempts to pass the final test, with a sufficiency threshold set at 75% of correct answers.

Results: The e-learning module was effective in improving the knowledge of ECPR. For the 220 HCP who participated, the mean scores for the pre-test and the post-test increased from 5.91 (SD 1.48) to 8.49 (SD 0.62) ($p < 0.001$). The mean difference was 2.59, with an SD of 1.53. A final survey to assess course satisfaction showed that 94% of participants considered it effective for consolidating their knowledge of ECPR.



Conclusions: Our study demonstrates that our e-learning module on ECPR improved the knowledge of HCP. The module was well-received and could be a helpful tool for new ECPR programs.

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ECMO supported patient outcome undergoing Trans-catheter Aortic Valve Replacement (TAVR)

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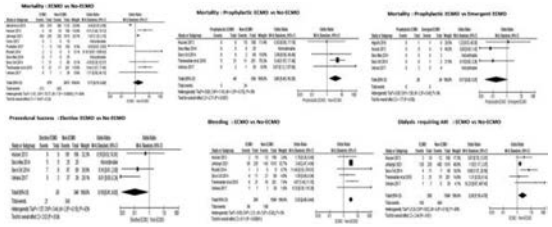
Objectives: To conduct a systemic review and meta-analysis of efficacy and safety of ECMO support during TAVR.

Methods: We conducted a systematic search of various bibliographic databases: PubMed, Embase, Cochrane, Scopus, Science Citation Index and Emerging Sources Citation Index from inception to May 27, 2022 using various relevant search terms and keywords. Studies that included patients 18 years of age and older, who underwent TAVR procedure and in whom ECMO was used emergently or prophylactically were included. Our primary outcomes of interest were patient mortality and procedural success rate. The key secondary outcomes were incidence of peri or postoperative complications including major bleeding, acute renal failure, myocardial infarction, vascular complication, and stroke.

Results: We identified eleven observational cohort studies including total of 2,275 participants (415 ECMO & 1860 non-ECMO). The unadjusted risk of mortality in ECMO supported patient was higher compared to non-ECMO patients (OR 1.73; 95% CI 0.70-4.28 P=0.24, I^2 =90%). In patients with prophylactic ECMO the unadjusted risk of mortality remained high (OR 3.89; 95% CI 1.45-10.39 P=0.007, I^2=0%) and reached statistical significance. Prophylactic ECMO use was associated with lower mortality compared to emergent ECMO use (OR 0.17; 95% CI 0.02-1.21 P=0.08, I^2=0%) but this was not significant. The procedural success rate was found to be lower in ECMO supported patient (OR 0.10; 95% CI 0.01–0.93 P=0.04, I^2=42%). We found significant increased risk of bleeding (OR 3.32; 95% CI 2.48-4.44 P<0.00001, I^2=0%), renal failure (OR 2.38; 95% CI 1.19-4.78 P=0.01, I^2=40%), post-operative myocardial infarction (OR 1.89; 95% CI 1.42-2.53 P<0.0001, I^2=0%) and stroke (OR 2.32; 95% CI 1.14-4.74 P=0.02, I^2=14%) in ECMO patients undergoing TAVR compared to those not on ECMO.



Conclusions: ECMO support in high-risk patients undergoing TAVR is not associated with improved clinical outcomes. Use of prophylactic ECMO has better outcomes than emergent ECMO. Overall, ECMO is associated with higher mortality and post-operative complications. Prophylactic ECMO could be used in selected high-risk cases for better outcomes in TAVR.

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Extracorporeal cardiopulmonary resuscitation – prognostic impact of initial rhythm

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Objectives: Patients (pts) with initial non-shockable rhythm (NSR) remain underrepresented in extracorporeal

cardiopulmonary resuscitation (eCPR) cohorts. We sought to evaluate the impact of rhythm on outcome in an all-comers real-life cohort.

Methods: 301 pts (median age 59 [51-67] years, 79% male gender) consecutively treated with eCPR for refractory cardiac arrest (RCA) from 01/2016 to 05/2022 were retrospectively analysed, stratified by initial findings of shockable rhythm (SR, n=152) or NSR (n=149).

Results: Coronary artery disease (83% vs 59%, p<0.001) and ischemic cardiomyopathy (28% vs 16%, p=0.024) were more prevalent in SR pts. No differences were detected in witness-of-collapse (SR 88% vs NSR 87%, p=0.93) or bystander CPR (SR 89% vs 85%, p=0.37). Mean low-flow time tended to be longer in NSR pts (84±45 min vs SR 74±29 min, p=0.16). Door-to-ECMO timing resembled (SR 15 [13-23] min vs NSR 17 [14-25] min), as did other intraprocedural parameters. Causes for RCA significantly differed (p<0.001): coronary event (SR 79% vs NSR 52%), primary arrhythmogenic event (SR 11% vs 7.8%), cardiogenic shock (SR 4.9% vs NSR 17%), aortic dissection (SR 0.8% vs NSR 5.8%) and pulmonary embolism (SR 2.4% vs 13%). Survival was higher in SR pts (28% vs 13% in NSR, p=0.001). Favourable outcome (cerebral performance category [CPC] ≤2) was higher in SR pts (19% vs 6.9%, p=0.002). Accordingly, NSR was found to be independently predictive of mortality (HR 1.84 [1.01 – 3.33]). Significant interactions for mortality and favourable neurological outcome were found for the application of suprarenine, such that its use significantly worsened prognosis in NSR but not in SR pts.

Conclusions: Despite similar baseline and procedural characteristics, mortality and adverse neurological outcome was significantly higher in pts with initial NSR in this large all-comers cohort. However, rates in NSR pts still remained below those in equivalent conventional CPR cohorts. Focused diagnostic algorithms preceding eCPR might enhance survival in this subgroup.

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Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) and levosimendan in aluminum phosphide-induced cardiogenic shock

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Objectives: Patients with aluminum phosphide-induced severe circulatory and cardiogenic shock represent a major challenge in the absence of specific antidotes. Conventional therapeutic approaches are not always successful with high mortality rates. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support alone provided mortality benefits in limited studies; however, early successful weaning is desirable. Levosimendan efficiently enhances myocardial function facilitating VA-ECMO weaning success. In this study, we describe the efficiency of levosimendan in aluminum phosphide-intoxicated patients receiving VA-ECMO support.

Methods: –

Results: *Case report:* We report three female patients 17, 32, and 15 years old referred to our center from the toxicology department with aluminum phosphide-induced cardiotoxicity and refractory cardiogenic shock after the ingestion of 0.75, 3, and 3 grams of aluminum phosphide, respectively. Given the escalating doses of noradrenaline and adrenaline exceeding 500 nanograms/kg/minute each, depressed ejection fraction below 10% and velocity time integral (VTI) of 2-4 cm, and ventricular arrhythmias, they were connected to VA-ECMO for hemodynamic support. After a failed weaning trial of VA-ECMO within 100, and 102 hours from ingestion, the first 2 patients received levosimendan as an adjuvant therapy, while the third patient received it 60 hours after the ingestion due to persistently depressed cardiac function. They received a loading dose of 6 micrograms/kg over 10 minutes followed by a maintenance dose of 0.1 micrograms/kg/minute. All three patients were weaned successfully 24, 48, and 68 hours after the initiation of levosimendan with a total ECMO run of 164, 138, and 108 hours, respectively. However, the third patient did not make it to ICU discharge and died 24 hours after decannulation due to reperfusion injury and multi-organ failure. None of the patients suffered adverse events attributed to levosimendan.

Conclusions: Levosimendan may represent a potential treatment option for aluminum phosphide toxicity improving contractility and accelerating VA-ECMO weaning. Further studies are still required.

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Nosocomial infections in adult patients undergoing postcardiotomy veno-arterial extracorporeal membrane oxygenation support

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Objectives: Extracorporeal membrane oxygenation (ECMO) is increasingly used in patients with refractory cardiopulmonary failure after cardiac surgery. Although nosocomial infections frequently occur during ECMO therapy, data regarding this complication remain scarce.

Aim of the study was to investigate various aspects of nosocomial infections (NI) in this specific, high-risk patient population.

Methods: We retrospectively analyzed data of 336 consecutive adult patients who received postcardiotomy ECMO therapy longer than 48 hours. The incidence, infection sites and risk factors of NI were identified. Moreover, we assessed the distribution of causative microorganisms and the impact of NI on patients outcomes.

Results: The 336 patients (aged 65.2 ± 15.02 years; 72.1% male) accounted for 366 VA-ECMO-runs with a total of 1781.3 VA-ECMO days. In 96 patients (28%), a total of 216 infections were identified, which counts for 12.1 infections per 100 ECMO days. Most common were infections of the respiratory tract (4.4/100 ECMO days), the bloodstream (2.3/100 ECMO days) and catheter related infections (2.2/100 ECMO days). Pneumonia was most frequently caused by Enterobacteria (26.1%) and Pseudomonas aeruginosa (25.0%), whereas Staphylococci (55.8%) and Klebsiella (19.5%) were the predominant germs in blood samples. NI were associated with a significantly higher risk for developing renal failure and bowel ischemia, but was not accompanied by increased mortality. ECMO support, ICU stay and total length of hospital treatment were significantly prolonged in patients affected by NI. Stepwise logistic regression analysis revealed that duration of ECMO therapy and dialysis were independent risk factors for nosocomial infections.

Conclusions: Patients treated with postcardiotomy ECMO are exposed to very high risk of acquiring NI. Ventilator associated pneumonia and bloodstream infections occured most frequently. Duration of ECMO support and renal replacement therapy were independent risk factors for NI, but NI were not associated with increased mortality.

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Peripheral versus central extracorporeal membrane oxygenation support for postcardiotomy shock

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Objectives: Venoarterial extracorporeal membrane oxygenation (VA-ECMO) application in postcardiotomy shock is increasing. Little is known about the effect of different cannulation strategies on morbidity, weaning success and survival. Therefore, we investigated clinical outcomes of patients supported by centrally and peripheral instituted VA-ECMO after cardiac surgery.

Methods: In our database, 474 patients could be identified who were supported with VA-ECMO after cardiac surgery. The cannulation strategies consisted of peripheral (femoral, axillary) cannulation (231 patients) or central cannulation (243 patients), either performed directly or through a subxiphoidally directed prosthesis connected with the ascending aorta.

Results: The average age of patients with central cannulation was 63±15 years. The peripherally cannulated patients were 64±15 years old. Gender distribution was similar in both goups (cental cannulation: 67.9%; peripheral cannulation: 70.6% male patients). Other demographic data was coparable within the two groups. Within both groups CABG was the predominant type of index surgery (central: 39. % vs peripheral: 31.7%) followed by combined (CABG and valve) procedures (central: 24.4% vs peripheral: 19.8%) and valve surgery (central: 19.6% vs peripheral: 31.7%). The duration of ECMO support did not differ significantly (central: 160±165 hours vs peripheral: 165±140 hours). Hower centrally cannulated patients were more likly to recive ECMO treatment immediately after surgery in the operating room (central: 62.9 % vs peripheral: 32.9 %). Weaning rates (central: 65.6 % vs peripheral: 60.4 %) and in-hospital survival did not differ between the groups (central: 44.2 % vs peripheral: 38.7 %).

Conclusions: Peripheral and central VA-ECMO configurations showed comparable weaning and survival rates. The rate of adverse events was comparable too.

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Outcomes of postcardiotomy venoarterial extracorporeal membrane oxygenation support in elderly patients

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Objectives: The indication for extracorporeal membrane oxygenation (ECMO) therapy in elderly patients is still controversial. The aim of the present study was to assess outcomes of elderly patients requiring VA-ECMO support for postcardiotomy cardiogenic shock.

Methods: Between January 2012 and December 2021 192 patients aged over 70 years underwent open-heart surgery in our department and suffered postoperative cardiogenic shock treated by ECMO implantation. Medical records of these patients were analyzed in retrospective manner to assess postoperative morbidity and mortality in this patient population.

Results: Regarding age patients were divided into three groups. Group 1: Patients older than 80 years (n = 23 patients; mean age 84 ± 2 years; 56.5% male). Group 2: Patients aged between 75 and 79 years (98 patients; mean age 77 ± 1 years; 63.3% male) and Group 3: Patients aged between 70 and 74 years (71 patients (group 3; mean age 72 ± 1 years, 67% male). The percentage of patients who required intraoperative VA-ECMO support immediately after surgery in the operating room was comparable between the groups (65.2%, 42.9%, 49.3%). All other patient received delayed ECMO support within 48 hours postoperatively on the intensive care unit. Mean duration of ECMO support was 118 ± 133 hours in group 1, 136 ± 142 hours in group 2 and 187 ± 174 hours in group 3. ECMO weaning rates in the 3 groups were 60.9%, 53.1% and 56.3% respectively. The percentage of patients discharged alive from hospital was 26.1% in group 1, 32.7% in group 2 and 33.8% in group 3. Regarding the length of ECMO support, the rate of successful ECMO weaning and hospital survival rate, no significant differences were found between the groups. The most frequent complications during ECMO therapy were acute kidney injury, pneumonia bleeding complication and sepsis.

Conclusions: Postcardiotomy ECMO support in elderly patients is associated with excess morbidity and mortality. But given the fact that ECMO therapy represents the last line of therapy for these critically ill patients, this treatment option should be considered also for selected elderly patients.

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The evolving face of ECLS - from ECMO team to ECLS network

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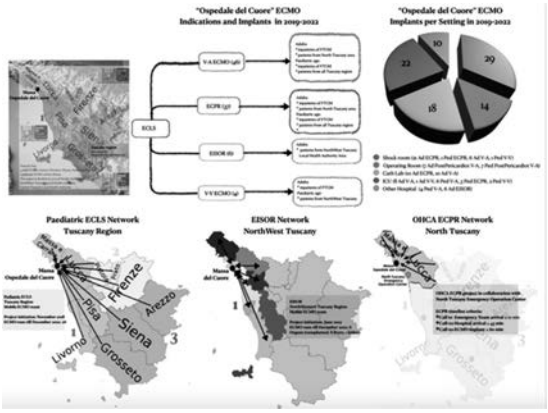
Objectives: From its establishment as rescue therapy in ICU or cardiac surgery operating theatre, ECMO has become a mainstream circulatory or respiratory support and resuscitative treatment. This paper analyzes the ECLS network of Ospedale del Cuore, Fondazione Toscana Gabriele Monasterio (FTGM), and represents all ECMO implants during 2019-2022.

Methods: After the skyrocketing increase in ECMO indications in the last decade, we have initiated regional projects, strengthened collaborations, and created new networks for ECLS implementation:

- Pediatric ECLS network of Tuscany region (end of 2018) - FTGM, University Hospital Meyer of Florence, and the pediatric network of Tuscany
- OHCA ECPR network of North Tuscany (2020) - FTGM and North Tuscany Emergency Operation Center.
- EISOR network of NorthWest Tuscany (2022) - FTGM and NorthWest Tuscany Local Health Authority.

We retrospectively revised the clinical records of 93 patients treated with ECLS support during 2019-2022 and analyzed the implementation settings and network functioning.



Results: During 2019-2022 the FTGM ECMO team implemented 93 ECMO treatments:

- 29 in Shock room (21 adult and 1 pediatric ECPR; 6 adult and 1 pediatric V-V)
- 14 in Operating Room (7 adult and 7 pediatric post-pericardiotomy V-A)
- 20 in Cath Lab (10 adult ECPR and 10 adult V-A)
- 22 in ICU (8 adult and 6 pediatric V-A; 1 adult and 2 pediatric V-V, 5 pediatric ECPR)
- 10 in other hospitals (4 pediatric V-A and 6 adult EISOR)

The mobile ECMO team performed 15 interventions: 9 pediatric ECMO implants and 6 EISOR.

Conclusions: With the expanded indications for ECMO support, creating an ECLS network is fundamental. For quality healthcare service delivery, a well-trained ECMO team is but one link in the chain of a good-functioning ECLS network.

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Evolution of left ventricle ejection fraction after the treatment of out-of-hospital cardiac arrest with extracorporeal cardiopulmonary resuscitation

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Objectives: Out-of-hospital cardiac arrest (OHCA) is a major public health issue for which extracorporeal cardiopulmonary resuscitation (ECPR) has become a second-line of treatment after the failure of conventional CPR. Yet, the short- and mid-term evolution of myocardial function in patients resuscitated with ECPR after acute coronary syndrome (ACS) remains unknown.

Methods: We conducted a retrospective observational study of patients admitted to a tertiary care university hospital in Paris, France. We reviewed patients admitted between January 1, 2015 and October 31, 2019 and treated with ECPR after a refractory OHCA following ACS. The objective of this study was to evaluate the evolution of left ventricle ejection fraction (LVEF) at 28 and 90 days after OHCA, as well as neurological outcomes. Survival with good neurological outcomes was defined as Cerebral Performance Category 1 or 2 (CPC 1 or 2) at 28 and 90 days.

Results: A total of 92 patients were included in the study. Cardiac ultrasound data at 28 days were available for 31/33 (94%) of surviving patients, and the median LVEF was 38% (30-50). Ultrasound data at 90 days were available for 24/27 (89%) of surviving patients and the median LVEF was 45% (37-50). LVEF improvement greater than 5% between 28 and 90 days was observed in 4/27 (15%) patients, LVEF worsening greater than 5% in 3/27 (11%), and similar LVEF at 28 and 90 in 20/27 patients (74%). Survival at 28 and 90 days was 33/92 (36%) and 27/92 (29%) respectively, whereas survival with good neurological outcomes at 28 and 90 days was 16/92 (19%) and 19/92 (21%) respectively.

Conclusions: Patients treated with ECPR following OHCA due to ACS had persistent myocardial dysfunction at 90 days and little or no LVEF recovery. Some patients had an early decline in LVEF. In any case, specialized care pathways should be developed for short-term follow-up of these specific patients in order to detect early complications related to left ventricular dysfunction and to promote early cardiological and neurological rehabilitation.

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Weaning attempt from VA-ECMO: echocardiographic parameters of contractile reserve

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Objectives: To analyse dynamic echocardiographic behaviour during scheduled weaning protocol from VA-ECMO between successfull and unsuccessfull weaning cohorts.

Methods: We designed a retrospective observational single-centre study from January 2019 to December 2022.

Clamping parameters	Successfully weaned (n = 28)	Not weaned (n = 3)		Net change from baseline	Successfully weaned (n = 28)	Not weaned (n = 3)	
LVEDD (mm)	45,9 ± 10,7	50,7 ± 10,2	NS	LVEDD (mm)	-1,3 ± 4,1	0,5 ± 2,1	NS
LVOT VTI (cm)	14,1 ± 3,3	13,2 ± 0,3	NS	LVOT VTI (cm)	2,9 ± 2,3	3,5 ± 2,6	NS
LVEF (%)	39,4 ± 13,2	25,0 ± 14,1	NS	LVEF (%)	5,7 ± 5,8	4,0 ± 5,3	NS
s'_mDTI (cm/s)	8,7 ± 3,1	7,7 ± 2,5	NS	s'_mDTI (cm/s)	2,1 ± 2,0	0,2 ± 1,1	NS
AV OT (ms)	218,0 ± 34,0	186,0 ± 22,6	NS	AV OT (ms)	9,4 ± 25,7	- 25,0 ± 7,1	NS
TAPSE (mm)	15,7 ± 5,2	14,7 ± 2,5	NS	TAPSE (mm)	1,5 ± 3,4	-2,2 ± 1,8	NS
s'_tDTI (cm/s)	11,7 ± 3,7	13,7 ± 1,1	NS	s'_tDTI (cm/s)	1,2 ± 2,7	-2,0 ± 4,2	NS

LVEDD: left ventricular end-diastolic diameter, LVOT VTI: left ventricular outflow tract velocity time integral, LVEF: left ventricular ejection fraction, s'_m TDI: mitral annulus systolic Doppler tissue imaging, AV OT: aortic valve opening time, TAPSE: tricuspid annular plane systolic excursion, s'_t TDI: tricuspid annulus systolic Doppler tissue imaging. Regarding our results, echocardiographic static measurements do not seem to be accurate weaning predictors from VA-ECMO support. 3/3 (100%) of unsuccessfully weaned patients had LVOT VTI > 10 cm, 2/3 (67%) s'_m VTI > 6 cm/s and 2/3 (67%) LVEF > 25%.Even though small sample size does not allow to detect differences, there is a clear net increase in s'_m DTI which was ten times higher in the weaned cohort. Nevertheless there were not marked differences in LVOT VTI nor LVEF net changes between groups. Net improve in AV OT and right ventricular parameters while reduction in support could have a role in predicting weaning success.

Results: A total of 31 patients were amenable to a weaning attempt after VA-ECMO support. Echocardiography measurements were perfomed at baseline and after 0.5 L gradually flow decreased until clamping. Clamping echocardiographic variables and dynamic changes with flow decrease are included in table 1.

Conclusions: Dynamic evaluation of echocardiographic parameters could be of help to decide whether or not to wean form VA-ECMO support.

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Use of ECMO as a bridge to recovery in acute post-operative cardiac failure in a patient suspected with Libman-Sacks endocarditis

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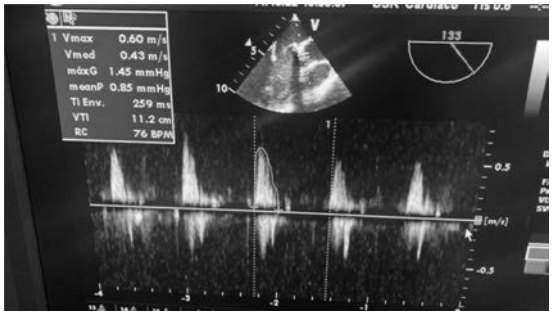
Objectives: Make a bibliographic review on the use of a circulatory support system in acute post-surgical failure in association with the complications of the underlying rheumatological diagnoses of our patient.

Methods: A medical-surgical case presentation was made with a 6-month follow-up with a review of the updated bibliography

Results: A 32-year-old female patient presented with a left parieto-occipital ischemic cerebrovascular event 6 months prior to surgery, study protocol was initiated for probable systemic lupus erythematosus. She was referred to cardiology due to an echocardiogram finding of a tumor in the posterior leaflet of the mitral valve that caused regurgitation, Libman-Sacks endocarditis was suspected. It is presented in a Heart Team session where surgical treatment is decided as the first option, plasty and wedge resection vs. mitral valve replacement. Surgery was performed without complications requiring mitral valve replacement with a biological prosthesis with the discovery of a tumor that invaded the entire posterior leaflet with a pump time of 92 minutes. Torpid immediate post-surgical evolution with acute heart failure, it was decided by the Heart Team to place VA ECMO as a bridge to recovery, which presented an improvement in parameters that was a candidate for weaning; presents FEVI improved from 20 to 35% and on the eighth day it is removed During his post-surgical period, she evolved with multiple thromboembolic events at different levels, finally reaching the diagnosis of Lupus and Antiphospholipid Antibody Syndrome.



Conclusions: A total of 73,000 ECMO procedures were recorded by the ELSO and greater than 25% were performed in adult patients. From 2006 to 2011, adult ECMO volumes increased greater than four times. ECMO is a viable rescue strategy for cardiac surgery patients with a 40% survival to discharge rate.

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Novel cannulation strategy with a bidirectional cannula for optimizing distal limb perfusion during peripheral veno-arterial extracorporeal membrane oxygenation: A preliminary, single-centre experience

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Objectives: Limb ischemia is an impactful complication of peripheral veno-arterial extracorporeal membrane oxygenation (V-A ECMO). Several techniques have been developed to prevent this adverse event, but it remains a major complication. In 2019, a new cannula with bidirectional flow (antegrade and retrograde towards the distal limb) has been introduced. A single-centre experience with this cannula in patients undergoing peripheral V-A ECMO is herewith reported.

Methods: This prospective observational study included adults (≥ 18 years) undergoing V-A ECMO from January 2021 to October 2022 with the use of a bidirectional femoral artery cannula. Primary outcome was limb ischemia requiring intervention. Secondary outcome

measures were: compartment syndrome, limb amputation, cannulation site bleeding, need for other surgical intervention due to cannula related complications, duplex ultrasound parameters from the femoral vessels, and mortality during hospital stay.

Results: Twenty-two patients were included. During ECMO support, limb ischemia requiring intervention occurred in one (4.5%) patient, while no patients developed a compartment syndrome, or required a fasciotomy or amputation. Significant bleeding was reported in two (9%) patients due to slight cannula dislodgement, easily solved with cannula repositioning. In-hospital survival was 45.5% (10 patients), and 4 patients still remain in the ICU, with successful ECMO weaning, at the moment of the abstract submission.

Conclusions: The bidirectional cannula is associated with a low risk for limb ischemia (related) complications, comparing to literature, and represents a safe alternative to dedicated distal perfusion cannula. Further studies are warranted to confirm these preliminary findings.

Conflict of interest: RL: Member of the Advisory Board for Eurosets and Fresenius, Consultant for Medtronic, LivaNova, CORCYM, Abiomed, Grant for research from Medtronic.

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Heparin monitoring during Impella^{TM}-support for cardiogenic shock: The benefit of parallel testing

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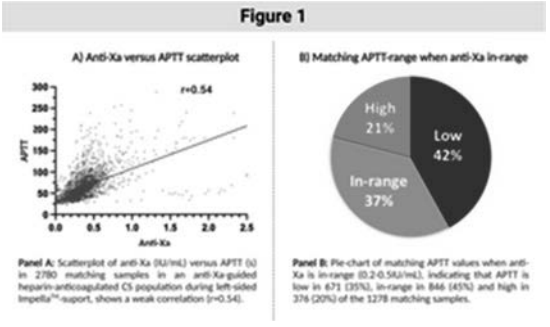
Objectives: Strict monitoring of unfractionated heparin (UFH) therapy is important to avoid complications during percutaneous ventricular assist device (pVAD)-support. Most frequently used is the APTT, though various confounding factors during critical illness affect it. Alternatively, the anti-Xa assay directly measures UFH-activity. Recently, an anti-Xa-guided protocol for UFH titration with parallel APTT measurements in pVAD-supported cardiogenic shock (CS) patients has been proposed. Here, we aim to investigate the correlation between parallel anti-Xa and APTT measurements in this setting.

Methods: Between April-2017 and June-2022, all CS patients with isolated left-sided Impella^{TM}-support (>24h) and UFH anticoagulation monitored by anti-Xa with APTT in parallel were assessed at two high-volume tertiary institutions. Anti-Xa was considered in-range between 0.2-0.3IU/mL or 0.3-0.5IU/mL based on the patient's profile. In-range APTT values were considered 40-60s and 60-80s respectively. Correlation between anti-Xa and APTT was assessed by a Pearson correlation model.

Results: Ninety-six Impella^{TM}-patients (79% men) with a median age of 55 (IQR 46-65) were included. Median support was 6 days (IQR 4-12). In a total of 2780 parallel samples, the overall Pearson correlation coefficient was 0.54 (Figure 1A). For samples with anti-Xa in range (0.2-0.3IU/mL or 0.3-0.5IU/mL) (N=1287), matching APPT was low in 540 (42%), in range in 478 (37%) and high in 269 (21%) samples (Figure 1B).



Conclusions: We highlight a weak correlation between anti-Xa and APTT in an anti-Xa-guided UFH-anticoagulated critical ill CS population during left-sided Impella^{TM}-support. UFH titration based on APTT alone would result in under- (21%) or overtitration (42%) in 63% of our cases, due to confounding factors influencing the APTT-assay in critically ill. Therefore, we strongly advocate a parallel anti-Xa/APTT anticoagulation monitoring strategy in this patient population.

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ECMO in drug intoxication. A nationwide retrospective study

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Objectives: This study aimed to analyse the utilisation of extracorporeal membrane oxygenation (ECMO) for patients experiencing cardiac failure, pulmonary failure or both due to drug intoxication. Furthermore, the aim

was to examine the hospital mortality of ECMO treatment and their predictive factors.

Methods: This study is based on inpatient data from every hospitalisations in Germany from 2005 to 2020. The data was provided by the Federal Statistical Office of Germany. To include patient stays due to intoxication and analyse these data, the international classification of diseases' codes and procedure keys were used. Intoxication from antiepileptic drugs (T42.3, T42.4), psychotropic substances (T43.0, T43.1, T43.3, T43.4), medication with effect primarily on the autonomic nervous system (T44.-) and primarily on the cardiovascular system (T46.0-T46.5, T46.7) were considered.

Results: 112 patients were hospitalised due to intoxication and treated with ECMO. 41.96% (n=47) patients received VV-ECMO and 58.04% (n=65) received VA-ECMO treatment. Mortality was 45.54% (n=51) overall, 40.43% (n=19) in the VV-ECMO group and 49.23% (n=32) in the VA-ECMO group. The median age was 48 (31.0-58.5) years. Increased mortality was associated with in-hospital resuscitation (OR: 9.75, 95% CI:3.70-25.70) and dialysis requirement (OR: 5.48, 95% CI:2.06-14.54). Age, as well as the ECMO mode (VV- or VA-ECMO) were not found to have a significant impact on mortality.

Conclusions: This is the first nationwide study on intoxicated patients receiving ECMO treatment. Data from intoxication studies require special attention to patient and substance characteristics and therefore careful interpretation. Although comparison with previous studies is difficult due to varying inclusion criteria, we found similar survival rates for the chosen substance classes. In this study, ECMO mode did not significantly impact mortality. Further research is needed to clarify the indications of ECMO treatment for different types of poisoning.

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Italian prehospital ECMO system: A national survey

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Objectives: The chain of survival represents the prehospital management of cardiac arrest. Early recognition of cardiac arrest, early cardiopulmonary resuscitation (CPR) and defibrillation have a great impact on early survival. In refractory cardiac arrest, advanced life support is performed to restore spontaneous circulation and extracorporeal life support can be provided with ECMO in selected patients. ELSO published guidelines of extracorporeal life support (ECLS) in which the inclusion criteria of ECLS in out-of-hospital cardiac arrest are age < 70 years old, witnessed arrest, no flow time < 5 minutes, initial cardiac rhythm as VF, VT, PEA, with a low flow time < 60 minutes and EtCO2 > 10 mmHg during CPR. Major comorbidities as tumoral illness, or cardiac, renal, liver end-staged diseases are contraindications to V-A ECMO. Globally, refractory cardiac arrest management is different: in France, ECLS is performed out-of-hospital, with reduction of low flow time transport related, while in Italy ECLS is performed in hub centers. In some regions a patient is eligible to ECPR directly from prehospital system, in others when the patient is in the emergency department.

Methods: A survey was conducted to analyze the national perspective of emergency medical service (EMS), analyzing regional EMS systems and regional reference legislation. All regional legislation was analyzed searching keywords as "ECMO" or "Prehospital cardiac arrest" OR "refractory cardiac arrest"

Results: From national survey, Italian EMS system are not homogeneous in OHCA management destinated to ECPR. The local legislation is different between 21 regions, with local protocol in some cases, in other there is no legislation. In relation to legislation, there is no national consensus on prehospital management of a patient who can be a candidate to ECMO.

Conclusions: Prehospital cardiac arrest has different treatment in relation to patient, to geographical setting, to EMS system, in relation to hospital resources. The Italian EMS system are not homogeneous, but it's different between regions. A major guidelines diffusion could improve an ECMO resource in selected patient affected by OHCA.

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The ProtekDuo as drainage cannula in venopulmonary-arterial (VP-A) ECMO configuration for circulatory shock

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Objectives: The ProtekDuo is a percutaneously, via right internal jugular vein inserted dual lumen cannula, that if connected to a pump, works as right ventricular assist device (RVAD) by draining blood from the right atrium (RA), and returning blood into the pulmonary artery (P), thereby bypassing the right ventricle (RV). When an oxygenator is added to the circuit, it may be used for venovenous (V-V) extracorporeal membrane oxygenation

(ECMO). Since the cannulas tip terminates in the P, this configuration is called venopulmonary (V-P) ECMO.

Methods: We describe a case study in which a patient with ProtekDuo and oxygenator is used in conjunction with an Impella CP (PROpella configuration) in acute biventricular failure with cardiogenic shock. The patient required reconfiguration to venopulmonary-arterial (VP-A) ECMO, secondary to leg ischemia and the need to remove the Impella CP. The ProtekDuo was subsequently used as double lumen drainage cannula, returning blood into a newly, percutaneously placed femoral arterial cannula, mimicking venoarterial (V-A) ECMO in VP-A configuration. The following day, an Impella 5.5 could be placed, the arterial cannula was removed, and the ProtekDuo was reconfigured back to its default V-P ECMO configuration with minimally invasive biventricular groin-free full mechanical circulatory support.

Results: While in VP-A ECMO configuration, good drainage blood flows of up to 4.5 LPM with around 4,000 RPM could be achieved, identical with the normal ProtekDuo forward flow when used as RVAD. None of the lumens collapsed secondary to negative pressure in the system. Keeping the ProtekDuo in situ allowed drainage without the need to place another drainage cannula, reducing procedural risk, and allowed to reconfigure back to use it as RVAD, once V-A ECMO was no longer needed and replaced by the Impella 5.5.

Conclusions: Drainage through both lumen of the ProtekDuo for VP-A ECMO is feasible and in our case without complications for a 24h period. This new method extends the ProtekDuo's spectrum and underlines its potential use as drainage cannula in various settings like on cardiopulmonary bypass for heart or lung transplantation.

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Selection of patients for extra corporeal cardiopulmonary resuscitation (ECPR) – a multivariate prediction model for good neurological outcome

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Objectives: In cardiac arrest (CA)-patients where cardiopulmonary resuscitation (CPR) is instituted early and gives enough blood circulation, the brain function will be preserved and ECPR might give a favourable neurological outcome. However, if the circulation is insufficient during CPR, ECPR will only prolong futile care at high cost. Despite that, data on optimal patient selection for ECPR is missing.

Methods: All 120 normothermic cardiac arrest patients, where extracorporeal membrane oxygenation (ECMO) was instituted during ongoing CPR, from 2010 to 2021 at Sahlgrenska University Hospital were included in the ECPR study. From 2016 and onwards CA characteristics and metabolic, circulatory, and neurological predictors were documented prospectively at the decision point of ECPR by the cardiothoracic anaesthesiologist at scene. After univariate analysis, predictors were analyzed by multivariate logistic regression with backward elimination. Multiple imputation (m=100) for missing values. Results were pooled according to Rubin rules.

Results: 33 of the 120 patients survived with a good neurological outcome outcome (Modified Rankin Scale 0-2) after 1 year. The final multivariate model with age, initial rhythm, no-flow time, CA-time, moving or breathing, pupil diameter, INVOS® regional cerebral oxygen saturation, end tidal CO_2 and arterial pH could predict good outcome with an AUC of 0.87. In 5-fold internal cross validation of the datasets, pooled-AUC for test-data was 0.82. The full multimodal model was significantly better in all datasets than the single mode models.

	All patients		Cross validation, test data	
	AUC (95% CI)	R2	AUC (95% CI)	R2
Full model	0.87 (0.78-0.93)	0.48	0.82 (0.71-0.90)	0.40
CA characteristic (age + rhythm + no-flow time + CA-time)	0.75 (0.65-0.83)	0.23	0.68 (0.58-0.77)	0.20
Metabolic (pHa + S-lactate)	0.60 (0.49-0.71)	0.05	0.51 (0.40-0.62)	0.01
Neurology (moving + breathing + pupil diameter)	0.74 (0.64-0.83)	0.26	0.69 (0.57-0.78)	0.27
CA circulation (end tidal CO_2 + INVOS®)	0.73 (0.58-0.84)	0.19	0.69 (0.53-0.82)	0.19

Conclusions: A rapid multimodal evaluation of easily accessible predictors during cardiac arrest can predict outcome in ECPR treatment.

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Patient and management variables associated to survival after post-cardiotomy extracorporeal membrane oxygenation in adults: The PELS-1 multi-centre cohort study

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Objectives: Extracorporeal membrane oxygenation (ECMO) for post-cardiotomy cardiogenic shock has been increasingly used without concomitant mortality reduction and poorly investigated long-term results according to available data. This study describes patients´ characteristics, in-hospital outcome, and 10-year survival after post-cardiotomy ECMO. Determinants for in-hospital and post-discharge mortality are investigated and reported.

Methods: The retrospective international multi-centre observational Post-cardiotomy Extra-Corporeal Life Support Study (PELS-1) includes data on adults requiring ECMO for post-cardiotomy cardiogenic shock between 2000 and 2020 from 34 centres. Variables associated with mortality were estimated preoperatively, intraoperatively, during ECMO, and after the occurrence of any complications, then analysed at different time points during a patient's clinical course, through mixed-Cox proportional hazards models containing fixed and random effects. Follow-up was established by institutional chart review or contacting patients.

Results: This analysis included 2058 patients (males: 59%) with a median age of 65.0 years (IQR:55.0-72.0). In-hospital mortality was 60.5%. Independent variables associated with in-hospital mortality were age (HR: 1.02, 95%CI:1.01-1.02), and preoperative cardiac arrest (HR:1.34, 95%CI: 1.08-1.66). In the sub-group of hospital survivors, the overall 1-year, 2-year, 5-year and 10-year survival were 89.5% (95%CI: 87.0-92.0), 85.4% (95%CI: 82.5-88.3), 76.4% (95%CI: 72.5-80.5), and 65.9% (95%CI: 60.3-72.0), respectively. Variables associated with post-discharge mortality included older age (HR:1.03, 95%CI: 1.02-1.05), atrial fibrillation (HR:1.45, 95%CI: 1.01-2.11), emergency surgery (HR: 1.68, 95%CI: 1.04-2.70), aortic valve surgery (HR:1.41, 95%CI: 1.07-2.24), postoperative acute kidney injury (HR:1.37, 95%CI: 1.01-1.95) and septic shock (HR: 2.59, 95%CI: 1.45-4.63).

Conclusions: In adults, in-hospital mortality after post-cardiotomy ECMO remains high, however two thirds of those who get discharged from hospital survive up to 10 years. Patient selection, intraoperative decisions, and ECMO management remain key determinants of survival in this cohort.

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Stellate Ganglion Block (SGB) with continuous infusion for management of electrical storm under Mechanical Cardiac Support (MCS)

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Objectives: •Review anatomy, side effects and complications related to SGB via peripheral nerve catheter

- Demonstrate proper technique of ultrasound guided stellate ganglion block in treating electrical storm
- Elucidate the advantages of a continuous bupivacaine infusion via a peripheral nerve catheter over a single injection SGB on the treatment of electrical storm in patients with MCS.

Methods: A 60-year-old gentleman with coronary artery disease suffered a non-ST-segment elevation myocardial infarction complicated by ventricular tachycardia and cardiogenic shock with cardiac arrest during angiography. The patient was initiated on emergent pVA ECMO with Impella CP and underwent revascularization with drug eluting stents to the RCA, LAD and ramus intermedius. Mechanical support was subsequently reconfigured to an Impella 5.5 and percutaneous RVAD. Unfortunately, despite optimization of hemodynamics with MCS, normalization of electrolytes, deep sedation, avoidance of catecholamine vasopressors, and aggressive anti-arrhythmic therapy, recurrent multifocal ventricular arrythmias persisted requiring repeated defibrillation. The patient was responsive to SBG blocks which were repeated seven times throughout his hospitalization. A peripheral nerve catheter was eventually placed to deliver a continuous infusion of local anesthetic (5cc/hr of 0.2% bupivacaine). This led to electrical quiescence of ventricular arrythmias off sedation for one week. Unfortunately, lack of meaningful neurological recovery in the setting of an embolic stroke led to transition to comfort care measures and withdrawal of support.

Results: Stellate ganglion blockade reduces the number of VT episodes and a 10-fold reduction in need defibrillation, but its effects typically last less than 12 hours. Placement of an ultrasound guided peripheral nerve catheter allows for a longer therapeutic effect and ability to promptly block the stellate ganglion without the associated repeated periprocedural complications.

Conclusions: Electrical storm is accompanied by a sympathetic surge making ventricular arrhythmias resistant to antiarrhythmic drugs. SGB continuous infusions should be considered as a viable and attractive adjunct in the management of VT storm while under mechanical cardiac support.

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The role of intraoperative hemoadsorption in cardiopulmonary unstable patients undergoing left ventricular assist device implantation

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Objectives: Left ventricular assist device implantation (LVAD) in preoperative ventilated or vasopressor supported patients is associated with increased morbidity and mortality due to postoperative vasoplegia. Preoperative hemodynamic or respiratory stabilization is not always feasible. The aim of this study was to evaluate the role of intraoperative hemoadsorption on the incidence of postoperative vasoplegia and short-term mortality in such patients.

Methods: Eligible candidates for this retrospective analysis were patients on invasive mechanical ventilation or vasopressor support (norepinephrine ≥0.05 µg/kg/min) undergoing LVAD implantation between December 2010 and December 2022. Patients were assigned to either the hemoadsorption or control group, according to application of intraoperative hemoadsorption. The primary endpoints were incidence of vasoplegia and 30-day mortality. Vasoplegia was defined as the need for norepinephrine 0.2µg/kg/min for at least 12 hours and absence of clinically relevant bleeding starting within the first 72 hours postoperatively.

Results: 75 hemodynamic or respiratory unstable patients underwent LVAD implantation. 40 patients received intraoperative hemoadsorption and 35 patients were operated on without intraoperative hemoadsorption. Baseline demographics and clinical status were comparable between both groups. The incidence of vasoplegia was 35% versus 57% (p=0.055) in the hemoadsorption group and control group, respectively. Mortality at thirty days was 23% versus 40% (p=0.101) in the hemoadsorption and control group, respectively.

Conclusions: Intraoperative hemoadsorption in cardiopulmonary unstable patients undergoing LVAD implantation seems to reduce the risk of postoperative vasoplegia and short-term mortality. These findings should be confirmed in larger cohorts.

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Bilateral femoral cannulation ss associated with reduced severe limb ischemia-related complications compared to unilateral femoral cannulation in adult peripheral V-A ECMO

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Objectives: Peripheral veno-arterial extracorporeal membrane oxygenation (V-A ECMO) is obtained through uni- or bilateral femoral cannulation. Whether one cannulation strategy is associated with a lower risk for limb-ischemia remains unknown. We aim to study if one strategy is preferable.

Methods: This retrospective cohort study included adult patients (≥18 years) who received peripheral V-A ECMO and were included in the Extracorporeal Life Support Organization Registry from 2014 through 2020. The primary outcome was the occurrence of limb ischemia, defined as a composite endpoint including the need for a distal perfusion cannula after six hours from implantation, compartment syndrome/fasciotomy, amputation, revascularization, and thrombectomy. Secondary endpoints included bleeding at the peripheral cannulation site, need for vessel repair, vessel repair after decannulation, and in-hospital death. Propensity score matching was performed to account for confounders.

Results: 19,093 patients underwent peripheral V-A ECMO through unilateral (n=11,965) or bilateral (n=7,128) femoral cannulation. Limb ischemia requiring any intervention was not different between both groups (bilateral vs. unilateral: OR 0.92, 95%CI 0.82-1.02); however, there was a lower rate of compartment syndrome/fasciotomy in the bilateral group (bilateral vs. unilateral: OR 0.80, 95%CI 0.66-0.97). Bilateral cannulation was also associated with lower odds of cannulation site bleeding (bilateral vs. unilateral: OR 0.87, 95%CI 0.76-0.99), vessel repair (bilateral vs. unilateral: OR 0.55, 95%CI 0.38-0.79), and in-hospital mortality (bilateral vs. unilateral: OR 0.85, 95%CI 0.81-0.91) compared to unilateral cannulation. These findings were unchanged after propensity matching.

Conclusions: Bilateral femoral cannulation is associated with fewer compartment syndrome/fasciotomy and lower in-hospital mortality compared to unilateral femoral cannulation and could become an important preventive measure for limb ischemia during peripheral V-A ECMO.

Conflict of interest: DB: Receives research support from ALung Technologies. He has been on the medical advisory boards for Abiomed, Xenios, Medtronic, and Cellenkos. He is the President-elect of the Extracorporeal Life Support Organization (ELSO) FST: Scientific Advisor for EUROSETS and XENIOS MB: Advisor for Eurosets srl (MO) Italy MLB: Member of the Medical Advisory Boards of Eurosets Srl., Medolla, Italy, and Xenios AG, Heilbronn, Germany, unrelated to this work DW: Proctor/consultant for Abbott, Scientific Advisor for Xenios/Fresenius RPB: ELSO Registry chair and reports grants from the US National Institutes of Health (R01 HL153519, R01 HD015434, and K12 HL138039) RL: Member of the Advisory Board for Eurosets and Fresenius, Consultant for Medtronic, LivaNova, CORCYM, Abiomed, Grant for research from Medtronic All other authors: Nothing to declare.

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Improving the quality of care for patients presenting in cardiogenic shock with acute coronary syndrome to a heart attack centre. A single centre experience

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Objectives: Patients treated with venoarterial ECMO (VA-ECMO) for cardiogenic shock (CS) complicating

acute coronary syndrome (ACS) were identified as a group with poor outcomes in our institution. We aimed to use quality improvement methodology to better understand this cohort and make systemic changes with the hope of improving survival.

Methods: Case files were reviewed for all patients treated with ECMO in 2018 within our hospital. All patients who presented directly to the cardiac catheter laboratory (cathlab) with ACS were identified and their clinical course analysed. A common theme was identified: non-survivors had late identification of CS, late admission to the intensive care unit and late use of VA-ECMO once severe end organ dysfunction had already developed. A multidisciplinary working group was established between key stake holders from intensive care and interventional cardiology to create a standardised approach for identification and management of cardiogenic shock in the cath lab. A hospital wide "shock call" was created which rapidly deploys a multidisciplinary team (MDT) 24 hours a day 7 days week. This team is comprised of senior practitioners specialised in cardiac, critical care, cardiac surgical and percutaneous mechanical circulatory support (MCS). Cardiogenic shock guidelines were created to support decision making, prioritising early identification of shock, shock team activation, early MCS and prompt admission of patient to a higher acuity setting.

Results: In 2018, 53 patients were treated with VAECMO in our institution, 34% (18/53) of these were for CS complicating ACS presenting directly to the cathlab. 11% (2/18) survived to hospital discharge. All patients had a delay of >12hours before initiation of VAECMO. In 2022, 43 patient were treated with VA-ECMO of which 7% (3/43) presented with ACS. VA-ECMO was initiated immediately all cases and 66% (2/3) survived to hospital discharge.

Conclusions: In our hospital early identification of patient with CS complicating ACS and rapid deployment of a shock team is feasible and resulted in reduced use of VA-ECMO and a higher proportion of survivors.

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One year ECPR results in a high volume ECMO center

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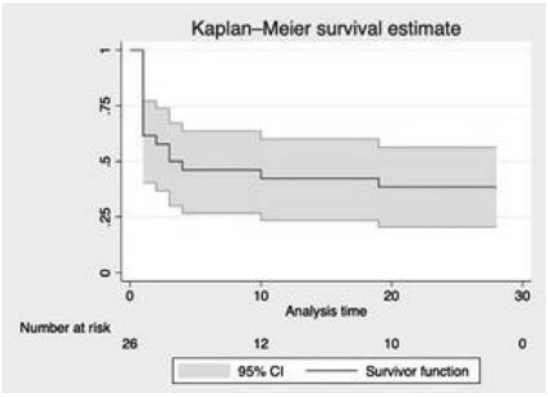
Objectives: To evaluate one-year results of an extracorporeal cardiopulmonary resuscitation (ECPR) program in a high volume ECMO centre.

Methods: Single-centre observational retrospective analysis of all patients requiring ECPR during the year 2022 for in and out of hospital cardiac arrest (IHCA and OHCA) with a follow up of 28 days. Data were obtained from clinical records. Variables were described using value and percentage, mean and standard deviation (SD) or median and interquartile range (IQR). Chi2 test, Fisher's exact test,Mann-Whitney's U Test and Student's T Test were used for comparisons. Survival was evaluated using Kaplan Meier estimator.

Results: During the study period ECPR was indicated in 26 patients. Mean age was 48.7 (SD 13.8) years and 20 (76.9%) were male. Twelve suffered

	All(n= 26)	Non-survivors(N=16)	Survivors(n=10)	p-value
Cardiovascular risk factors, n, %	16 (61.5%)	10 (62.5%)	6 (50%)	0.609
Initial rhythm (shockable), n, %	13 (50%)	7 (43.8%)	6 (60%)	0.402
No flow time (min), mean, SD	4 (13.9)	6.7 (17.7)	0	0.239
Low flow time (min), median, IQR	56 (30-66)	60 (34-85)	42.5 (29-61)	0.202
Cannulation time (min), median, IQR	15 (11-19)	14 (11-19)	15 (12-19.5)	0.946
pH pre ECMO, mean, IQR	6.9 (6.8-7.01)	6.9 (6.8-6.94)	6.9 (6.9-7.1)	0.420
Lactate pre ECMO (mmol/L), mean, SD	12 (5.9)	11.5 (6.7)	12.6 (5.4)	0.709
ECMO duration (days), median, IQR	2 (1-4)	1 (1-2.5)	2.5 (2-8)	0.007
Hospital length of stay (days), median, IQR	10.5 (1-15)	2.5 (1-7.5)	20.5 (12-43)	<0.001

OHCA and 14 IHCA. Details about comorbidities, cardiac arrest characteristics and ECMO cannulation can be seen in Table 1. Ten (38.5%) patients survived to 28 day follow up, all with cerebral performance category 1-2 and 2 (7.7%) patients became donors. Figure 1 shows Kaplan-Meier estimator.



Conclusions: Survival with good neurological outcomes after prolonged ECPR is possible when performed by experienced teams.

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Results of the beginning of an ECMO program in Latin America

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Objectives: The first case in our institution was carried out in 2019, and 5 subsequent cases followed until November 2022.-Describe the first cases of a recently established ECMO program in Mexico. -Describe the characteristics of the cases and the evolution of the program, from the beginning until now.

Methods: A retrospective descriptive single-center study on patients with ECMO. Medical records of 6 patients who presented from October 2019 to November 2022 were reviewed.

Results:

Patient characteristics	
	All patients (n=6)
Age in years, median (IQR)	56 (38-75)
Male, n (%)	2 (33%)
Peripheral ECMO AV, n (%)	6 (100%)
Mode of circuit, n (%)	
Jugulo-femoral	3 (50%)
Femoro-femoral	3 (50%)
Indication of ECMO, n (%)	
Cardiogenic shock + mitral valve replacement	2 (33%)
Cardiogenic shock + aortic valve replacement + CABG	1 (17%)
Failure weaning from CBP	2 (33%)
Cardiogenic shock + septal rupture post-AMI	1 (17%)
Place to start ECMO, n (%)	
OR	5 (83%)
ICU	1 (17%)
LV venting, n (%)	
IABP	3 (50%)
Survival, n (%)	
Wean off ECMO	5 (83%)
To hospital discharge	1 (17%)
28-day survival	1 (17%)
Duration of ECMO (days)	6.6 (3-9)
Lenght of ICU stay	17.3 (3-42)
Complications, n (%)	
Bleeding	3 (50%)
AKI	2 (33%)
Stroke	1 (17%)
Limb ischemia	3 (50%)
Cause of death, n (%)	
Lethal arrythmia	3 (60%)
Septic shock	2 (40%)

All patients were cannulated with peripheral AV ECMO, and different configurations were used, jugular-femoral and femoral-femoral. The main indication was a post-cardiotomy cardiogenic shock, the main difference was the time of presentation from pump output failure until hours later in the ICU. 83% were placed in OR, and only 17% were placed in ICU. In 5 patients it was possible weaning ECMO however, only one patient survived 28 days. The main complications were bleeding and lower limb ischemia. In all patients, a perfusion bridge was placed distal to the arterial cannulation site; however, we did not have a continuous monitoring system, which could have contributed to 50% of ischemic complications. The last case was handled with more organized management, action protocols and responsibilities by service began to be established, which translates directly into a positive result with the patient.

Conclusions: In Latin America, where human and economic resources are restricted, it is possible to establish an ECMO program, however, it is not easy. The

establishment of a work protocol is needed, which is adjusted to the specific needs of the staff and the center. The ELSO has specific recommendations: at least one ECMO physician, training of ECMO specialists, patient selection, and continuing education. Teamwork is essential to obtain good results.

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From out-of-hospital cardiac arrest to ECMO: Lombardy AREU emergency medical service management protocol

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Objectives: Extracorporeal cardiopulmonary resuscitation (ECPR) is an advanced method over classical advanced life support (ALS). ECMO is applicable in selected patients, according to ELSO 2021 ECPR guidelines, in ECMO centers. In Lumbardy Emergency Medical Service (EMS) System, OHCAs candidates to ECLS are performed in selected ECMO Centers, defined by a regional legislation. The EMS System is responsible of prehospital cardiac arrest management

Methods: The out-of-hospital cardiac arrest is managed by a technician, the first responder. He manages the emergency call, giving prehospital instruction to perform chest compression. During the first interview, he identifies if the cardiac arrest is witnessed and the patient age. During this time, an ambulance is engaged to respond and a nurse assesses, in according to emergency control room doctor, the possibility of an ECMO code, with engagement of an advanced medical car. The health care providers explore the hospital resources in relation to the available ECMO center, in relation to geographical and emergency medical vehicles engaged (i.e. road versus air transport). When the first responder is on site, a nurse or a doctor receives medical data, to confirm the ECMO code. If the inclusion criteria are confirmed, the patient is candidable to ECMO, and he is transported to the closer available ECMO center.

Results: All patient with inclusion criteria area transported as ECMO code to ECMO centers. Cannulation are performed in case of absence of major contraindications. To increase the possibility of organ donor in cardiac death (DCD), the inclusion criteria to ECMO code were expanded.

Conclusions: The ECMO center in Lombardy were reduced from 13 to 12, but all victims of refractory cardiac arrest have the change to ECLS, in selected inclusion criteria, in relation to availability of ECMO centers. The ampliation of inclusion criteria increases the possibility of organ donor recruitment and all ECMO centers are informed on the prehospital emergency management to determine the application of ECLS. In this configuration, ECLS and DCD are combined, indetifying the patient who can be a candidate to ECMO implant

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Risk factors of extracorporeal membrane oxygenator weaning failure after major cardiac surgery

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Objectives: This study aims to find out the factors related to extracorporeal membrane oxygenator weaning-off among patients who applied extracorporeal life support for low cardiac output syndrome after major cardiac surgery.

Methods: We evaluated 203 adult patients (aged 62.0 +- 13.4 years, 97 female patients) undergoing extracorporeal life support to manage low cardiac output syndrome after major cardiac surgery and divided them into two groups, the success of extracorporeal membrane oxygenator weaning-off group and weaning failure group. Several factors (operation time, cardiopulmonary bypass time, aortic cross-clamp time, EuroSCORE II, ejection fraction, blood lactate levels, cardiac marker levels, etc.) were compared and analyzed between the two groups, using the chi-square test.

Results: Ninety-two patients (45.3%) were weaned off extracorporeal life support successfully. Older age (mean age, 63.7yr vs 59.9yr, p=0.047), and longer cardiopulmonary bypass time (mean time, 257.9 min vs 212.3 min, p=0.013) emerged as related factors of extracorporeal membrane oxygenator (ECMO) weaning failure. Higher serial lactate levels (24hr, 48hr, and 72hr from the start of ECMO support) and maximum creatinine kinase muscle brain (CK-MB) levels, since ECMO support start, are also revealed as related factors of ECMO weaning failure. More blood transfusions are also related to ECMO weaning failure.

Conclusions: We could find out the risk factors of extracorporeal membrane oxygenator (ECMO) weaning

failure. The longer cardiopulmonary bypass time and the more total transfusion mean more possibility of ECMO weaning failure. After the ECMO support, if the lactate level or CK-MB level decreases rapidly, more possibility of ECMO weaning is expected.

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Retrospective analysis of liver transplantation using brain death donor after ECPR

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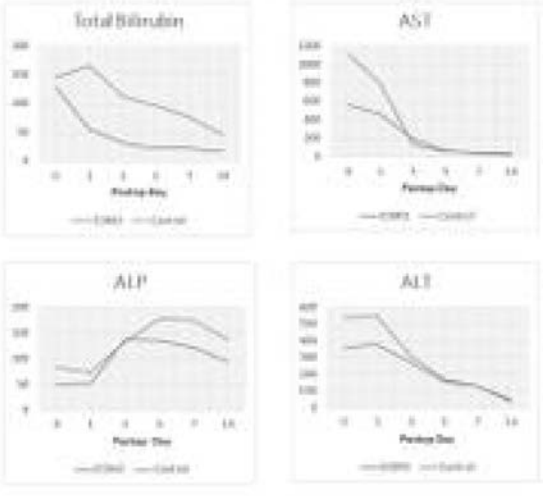
Objectives: To analyse the short term and intermediate outcome of liver graft recipient receiving liver graft from E-CPR brain death donor.

Methods: Retrospective analysis of medical record ECMO data from year 2017 -2020 for basic demogrphic parameters and organ function along ECMO support. Propensity score matching ECMO brain death liver graft recipient with non-ECMO brain death liver graft recipient in 1:3 ratio with regard to cadaveric donor age, recipient age, graft weight, ischaemic time, meld score, recipient OT blood loss.

Results:



62 ECPR patients retrieved from Jan2017 to June2020 with overall hospital survival of 18/62 (29%). 5 patients become actual liver donor. All liver graft sustained initial significant injury from cardiac arrest with liver function recovery from ECMO support. (Table 1)

Patient	1	2	3	4	5
Sex/ Age	M/62	F/64	M41	M/59	F/41
Duration of ECMO support (day)	7	4	5	5	5
Worst Blood parameter	7.0	6.97	6.79	7.08	6.83
	8.5	10.9	8	11.2	9.2
pH	8	23	20	37	19
Lactate (mmol/L)	170	124	79	118	138
Bilirubin (umol/L)	71/	105/	104/	203/	458/
ALP (U/L)	347	366	344	1002	1366
ALT/AST (U/L)					
Blood Parameter	7.54	7.43	7.45	7.43	7.51
before organ	1.5	1.0	1.5	1.8	1.6
Procurement	6	21	17	37	15
pH	170	119	74	96	138
Lactate	44/70	16/73	73/	70/158	148/
Bilirubin			218		239
ALP					
ALT/AST					

Early graft function was comparable between two groups (Figure 2). 2 years survival was 80% (4/5) and 1 patient die due to nosocomial pneumonia 1 month post liver transplantation.

Conclusions: After ECPR , ischaemic liver injury recovered with ECMO support. Outcomes of liver grafts retrieved from E-CPR brain death donor were comparable to conventional non-ECMO brain death donor despite sustaining substantial ischaemic insult from cardiac arrest.

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Optimal timing of extracorporeal membrane oxygenation (ECMO) application for the prognosis of patients with acute coronary syndrome (ACS) accompanying cardiogenic shock

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Objectives: To find out the optimal use and application timing of the extracorporeal membrane oxygenatio device in patients with cardiogenic shock.

Methods: The RESCUE study (Retrospective and Prospective Observational Study to Investigate Clinical Outcomes and Efficacy of Left Ventricular Device for Korean Patients With CS) is multicenter, retrospective, and prospective registry of patients that presented with CS. From January 2014 to December 2018, 1247 patients with CS were enrolled from 12 major centers in Korea. Among enrolled patients, ECMO was applied to 238 of 693 patients who performed percutaneous coronary intervention (PCI) with

acute coronary syndrome. The primary endpoint was a composite of in-hospital, 30-day, 6-month and 12-month mortality according to ECMO application timing.

Results: Table 1. Clinical characteristics of patients with ACS with CS who performed PCI according to ECMO timing

	Before PCI (n=95)	During or after PCI (n=116)
Male	75 (79%)	83 (72%)
Cardiac arrest as presentation	65 (68%)	60 (52%)
ECPR	63 (66%)	60 (52%)
STE-ACS	72 (76%)	85 (73%)
NSTE-ACS	23 (24%)	31 (27%)
LVEF, mean ± SD	24.47 ± 13.78	25.68 ± 13.55
ECMO only	85 (89%)	95 (82%)
ECMO + IABP	10 (11%)	21 (18%)
CRRT	35 (37%)	39 (34%)

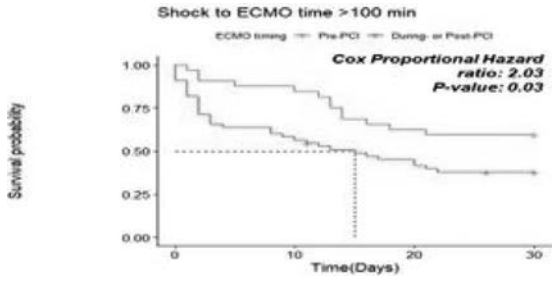

Figure 1. KM survival curve according to shock to ECMO application time

Conclusions: According to ECMO application timing, prognosis of ACS patients with cardiogenic shock was different. In case of exceed 100-minute, early initiation of ECMO application was associated with improved prognosis in 30-day mortality.

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Understanding in-hospital death according to On-ECMO or post-weaning mortality in adult post-cardiotomy Veno-Arterial extracorporeal membrane oxygenation: Observations from the PELS-1 cohort study

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Objectives: Post-cardiotomy veno-arterial extracorporeal membrane oxygenation (PC V-A ECMO) is characterized by a discrepancy between weaning and survival-to-discharge rates. This study analyzes the differences between PC V-A ECMO patients who survived, those who died while on ECMO support, or those who died after ECMO weaning. Causes of death and variables associated with on-ECMO and post-weaning mortality are investigated.

Methods: The current analysis of the retrospective, multicenter, observational Post-cardiotomy Extracorporeal Life Support Study (PELS-1) includes adults requiring PC V-A ECMO between 2000 and 2020. Variables associated with each type of mortality were modeled using mixed-Cox proportional hazards including random effects for center. Associations between variables known at ECMO initiation and on-ECMO mortality were investigated on the whole population. Association between variables likely known at the moment of ECMO weaning, including complications, and post-weaning mortality were investigated in patients who underwent ECMO weaning.

Results: This analysis included 2058 patients [males: 59%; median age:65.0 (IQR:55.0-72.0 years)]. Weaning rate was 62.7%, while survival to discharge was 39.6%. Deceased patients (n=1244) included 754 on-ECMO deaths [(36.6%; median support time:79 (IQR:24-192 hours)], and 476 post-weaning deaths [(23.1%; median support time:146 (IQR:96-235.5 hours)]. Multi-organ failure (n=431/1158, 37.2%) and persistent heart failure (n=423/1158, 36.5%) were the main causes of death in both groups, followed by bleeding (n=56/754, 7.4%) for on-ECMO mortality and sepsis (n=61/401, 15.4%) for post-weaning mortality. Variables specifically associated with on-ECMO death included emergency surgery, preoperative cardiac arrest, cardiogenic shock, right ventricular failure, CPB time, and ECMO implantation timing. Diabetes mellitus and post-operative complications (bleeding requiring thoracotomy, cardiac arrest, bowel ischemia, acute kidney injury and septic shock) were specifically associated with post-weaning mortality.

Conclusions: In adult PC V-A ECMO, in-hospital mortality occurs in 60% of patients. While patients with a more unstable pre-operative situation die on ECMO, one third of the overall in-hospital deaths occurs after ECMO weaning and is associated with a higher occurrence of complications. This underlies the importance of several factors which may still negatively influence an apparent favorable in-hospital course after ECMO support.

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The importance of timing in post-cardiotomy Veno-Arterial extracorporeal membrane oxygenation: The PELS-1 multicentre observational study

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Objectives: Post-cardiotomy veno-arterial extracorporeal membrane oxygenation (PC V-A ECMO) can be initiated intra-operatively or post-operatively based on indications, settings, and patients. Data on the characteristics and consequences of implantation timing are

scarce, and no clear guidelines or studies on this topic are available. Therefore, we compare characteristics, in-hospital and long-term survival between patients who received an intra-operative ECMO implantation or a post-operative ECMO implantation.

Methods: The retrospective, multicentre, observational Post-cardiotomy Extracorporeal Life Support Study (PELS-1) includes adults requiring PC V-A ECMO for post-cardiotomy shock between 2000 and 2020. We compare patients who received ECMO implantation in the operating theatre (intra-operative) with those in the intensive care unit (ICU, post-operative). Outcomes of interest included in-hospital and post-discharge results.

Results: We studied 2003 patients (women:41.1%), with a median age of 65 years (IQR:55.0-72.0). Patients who received intra-operative ECMO (n=1287), compared to those who received a post-operative cannulation (n=716), had worse pre-operative risk profiles. Cardiogenic shock (45.3%), right ventricular failure (15.9%), and cardiac arrest (14.3%) were the main indications for post-operative ECMO initiation, with cannulation occurring after (median) 1 day (IQR:1-3 days). Compared to intra-operative PC V-A ECMO, post-operative ECMO patients experienced more complications, cardiac reoperations (19.7% vs. 24.8%, p=0.011)., and percutaneous coronary interventions (1.8% vs. 3.6%, p=0.026) and had higher in-hospital mortality (64.5% vs. 57.5%, p=0.002). Among hospital survivors, ECMO duration was shorter after intra-operative ECMO (median:104, IQR:67.8-164.2 hours) compared to post-operative ECMO (median:139.7, IQR: 95.8-192 hours, p<0.001) while long-term survival was similar between the two groups (p=0.86).

Conclusions: Intra-operative and post-operative PC V-A ECMO implantation are associated with different patients' characteristics and survival, with higher in-hospital mortality and complications. Strategies to identify the optimal location and timing for PC V-A ECMO initiation are warranted to optimize in-hospital outcomes.

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The evaluation of infections in adult patients with extracorporeal cardiopulmonary resuscitation after cardiac arrest

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Objectives: Extracorporeal cardiopulmonary resuscitation (ECPR) is emerging as a modality to improve prognosis by augmenting perfusion to vital end-organs by utilizing extracorporeal membrane oxygenation (ECMO) during CPR and stabilizing the patient for interventions aimed at reversing the etiology of the arrest. Rapid cannulation plays a crucial role in reducing the hypoxic brain injury, because it can reduce the low flow time during ECPR. However, in emergent ECPR practice, it is very difficult to perform a clean procedure quickly. Cannulation of major vessels provides entry for infectious agents along with additional invasive devices such as endotracheal tubes and central venous catheters. Here we aimed to present infection rates in patients receiving ECPR support.

Methods: This is a retrospective cohort study conducted between January 2020 and December 2022. Patients 18 years and older treated with ECPR using veno-arterial (V-A) ECMO support for in-hospital cardiac arrest were included. Age, gender, comorbidities, body mass index (BMI), cause of arrest, laboratory data, ECMO duration, site of infection, causative microorganism, intensive care unit (ICU) lenght of stay and mortality were recorded. Data are expressed as number (%) or median (minimum-maximum).

Results:

Table1. Baseline clinical and laboratory findings

Age,years	54 (25-67)
Gender,male	26 (89.6)
BMI, kg/m²	24.5 (21.3-29.8)
Comorbidities	
Ischemic heart disease	16 (55.1)
Diabetes mellitus	11 (38)
Hypertension	9 (31)
Chronic kidney disease	8 (27.5)
History of PCI	8 (27.5)
History of CABG	6 (20.6)
History of CVD	4 (13.7)
Malignancy	2 (6.8)
No medical history	2 (6.8)
Cause of arrest	
Ischemic	18 (62)
Refractory arrhythmia	5 (17.2)
Myocarditis	3 (10.3)
Valvular heart disease	2 (6.8)
Pulmonary thromboembolism	1 (3.4)
Laboratory findings on the day of ECPR	
WBC (x 10^3/µL)	18.3 (10.4-25.6)
N/L	9 (3.3-16.3)
C-reactive protein (mg/L)	136 (85.3-330)
Creatinine (mg/dL)	1.09 (0.8-3.7)
ECPR duration (days)	3 (2-8)
ICU length of stay (days)	7 (4-21)
Mortality	15 (51.7)

BMI = body mass index, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting, CVD: Cerebro-vascular disease, ECPR = extracorporeal cardiopulmonary resuscitation, WBC: White blood cell, N/L: Neutrophil to lymphocyte ratio, ICU: Intensive care unit

A total of 29 patients (26 males, 3 females; median 54 years [25 -67]) included the study. Ischemic heart disease was the most common predisposing factor and followed by DM (Table1). 12 (41,3%) patients had culture proven infection, of this 8 (%66,6) were pneumonia. The most common cause of this was *Klebsiella* spp. (37,5%)

Conclusions: Infections are common in ECMO patients and are associated with prolonged hospital admission. Pathogens are predominantly hospital-acquired Gram negative bacteria. Careful implementation of infection control measures and rational antimicrobial management is necessary to minimize infection rates.

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Impact of continuous renal replacement therapy (CRRT) on outcomes of patients on veno-arterial extracorporeal membrane oxygenation (VAECMO)

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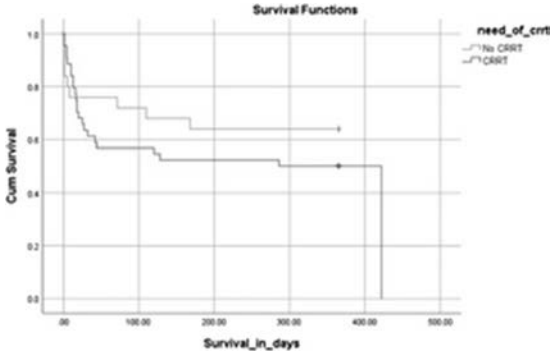
Objectives: 1. To study the baseline characteristics of patients receiving VAECMO alone and concurrent VAECMO/CRRT. 2. To compare the clinical outcomes and survival in patients receiving VAECMO and concurrent VAECMO/CRRT.

Methods: Retrospective observational study was carried out at tertiary center. Analysis includes all adult patients who were placed on VAECMO between January2019 to March2022. The study population was classified into two groups: with CRRT and without CRRT. Demographic data, baseline clinical characteristics, treatments administered, laboratory parameters, mechanical ventilator and ECMO data and survival outcome were collected and analyzed.

Results: Total - 70 VA ECMO patients [44(63%) patients required CKRT]

The pre-ECMO data and initial ECMO parameters were observed similar between the groups. Median duration of ECMO (3 days vs. 6.5 days, p=0.003) was significantly higher in CRRT group; however, there was no difference in mortality, complications, duration of ICU stay (13 days vs. 24,p= 0.17), hospital stay (44 days vs. 38 days, p=0.3) and mechanical ventilation(7 days vs 12.5, p= 0.3) between the two groups. The survival function of the study groups is shown in figure.



Conclusions: The study demonstrated that patients on VAECMO who required CRRT had longer duration of ECMO run.

Adult - Lab session - fundamental research

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Von Willebrand factor fiber formation in a minimized ECMO-perfusion model – effect of N,N'-diacetyl-L-cystine

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Objectives: Clot formation remained a critical complication during extracorporeal membrane oxygenation (ECMO). Previous studies demonstrated the importance of the von-Willebrand-factor (vWF) in

Demographics	Total (n=70)	VAECMO(n=26)	VAECMO+CRRT(n=44)	p-value
Age,median(IQR)	60(45.5-67.5)	59(43.5-66)	61.5(44.7-68.7)	0.45
BMI,median(IQR)	27(23.7-31.2)	29.1(23.9-31.4)	26.6(23.6-31.2)	0.67
Gender(male), n(%)	39(55.7)	13(50)	26(59)	0.45
Immunocompromised, n(%)	9(12.8)	3(11.5)	6(13.6)	0.8
Obesity, n(%)	12(17.1)	3(11.5)	9(20.4)	0.33
Pre-existing cardiac condition, n(%)	41(58.7)	15(57.6)	26(59)	0.9
Pre-existing respiratory condition, n(%)	29(41.4)	11(42.3)	18(41)	0.9
Pre-existing CKD, n(%)	19(27.1)	6(23)	13(29.5)	0.5

shear-induced clot formation in membrane oxygenators (MOs). A minimized ECMO-model was used to reproduce shear-induced vWF and platelet rich aggregates. The thrombolytic activity of N,N'-Diacetyl-L-cystine (DiNAC) was tested.

Methods: A perfusion system which contained a flow chamber with an inoculated ECMO chaining thread (Ibidi, Gräfeling, Germany) was observed under a fluorescence microscope (Keyence, Neu-Isenburg, Germany). vWF-drug Fanhdi (Grifols, Barcelona, Spain) was added to the system. The formation of vWF-fibers under flow (12 mL / min, 37°C) were visualized by using FITC-conjugated anti-vWF antibody. PE-conjugated anti-CD42 antibody incubated platelet rich plasma (PRP) was used to generate vWF-platelet aggregates. Three different concentrations of DiNAC (6 mM, 12 mM, 20 mM) were tested.

Results: Within few seconds, first vWF-fibers appeared on the chaining thread that increased with a velocity of 0.04 ± 0.02 mm² / min for the next 5 minutes followed by a deceleration of the vWF accumulation (0.02 ± 0.01 mm² / min, 5-30 min). PE-stained platelets attached immediately to the vWF-fibers and lead to the stagnation of vWF-fiber formation. An increase in platelet concentration did not affect aggregation as well as vWF-fiber formation. DiNAC dose-dependently lysed the vWF-platelet aggregates (p = 0.048) but had no effect on the vWF fiber formation.

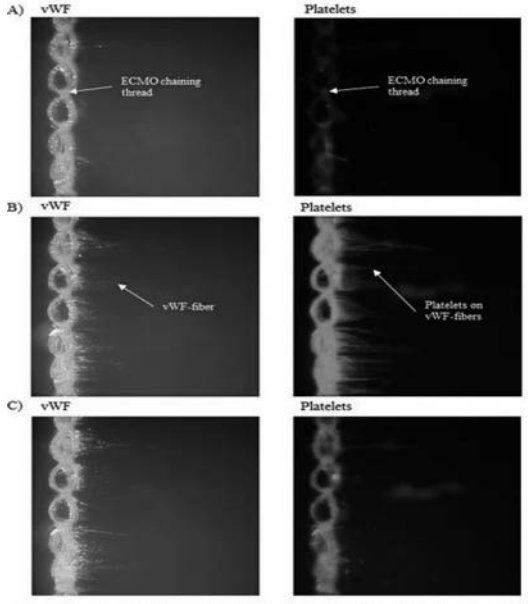

Fig. 1: Shear induced formation of vWF-fibers, binding of thrombocytes to vWF-fibers and effect of DiNAC (20 mM) on vWF and platelets area.
The images on the left side show the FITC-conjugated anti-vWF antibody stained vWF area, whereas the platelets area, which is stained by a PE-conjugated anti-CD42 antibody, is displayed by the images on the right side. Flow conditions: Temperature: 36.0°C – 37.0°C, flow rate: 12.0 mL / min – 13.0 mL / min.
A) 5 min after Fanhdi-vWF application. B) 30 min after Fanhdi-vWF application and immediately after PRP (platelet rich plasma) application. C) 30 min after DiNAC application (20 mM).

Conclusions: ECMO chaining threads caused vWF-fiber formation under flow conditions. Perfusion with DiNAC interfered the interaction between vWF and platelets. This could be an interesting finding regarding the prevention and dissolution of thrombi in MOs.

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Microbiological study of cannulae after ECMO support: A retrospective study including 336 samples

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Objectives: We aimed to describe the results of microbiological findings of the cannula culture after removing ECMO support in our population. We studied the impact of the facility in which the cannulation was performed and the cannulation site on the results of cultures. We investigated the impact of these results on outcomes.

Methods: Single-center retrospective study including 292 V-V and V-A ECMO patients admitted to the Vall d'Hebron University Hospital (Barcelona, Spain) between January 2016 and July 2022. Antibiotic prophylaxis is routinely used since cannulation until ECMO withdrawal with either Vancomycin/Daptomycin. During decannulation ECMO cannulae are aseptically collected, sectioning the distal portion of the catheter (5cm) which is transported to the laboratory for standard catheter culture. We performed a descriptive analysis by calculating frequencies and percentages of qualitative variables. We did a bivariate statistical analysis by chi ^{2}-test.

Results: A total of 292 patients were admitted and in 51% cannulae were correctly sent and cultivated in our laboratory. Antibiotic prophylaxis was used in 276 patients (95%). The total number of cannulae cultivated was 336, of which only 26% were positive. Of these, almost half of the cultures were positive for coagulase-negative staphylococci (CNS) (47.7%). The second microorganism more frequently isolated was candida

spp (32%), followed by klebsiella spp (11.36%), pseudomonas spp (4.54%), and enterococcus faecium (3.4%). We did not find statistical significance between the facility of ECMO cannulation and the incidence of cannula infection. The same was true for the site of cannulation. The 28-day survivance of patients with at least one cannula infection was 72%, equal to the survival of patients with negative cultures.

Conclusions: One of four patients receiving ECMO support may suffer colonization/infection of cannulae, despite receiving antibiotic prophylaxis. This frequency seems to be the same independently of the site of cannulation and the facility in which the process was performed. Positivity of cannulae cultures were not associated with higher mortality. Prospective investigations are needed to confirm these findings and an evidence-based definition of colonization and infection is strongly needed.

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Viscoelastic tests may aid in identifying candidates for eCPR

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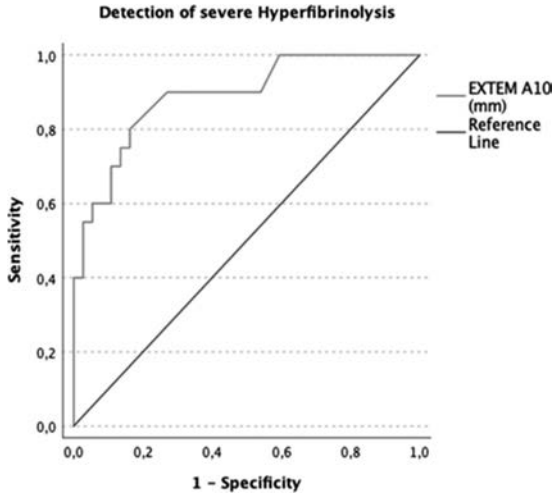
Objectives: Extracorporeal resuscitation is a treatment option for patients with ongoing cardiac arrest. Prediction of neurologic outcome remains difficult. Low-flow time is an important prognostic parameter but even after low-flow-times of > 2h reasonable rates of neurologic intact survival are reported in some case series. Hyperfibrinolysis is known to be associated with poor outcome after cardiac arrest and may be a marker of poor tissue perfusion but has not yet been evaluated in eCPR candidates.

Methods: Fibrinolytic activity was evaluated using thrombelastometry at the time of hospital admission and is given as maximum lysis (%). ROC analyses were performed for hyperfibrinolysis to predict poor outcome. Poor outcome was defined as death or a CPC> 2 at hospital discharge. Low early values of clot firmness (EXTEM A5, A10) were analyzed in their ability to detect hyperfibrinolysis earlier.

Results: Of the 57 patients, 9 patients developed ROSC. In 33 patients, eCPR was performed. 15 patients did not meet criteria for eCPR and died. Hyperfibrinolysis exceeding the normal reference value of ML 15% was detected in 63,2% of patients. Of the patients with a poor outcome, 75% (N=21) had hyperfibrinolysis at admission. Maximum lysis in EXTEM resulted in an area under the curve (AUC) of 0.83 [95% CI 0.7–0.96] for poor outcome (p = 0.001).) Low early value of clot firmness EXTEM A10 had a good ability to predict severe hyperfibrinolysis (AUC of 0.89 [95% CI 0.8–0.98; p=0.001].



Conclusions: Extem A10 is available early in the course of treatment and shows a good prediction of hyperfibrinolysis. It may therefore be a useful parameter to rule out severe tissue hypoperfusion and guide decision making concerning ECMO-therapy in cases with prolonged low-flow times.

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Behaviour of thermodilution signals in a closed extracorporeal circuit - a bench study

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Objectives: Thermodilution is a well-established concept for cardiac output measurement, but it does not provide accurate results in the setting of ECMO and the behaviour of thermodilution signals in extracorporeal circuits is unknown. We therefore investigated thermodilution curves within a closed circuit system and assessed the impact of injection volume, flow and distance on the behavieour of thermodilution signals.

Methods: We injected 3, 5, 7 and 10 ml of saline at room temperature (23°C) into a heated closed circuit at flow settings of 0.5, 1, 1.5 & 2 L/min. Four Swan-Ganz-catheters at distances of 40, 60, 80 and 100cm from the injection port recorded temperature differences (Figure 1A). Area under the curve (AUC), rise time,

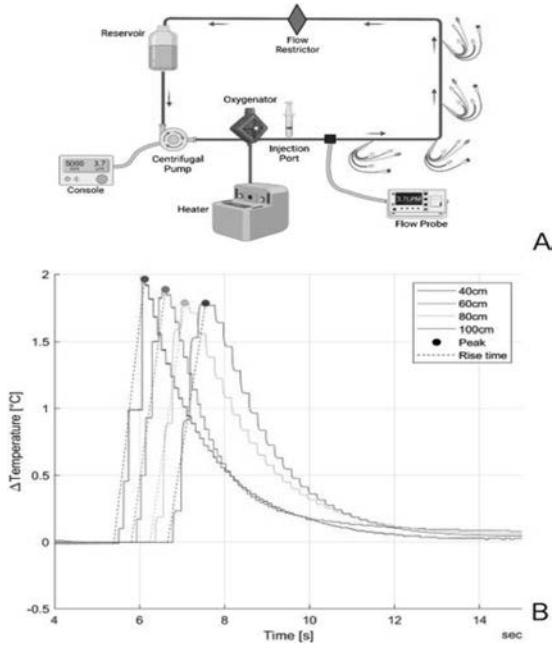
Table 1

	Intercept	Catheter 60cm [Change compared to catheter at 40cm]	Catheter 80cm [Change compared to catheter at 40cm]	Catheter 100cm [Change compared to catheter at 40cm]	Injection volume [change per 1ml]	Circuit flow (change per 1 L/min)
Peak Temperature	0.81 +/- 0.15 (p < 0.001)	-0.15 +/- 0.04 (p < 0.001)	-0.26 +/- 0.04 (p < 0.001)	-0.23 +/- 0.04 (p < 0.001)	0.22 +/- 0.02 (p < 0.001)	-0.44 +/- 0.08 (p < 0.001)
Rise Time	1.91 +/- 0.43 (p < 0.001)	0.08 +/- 0.08 (p = 0.040)	0.74 +/- 0.08 (p < 0.001)	1.00 +/- 0.08 (p < 0.001)	0.05 +/- 0.05 (p = 0.037)	-0.89 +/- 0.23 (p < 0.001)
Exponential Decay	-0.156 +/- 0.059 (p < 0.001)	-0.116 +/- 0.019 (p < 0.001)	0.041 +/- 0.019 (p < 0.001)	0.020 +/- 0.019 (p = 0.039)	0.002 +/- 0.006 (p = 0.544)	-0.25 +/- 0.03 (p < 0.001)
AUC	694.9 +/- 294.9 (p < 0.001)	-23.3 +/- 18.3 (p = 0.013)	-11.3 +/- 18.3 (p = 0.230)	-10.2 +/- 18.3 (p = 0.276)	88.0 +/- 33.3 (p < 0.001)	-530.2 +/- 152.1 (p < 0.001)
Catheter constant	6.25 +/- 0.74 (p < 0.001)	-0.17 +/- 0.27 (p = 0.224)	0.08 +/- 0.27 (p = 0.567)	0.10 +/- 0.27 (p = 0.466)	-0.05 +/- 0.08 (p = 0.214)	0.00 +/- 0.37 (p = 0.996)

peak temperature, the exponential temperature decay and catheter constants were analysed from each injection (Figure 1B). Linear mixed-effects models evaluated the impact of circuit flow, distance and injection volumes.

Results: 78 injections (312 signals) were analysed. Properties of the thermodilution signal changed significantly with flow, distance, and injection volume (Table 1). Catheter positioning did not impact AUC and the resulting catheter constants were independent of experimental conditions.

Figure 1



Conclusions: In vivo calibration of catheter constants derived in an in-vitro circuit appear to be reasonable and reliable. Indices dependent on exponential decay may change significantly with injection volume and distance to the injection port.

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Clot localization within membrane lungs using different imaging methods and histological clot characterization as a way to prevent thrombosis in extracorporeal membrane oxygenation

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Objectives: Intra-device clot formation remaines a critical complication during extracorporeal membrane oxygenation (ECMO). Precise localization of clots within the membrane lung (ML) and identification of clot components will increase the understanding of clot-forming mechanisms to prevent thrombosis.

Methods: Clot structures within an end-of-therapy ML (Cardiohelp, Getinge, Rastatt, Germany) were visualized using different imaging methods (multidetector CT (MDCT), microcomputed CT (μCT), fiber mat imaging (FMI)). Randomly selected gas fiber samples were stained with platelet markers (CD42b, CD62P), von Willebrand

factor (vWF), and nucleated cells with DAPI (4',6-diamidino-2-phenylindole).

Results: The calculated clot volume was independent of the imaging method ($V_{\mu CT}$ = 104 ml, 37% of ML blood volume; V_{MDCT} = 122 ml, 40%; V_{FMI} = 103 ml, 37%). The observed clot structures were evenly distributed within the ML except in the vicinity of blood inlet and outlet. In thrombotic regions a continuous multi-layer of extended vWF, leucocytes, and activated platelets was spanning neighboring gas fibers. Clot-free areas were covered with high density of leucocytes (2077 ±1023 nuclei/mm^2). The latter remained unchanged along one gas fiber mat but significant differences were detected at different levels of the ML ($p \leq 0.010$). While the frequency of neutrophile extracellular traps (NETs) was low (< 1%), its precursors (decondensed swollen nuclei) amounted to 13 ±9%. Platelet-leucocyte-aggregates (PLAs) dominated with 30 ±21%. PLAs included significantly more vWF structures (81 ±24%) than activated platelets (63 ±23%, $p < 0.001$).

Conclusions: All imaging methods detected similar clot volumes within the ML. While clots consisted of multi-layered deposits, inflammatory response with a high occurrence of NETs and PLAs played a key role on the surface of clot-free fibers. These deposits may be responsible for activation of the coagulation cascade and triggering clot formation.

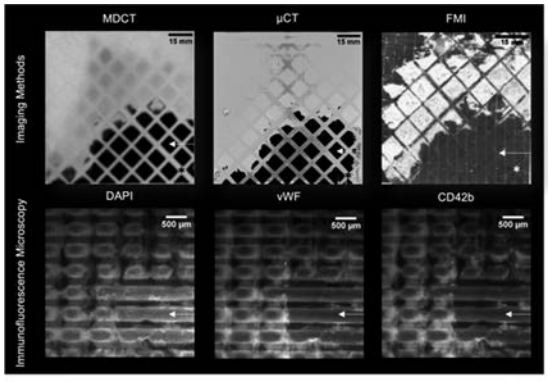

Fig. 1: Imaging of clot formation and clot-free areas (arrow) at the dividing wall and equivalent fiber mat regions investigated with histological staining. * Position of inlet, MDCT, multidetector computed tomography; µCT, microcomputed tomography; FMI, fiber mat imaging; DAPI, Nucleated cells; vWF, von Willebrand factor; CD42b, Thrombocytes.

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Watershed region tide - computational fluid dynamics simulations of the ECMO-failing heart circulation

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Objectives: Computational fluid dynamics (CFD) enables the study of different fluid dynamic scenarios, alloying the quantification of variables not measurable at the bedside. CFD simulations of the ECMO-failing heart circulation were used to (i) quantify total flow and pressure and (ii) describe the watershed region produced by the collision of native and ECMO flow.

Methods: A patient-specific geometry of the whole aorta was reconstructed from the CT dataset. Performing CFD simulations, the corresponding virtual twin was built, and 13 scenarios were simulated:

- healthy conditions;
- shock without ECMO support;
- 5 shock simulations: reduction of 30% of the native cardiac output (-30% CO), - 50% CO and -70% CO with 5 different ECMO support levels (ECMOf): 2 to 6 l/min.

Results: With increasing degrees of shock, the location of the watershed region ascends along the aorta as ECMO support increases:

- in -30% CO in the aortic arch for ECMOf 6 l/min;
- in -50%% CO in the descending area of the aortic arch with ECMOf 4 l/min;
- in -70%% CO in the epiaortic branches with ECMOf of 4 l/min. In diastole, there is a retrograde shift of the watershed region in the aortic arch, and ECMO flow reaches the epiaortic vessels. Neither in systole nor diastole, the coronary arteries were perfused by ECMO flow.

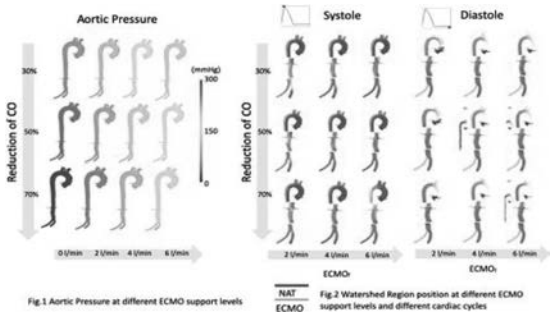

Fig.1 Aortic Pressure at different ECMO support levels

Fig.2 Watershed Region position at different ECMO support levels and different cardiac cycles

Conclusions: ECMO support of approximately 2 l/min in -30% CO, 3 l/min for -50% CO and 4 l/min for -70% CO avoids excessive pressure increase, providing a total flow equal to that of healthy conditions. The watershed region ascends along the aorta as ECMO support increases and during diastole.

Adult - Nurse

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Exploring the scope of nursing practices in the care of ECMO supported patients in Israel

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Objectives: The growing implementation of extracorporeal membrane oxygenation (ECMO) for patients with COVID-19 has led to increased involvement of nurses in treating ECMO-supported patients (ECMO-SP). In June 2021, the Israeli Ministry of Health's Nursing Administration published the first director's circular in the world to detail the nursing scope of practice in caring for ECMO-SP. This study aimed to examine how often nurses perform various activities while caring for adult ECMO-SP.

Methods: A cross-sectional study. A convenience sample consisted of 76 registered ICU nurses (mean age 41.3±8.7 years; 71% female). A 20-item Nursing Activities in the Care of ECMO-SP instrument was developed based on the Israeli Ministry of Health's procedure on Nursing Practice in the Care of ECMO-SP and a literature review. The instrument examined how often nurses perform various activities on a Likert scale ranging from 1 (Never) to 5 (Always). Exploratory and confirmatory factor analyses (EFA and CFA), as well as descriptive statistics and Pierson's correlations were performed.

Results: When examined in EFA and CFA, the instrument yielded acceptable fit indices. The instrument contains four subscales with the following mean ± SD scores: Factor 1. Nursing care of ECMO-SP not related to the ECMO device (7 items, a=0.90), M±SD=4.66±0.61; Factor 2. Activities on the ECMO device during emergencies (5 items, a=0.82), M±SD=2.1±0.91; Factor 3. ECMO device calibrating and monitoring (4 items, a=0.72), M±SD=3.26±1.0; and Factor 4. Medication and blood administration through the ECMO device (4 items, a=0.73), M±SD=1.52±0.60. Of the 20 nursing activities, 10 (50%) were reported as "never" or "rarely" performed. Nine out of 20 items (45%) were reported as "very often" or "always" performed.

Conclusions: Ten out of 20 (50%) activities while caring for ECMO-SP listed in the scope of practice as permissible for nurses to perform were reported as not performed at all or performed rarely. Policymakers need to act so that the activities listed in the nursing scope of practice are carried out by nurses in practice.

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Training needs for ECMO nurses: Analysis, results and what's beyond

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Objectives: Nurses attending ECMO patients must have specialized knowledge and skills. At Careggi Teaching Hospital and ECMO center, as well as in other hospitals worldwide, new personnel have been summoned to face the increased number of critical patients due to the COVID pandemic. Therefore, the number of nurses with poor ECMO experience has recently skyrocketed. During the work shifts inexperienced nurses have been coached by experienced ones. This organization has permitted to manage a volume of fifty-nine ECMO patients during the pandemic without significant adverse events.

Methods: We led a survey among the nurses of the ICU and ECMO unit to assess their perceived training status and educational needs. In November 2022 seventy-two nurses received an anonymous questionnaire made of 21 items based on Likert scale. The questionnaire consisted of three parts investigating the general knowledge of ECMO support and maintenance, their perceived level of competency in several conditions and, finally, their expectations for future training.

Results: The most relevant results are presented in figure 1.

Topic	Level	Percentage
Indications and initiation of ECMO treatment	Know a little	37.1%
Knowledge about monitoring pressures	Limited knowledge	25.8%
Coagulation Management	Feel poorly prepared	45.2%
Air embolism Troubleshooting	Not able to intervene	50.0%
Membrane Lung failure due to coagulation	Poorly prepared Very poorly prepared	46.8% 11.3%
Training received during COVID pandemic	No training received Superficial training	6.5% 48.4%

Figure 1

From the analysis of the survey we have assessed that in our institution, an educational programme for nurses actually involved in managing ECMO patients is an urgent need and should cover both ordinary management and emergency situations. Real life scenarios and crisis resource management events should be the focus of the programme.

Conclusions: Training in ECMO is crucial for patient safety. After COVID pandemic, in our ECMO center, capabilities and knowledge of newly recruited nurses treating ECMO patients are suboptimal/unsatisfactory. A questionnaire to analyze the actual level of competence of the personnel involved can help to tailor a more effective educational programme to meet their real needs and to select the appropriate improvement actions.

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ECMO follow-up clinic at Rigshospitalet, Copenhagen. 1 out of 2 ECMO-centers in Denmark

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Objectives: There is little knowledge about how adult patients (>18 years), who have been treated with ECMO,

copes after illness, and what challenges they have afterwards. It it necessary to collect data on what we, in intensive care, can do to optimize the time after discharge for this specific group of patients. Therefore our aim is to gather knowledge of the physical, psychological and neurocognitive outcomes of those of our patients, who have undergone treatment with ECMO at the ICU, and to make the necessary interventions, when or if needed.

Methods: The patients attend the ECMO follow-up clinic, 6 and 12 month after discharge from the hospital. They fill out 2 questionnaires; HADS (Hospital Anxiety and Depression Scale) and SF12 (Shortform survey of quality of life measures) in advance. Their physical condition will be assessed by a physiotherapist -6 min walktest, handgrip test and sit to stand test (30sec). Afterwards they meet with af physician and a nurse. The session starts with the MoCA test (The Montreal Cognitive Assessment) and then follow a semi structured interviewguide.

Results: From the start in january 2022 until january 2023, there have been 22 patients at the 6 month follow-up and 13 patients at the 12 month follow-up. It is a very heterogenous group. 12 V-A and 10 V-V ECMO with different diagnostics. Until now, most patients have shown a need for intervention of various kinds. They are challenged both physical, phycological and cognitive. Data will be presented based on screening and cases.

Conclusions: After 1 year of ECMO follow-up clinic, we have decided to make it permanent. We see great potential in gathering more knowledge about the longterm outcome in this group of patients, where the current knowledge is sparse, at an international level. Furthermore we believe that we can improve and optimize quality of life for these patients.

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A theory based introduction to the concept of psychological safety in high fidelity ECMO simulations

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Objectives: High fidelity simulations (HFS), are very useful educational strategies, aimed to offer a safer and relaxed learning environment for students, practicing real-life scenarios. Participants are encouraged to speak up, express and share their feelings and emotions during ECMO simulations. Building a psychologically safe learning environment in the context of High Fidelity ECMO Patient Simulations, to allow students to feel safe when making mistakes in the simulation suit, without the stress of feeling emotionally uncomfortable and the pressure of performing in front of peers.

Methods: The concept of Psychological Safety in High Fidelity ECMO Patient Simulation is being introduced into all the ECMO-specific training in our organisation. Especially in the ECMO Clinical Specialist Nurse course, where simulations play a very important role in the learning experience of the candidates. Students are encouraged and reminded at the beginning of simulations that they should feel able to speak up and take personal risks as well as share their emotions at any time of the scenarios. Confidentiality and mutual respect are always maintained throughout the course. Real life experiences are re-created during simulations, including life-threatening emergencies, patients' death and stressful situations, educators and course facilitators include emotional stressors and human factors from real-life experiences (mostly from previous episodes or after reflecting on clinical incident situations). Facilitators are aware of the emotional impact and stress that high fidelity simulations can have on participants, continuously assessing learners' emotional status and responses.

Results: High fidelity simulation, can cause negative emotions to participants, due to stress and anxiety, related to the fears of without fear of judgment, shame or career repercussion and consequences. Fostering psychological safety during High Fidelity ECMO Simulations allows healthcare professionals to feel able to participate in training without fears and enhances their learning experience, motivating them and prompting them to learn from error and encouraging to report adverse patient events.

Conclusions: Psychological safety in healthcare simulations aims to amplify learners' experience during high fidelity ECMO simulations, allowing them to feel safe and comfortable whilst learning.

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Simulation training in an experienced ECMO program

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Objectives: ECMO is an advanced lifesaving treatment for critically ill patients with severe respiratory, cardiac or combined cardio-respiratory failure. In an experienced ECMO center without perfusionists it is

imperative that ECMO specialist physicians and ECMO specialist nurses maintain bedside competence for safe management and troubleshooting in case of emergency.

Methods: In our program the simulation training is led by experienced ECMO specialist physicians and ECMO specialist nurses (also ECLS primers) who are qualified simulation instructors trained at Center of Advanced Medical Simulation Training (CAMST). The training is held in a simulation lab at the clinical training center, part of our University Hospital. The training set up is made to look authentic to create a familiar environment during simulation exercises. For each simulation the instructor team assemblies a mockup ECMO patient in form of a mannequin and a primed ECMO circuit attached to a 5-liter bag of fluid hidden under the bedding of the mannequin. Cannulas are inserted into the tubing, and pressure is applied to the fluid compartment with ratchet straps setting patients' blood pressure. For realistic scenarios swivels are attached to the circuit with Fogarty catheters inserted through them. When the balloon is inflated, this acts as an obstruction in the circuit. These are hidden from the trainees. Apart from obstructions in the circuit, other scenarios, for example air entering the circuit, power failure, oxygen failure, can be simulated.

Results: Each staff member in our program simulates at a minimum once a year. Each simulation session starts with a lecture on crew resource management (CRM) The staff plays the role they normally have in the team. Focus for the simulation is to act on events as a team where tasks are clearly alllocated, and the participants practice their communication skills. A debriefing is held after each scenario. Part of this debriefing, CRM principles such as team members awareness of the situation, decision making, prioritising, communication, leadership, being able to follow the team leader, asking for help early and allocation of resources, are discussed. Participants use our programs ECMO A-B-C algorithm to solve problems in the ECMO circuit as well as for the timeout after any incident to assure that the ECMO circuit is complete and running according to pre-defined settings (patients need)

Conclusions: ECMO is an advanced treatment that require specific training and expertise. To ensure safe ECMO management given the known complications, emergencies have to be solved by bedside staff 24/7 and thus, it is imperative that all staff members train together as a team in clinically familiar environment which is effectively performed during simulation sessions.

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Evaluating structural training of critical care nurses in a nurse governed ECMO programme

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Objectives: The purpose of this study is to identify the benefit of a structured extracorporeal life support (ECLS) training program for both novice and experienced nurses with various ICU backgrounds. The need for ECMO training programs at institutions that provide ECLS has been established.[1] [1] Gannon WD, Craig L, Mauldin C, Troutt A, Warhoove M, Tipograf Y, Hogrefe K, Rice TW, Shah A, Bacchetta M. Curriculum to Introduce Critical Care Nurses to Extracorporeal Membrane Oxygenation. Am J Crit Care. 2020 Jul 1; 29(4): 262-269. Doi: 10.4037/ajcc2020739. PMID: 32607573

Methods: Evaluation of the training and education topics and pathway was completed by evaluating the learner response to confidence surveys and exams. The study consisted of a 15-question survey distributed pre and post training, as well as a pre and post exam evaluating specific specialized ECMO concepts and interventions. Data was collected utilizing Survey Monkey. Differences in proportions were initially analyzed using two proportion z test and subsequently divided into additional groups of specialist confidence to be analyzed using x2 or Fishers exact test. All statistical analysis were performed using Stata. Results were considered significant at a P-value of 0.05.

Results: In total, 37 specialists (ECMO Bedside Nurses and ECMO Specialists) responded to the pre and 30 responded to the post survey. 43.2% of specialists had 1-3 years of critical care experience. 75.7% of those surveyed had no prior ECMO experience. Compared to pre-confidence survey results, there was a statistically significant increase in confidence of specialists ability to function within their role after training completion. Pre and post-test training exam scores were evaluated with a noted statistically significant increase in exam scores related to ECMO management within scope and role.

Conclusions: Identifying a framework of replicable, evidence-driven educational methods that improve both staff confidence and competence of Extra Corporeal Membrane Oxygenation (ECMO) would be invaluable to providing improved patient outcomes.

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The role of ECMO nurses in weaning V-A ECMO patients with Pump-Controlled Retrograde Trial Off (PCRTO)

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Objectives: PCRTO is a weaning technique by mimicking normal physiological blood flow direction, which involves a retrograde blood flow from the arterial ECMO cannula to the venous side via the pump head. Its feasibility has been demonstrated in both adult and pediatric populations and has become a routine weaning strategy at our center. A PCRTO protocol was established, the safety and responsibility of ECMO nurses were evaluated.

Methods: We retrospectively reviewed all V-A ECMO patients who have undergone PCRTO at a tertiary ECMO center from January 2019 to July 2021. PCRTO was initiated by serial decremental pump revolutions until a retrograde blood flow at 10ml/kg/min from the arterial to the venous cannula. The distal reperfusion catheter was kept patent with pressurized normal saline. ECMO nurses carried out meticulous monitoring of patient's physiological parameters and ECMO circuitry. Serial blood sampling and echocardiogram assessment were utilized to evaluate the readiness to wean off V-A ECMO support.

Results: A total of 57 runs of PCRTO in 36 patients were commenced and terminated by ECMO nurses, 45 (78.9%) of the trials were conducted uneventfully. Every trial was carried out by 1 ECMO nurse with a minimum of 5 years of ECMO experience. The total number of nursing-supervised hours during PCRTO were 156 hours. The major reasons for the premature termination of PCRTO were right ventricular failure (n = 4) and lower limb hypoperfusion (n = 4). Early subtle changes in patient's vital signs and Near Infrared Spectroscopy (NIRS) reading on bilateral lower limbs were captured by the ECMO nurses. ECMO nurses paid special attention to any signs of clot aggregation or migration during each trial and upon restoration veno-arterial flow. There were no thrombotic or embolic events arising from PCRTO in our cohort.

Conclusions: Our center experience suggests that protocolized application of PCRTO during V-A ECMO weaning is practicable and safe. PCRTO requires well-trained and experienced ECMO nurses to detect and manage ongoing changes.

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Nurse perception on ECMO care: A literature review

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Objectives: The nursing care is more complex in relation to new technologies, new diseases, new globally emergencies. In relation to technology, nurses acquired more competences in relation to advanced therapy, in respiratory, circulatory, and renal support. The nursing workload increases in complexity and in responsibilities, without a staff increasing in relation to nursing activities. ECMO was widely applied to manage acute respiratory distress syndrome and circulatory failure, in case of cardiac arrest or cardiogenic shock, configuring as a therapy bridge to decision, to restore, to transplant or to nowhere. During the last years, nurses were involved to a rapid and continuous changing, to respond adequately to new health challenges, understanding or not their role and responsibilities in globally health care system. Nurse manages different variables, well represented by nursing activities score, but in nursing ECMO care, these variables are more complicated, in relation to ECMO device and to ECMO patient. What is the globally perception of nurses involved in ECMO care?

Methods: A literature review was applied on PubMed. The inclusion criteria were all articles about ECMO, including pediatric and/or adult population, with a publication less than ten years.

Results: A total of sixteen articles were found, with reduction to ten for relevance. The excluded articles talked about non ECMO care or patient's perceptions. Articles included in the research talk about nursing perceptions (40%), education (30%), ethics in ECMO care (20%), professional experience in ECMO Covid (10%).

Conclusions: The nursing perception on ECMO nursing care are different. They recognize the central role in ECMO care, but over workload, without staff increasing, less peer support, a low teamwork and personal differences in technical and non-technical skills increase some barriers to nursing perception of themselves. Nurses allocate their competence on experience and continuous training, but also a good teamwork and a professional recognition by other health care professions or by nursing supervisors can

increase nursing perception and reduce the abandonment of nursing profession.

Adult - Perfusion

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Mortality on extracorporeal membrane oxygenation: Evaluation of independent risk factors and causes of death comparing venoarterial and venovenous support

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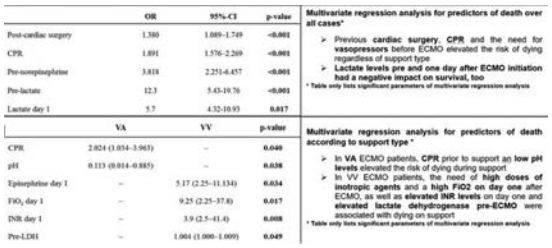
Objectives: Extracorporeal membrane oxygenation (ECMO) has become an indispensable treatment option for cardiopulmonary diseases in intensive care and emergency medicine. Despite increasing ECMO experience, mortality during support remains high and the actual causes of death on support have not been studied sufficiently. The present study focuses on mortality during support, comparing veno-arterial (VA) and veno-venous (VV) ECMO support.

Methods: Of 2016 patients receiving VA or VV ECMO-treatment at our institution from 2006–2021, 759 patients (37.7%) died during ECMO support or within 24 hours after its termination. The underlying causes and predictors of death were analyzed.

Results: The causes of death were different for VA ECMO and VV ECMO. VA ECMO patients mostly died from cerebral hypoxia (34%), low-cardiac output (LCO; 24.1%) and multi-organ failure (MOF; 21.6%), and bleeding (8%), whereas in VV ECMO cases, respiratory insufficiency (28.2%), and sepsis (20.4%) dominated. Patients with ECMO-assisted cardiopulmonary resuscitation (eCPR) mostly died of cerebral hypoxia (45.3%) or LCO (22.3%), while post-cardiotomy patients mainly died of LCO (39.6%) and MOF (33.6%). Multivariate regression analysis revealed previous cardiac surgery (p=0.035), CPR (p=0.004), the need of high doses of vasopressors (p=0.011), and elevated lactate levels pre-ECMO (p≤0.001) as risk factors for death. When adjusted according to support type, death on VA ECMO was associated with CPR and acidic pH, on VV ECMO with high inotropic doses pre-ECMO, high fraction of inspired oxygen on day 1, as well as elevated lactate dehydrogenase, C-reactive protein and international normalized ratio.



	OR	95%-CI	p-value
Post-cardiac surgery	1.380	1.089–1.749	<0.001
CPR	1.891	1.576–2.269	<0.001
Pre-norepinephrine	3.818	2.251–6.457	<0.001
Pre-lactate	12.3	5.43–19.76	<0.001
Lactate day 1	5.7	4.32–10.93	0.017

Multivariate regression analysis for predictors of death over all cases*

- Previous **cardiac surgery**, **CPR** and the need for **vasopressors** before ECMO elevated the risk of dying regardless of support type
- **Lactate levels pre and one day after ECMO initiation had a negative impact on survival, too**

* Table only lists significant parameters of multivariate regression analysis

	VA	VV	p-value
CPR	2.024 (1.034–3.963)	–	0.040
pH	0.113 (0.014–0.885)	–	0.038
Epinephrine day 1	–	5.17 (2.25–11.334)	0.034
FiO_2 day 1	–	9.25 (2.25–37.8)	0.017
INR day 1	–	3.9 (2.5–41.4)	0.008
Pre-LDH	–	1.004 (1.000–1.009)	0.049

Multivariate regression analysis for predictors of death according to support type*

- In **VA** ECMO patients, **CPR** prior to support an **low pH levels** elevated the risk of dying during support
- In VV ECMO patients, the need of **high doses of inotropic agents** and a **high FiO2 on day one** after ECMO, as well as **elevated INR levels** on day one and **elevated lactate dehydrogenase pre-ECMO** were associated with dying on support

* Table only lists significant parameters of multivariate regression analysis

Conclusions: Even in centers with large experience, overall mortality remains high during ECMO support. The causes of death differ between VV and VA ECMO depending on the underlying diseases responsible for the need of extracorporeal support.

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Which is the optimal method for an intra-hospital ECMO transport? Single center experience

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Objectives: Intra-hospital transport of a patient in ecmo is often necessary for further diagnostic examination. The procedures may be influenced by the structural peculiarity of the hospital. The aim was to find our best method of transportation in terms of safety, time and number of operators involved.

Methods: We compared two different transport configurations: A) hospital icu bed + ecmo trolley system + iabp cart B) transport stretcher + ecmo with support on the stretcher + iabp cart Analyzing the time taken by the icu to the cath lab or ct scan room, the number of operators involved, the size and the number of elevators for the same intra-hospital path.

Results: The distance from the icu to the ct scan room is 350 metres (a1 - b1) and from the icu to the cath lab is 270 metres (a2 – b2) a1) time taken to the ct scan room is 9 minutes and 45" with 5 operators a2) time taken to the cath lab is 11 minutes and 38" with 5 operators b1) time taken to the ct scan room is 4 minutes with 3 operators b2) time taken for the cath lab is 3 minutes and 50" with 3 operators

Conclusions: In our experience we have seen that method "a" requires more travel time associated with necessarily longer paths due to the size of the icu bed and the ecmo/iabp trolley in relation to the size of the elevators; Furthermore, the maneuvers in ct scan are more difficult due to the narrow dimensions of the room. Method "b" appears to be faster thanks to shorter paths, it requires fewer operators due to the absence of the ecmo trolley and it proves to be safer because it is a solidarity system avoiding any traction or damaging of the circuit between the transport stretcher and the ecmo trolley

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Is it safe to maintain a pre-primed ECMO circuit?

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Objectives: Our center is involved in ECMO and ECPR programme. In order to reduce the ECMO implant time in emergency and to avoid mistake during the preparation of the circuit, it is easy to have a pre-primed ECMO circuit available. Our goal is to evaluate whether the pre-primed ECMO circuits could develop alterations of the sterility of the priming.

Methods: Every Monday a sample of ECMO priming is taken and send to the analysis laboratory of our centre for evaluation of:

- tests of sterility
- direct microscopic examination and culture examination.

Results: 92 ECMO were implanted in our center between 2019 and 2022. 260 priming analysis were performed . Of the total of 260 analysis only 2 samples were positive, one for E.Coli and one for S.Epidermidis (0.7%).The average stay of a pre-primed circuit was 19,26 days. The calculated standard deviation is equal to 18,40 days. The longest stay of a pre-primed circuit was 72 days.

Conclusions: In our experience, having a pre-primed ECMO circuit in emergency situations is safe and avoids time delay for the preparation of the circuit,because of during the night and during the week-end the presence of the equipe is on call. The 99.3% of the implanted ECMO circuits resulted free of alteration of the priming's sterility; only 0.7% of the samples resulted positive. In the two cases the positivity of the sample occurred after a week from the priming; we suppose that there has been an alteration in the sampling phase or during the circuit preparation time. In both cases the circuit was replaced with a new one. Based on the results we also have observed that there are no alterations in sterility in circuits pre-primed for a long time.

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Critical leg ischemia contralateral to arterial canula site in patients with peripheral VA-ECMO: Incidence, mechanism and challenges of treatment

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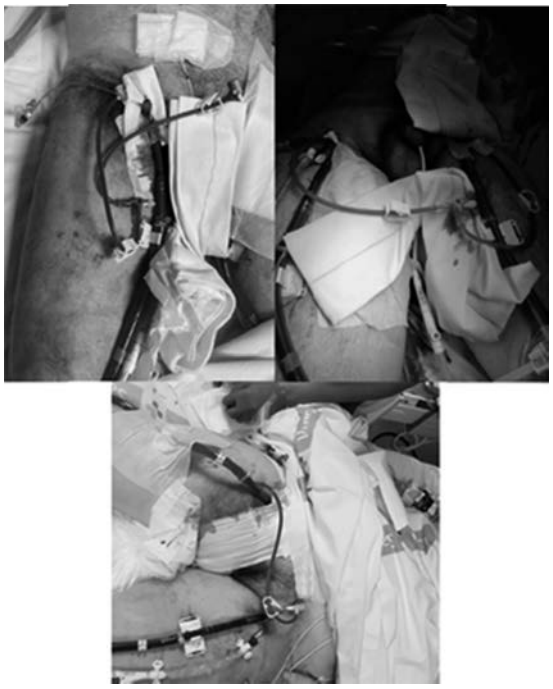
Objectives: Ipsilateral leg ischemia where the arterial cannula is placed in patients with peripheral VA-ECMO is common. However, perfusion compromise of the contralateral extremity is scarcely described. We present a single center retrospective review of this rare, but seriously vascular complication.

Methods: From January 2019 to December 2022, a total of 111 VA-ECMO were implanted in patients suffering by cardiogenic shock and cardiac arrest. Four of them (3,6%) presented critical leg ischemia contralateral to arterial cannula site. Median age of 59 years old (range 55-70), three of them males. In three cases VA-ECMO was inserted during cardiac arrest. Etiologies of critical contralateral leg ischemia were as follows: flow obstruction by left ventricular unloading device (n=2), retrograde dissection triggered by ECMO canula (n=1) and thromboembolism (n=1)

Results: Critrical leg ischemia was developed within 24 hours of ECMO implantation. It was resolved by placing an additional perfusion line in the superficial femoral artery connected to arterial ECMO cannula (surgical cut-down (n=2) and percutaneous eco-guided (n=2)). 75% survived to ECMO withdrawal after a median support of 7 days. A concomitant trombectomy besides ECMO explantation was needed in two cases. All weaned patients had no sequels of critical leg ischemia.



Conclusions: Contralateral to arterial ECMO canula critical leg ischemia is triggered by presence of left ventricle unloading devices, followed by thromboembolism and vascular complication of arterial cannula insertion. Close perfusion monitoring of both lower extremities is therefore of great importance. Additional distal perfusion line placed percutaneously eco-guided

or by surgical cut-down may resolve perfusion until VA-ECMO explant and vascular revision.

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Pre-primed ECMO in a clinical setting

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Objectives: In experimental studies extracorporeal membrane oxygenation (ECMO) systems has been wet primed for up to 65 days with sterility intact. However, few circuits have been tested and clinical studies are missing. Therefore, this study was undertaken with the aim to investigate if oxygenator function is intact despite dry set up followed by wet priming beforehand and if sterility testing of a preprimed ECMO is necessary in a clinical setting.

Methods: The Cardiohelp system HLS set 7.0 advanced was used. The circuits were assembled dry and when the previous wet circuit was used the dry circuit was primed with Ringer-Acetate. After ECMO start the whole prime bag was sent for sterility control to detect the presece of contaminating bacteria and funghi. ECMO data regarding oxygenation, carbon dioxide removal and pressure drop was measured at 0, 12, 24 h and once a day after that until the end of the treatment.

Results: 107 circuits were primed. Mean dry set up time was 11,8 days (range 0-89), mean wet prime before use 8,8 days (range 0-57) and mean total set up time, dry + wet, was 20,5 days (range 0-90). Mean ECMO run was 3,1 days (range 0-84). One circuit was changed after 48 hours due to high membrane pressure drop. There was no correlation between number of days primed and any clinical measurements of oxygenator oxygenation, carbon dioxide removal or pressure drop. Two circuits showed bacterial growth, one with coagulase-negative staphylococci and another with cutibacterium acnes. Both circuits had been primed for teen days each. The affected patients died in three respectively six days due to other causes.

Conclusions: Hollow fiber membrane oxygenator with diffusion membrane can be safely wet primed up to 57 days in a clinical setting without effect on clinical oxygenator function. The Sterility control revealed two contaminated circuits and shows that testing can be of importance when using preprimed ECMO in a clinical setting to identify and treat contamination.

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Smaller arterial cannula diameter in venoarterial ECMO has equivalent indexed blood flow without increased haemolysis: A single centre, retrospective cohort study

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Objectives: There are a number of potential advantages to inserting a smaller arterial cannula in venoarterial ECMO (VA ECMO), including ease and speed of insertion and possibly reduced cannula related adverse events. There are concerns, however, that inferior flow is achieved with increased rates of haemolysis as compared to a larger arterial cannula. The aim of this study was to explore the relationship between arterial return cannula diameter and blood flow indexed to body surface area (BSA) during VA ECMO, along with associated adverse events and technical induced haemolysis. We hypothesised that smaller cannula diameter would not be associated with lower indexed blood flow and would have similar or lower rates of adverse events.

Methods: We identified 158 adult patients who received VA ECMO at our institution from the national ECMO database (EXCEL) between February 2019 and July 2021. We classified patients into a small cannula group (15 Fr diameter, n=45) and a large cannula group (≥17 Fr diameter, n=113), comparing blood flow rate per BSA, cannula related adverse events and haemolysis data.

Results: ECMO blood flow indexed to BSA was not significantly different between small and large cannula groups at 4 hours (1.66 ± 0.11 vs 1.75 ± 0.17 L/min/m^2; p=0.17) and 24 hours (1.61 ± 0.13 vs 1.73 ± 0.20 L/min/m^2 ; p=0.11). There was no significant difference in rates of moderate haemolysis (2.2% vs 5.3%; p=0.39) or severe haemolysis (0% vs 2.7%; p=0.27) between small and large cannula groups, nor was there a significant difference in the rate of cannula related adverse events between the groups (46.6% vs 47.7%; p=0.93).

Conclusions: We observed similar ECMO blood flow rate indexed to BSA when comparing small vs large arterial cannula diameter in peripheral VA ECMO, with no increased rates of haemolysis or cannula related adverse events. Further research into cannula size is needed.

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Case report: The use of ECPELLA in a refractory cardiogenic shock after complex coronary artery bypass graft surgery

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Objectives: Background: The importance of mechanical circulatory techniques in refractory cardiogenic shock has been growing over the last few decades. The combination of ECMO and Impella (ECPELLA) is a new and appealing technique for the unloading of the left ventricle to prevent the increase in afterload caused by ECMO. However, this is a technique that still requires further research.

Methods: -

Results: Case presentation: A sixty-seven year old female presented with complaints of fatigue for moderate exercise, has been diagnosed with severe three vessel coronary artery disease. The patient underwent elective coronary artery bypass graft surgery, without any complications during the intraoperative period. On day one after surgery, the patient suffered an episode of hemodynamic instability, accompanied by severe left ventricular dysfunction and respiratory arrest. It was decided to perform emergent catheterization to acess the permeability of the grafts which showed that they were occluded. The patient underwent emergency surgery, and all the coronary arteries were revascularized by re-doing all the anastomoses. In the immediate postoperative period, generalized hypokinesia and right ventricle failure were identified, which resulted in refractory cardiogenic shock, despite maximum adrenergic support and intra-aortic ballon assistance. The worsening of the clinical condition motivated, firsty, the implementation of VA-ECMO as a cardiorespiratory assistance device (bridge to recovery), and in the next day, the implantation of Impella, for left ventricle unloading and support. After this, the patient cardiac condition steadily improved and VA-ECMO and Impella were removed on the 5th day and the 12th day after surgery, respectively. The patient clinical evolution was affected by several factors, like bleeding on the cannulation site, febrile syndrome of unknown aetiology, suspected cerebrovascular event and acute kidney injury.

Conclusions: In this case-report, the concomitant use of VA-ECMO and Impella (ECPELLA) remarkably improved refractory cardiogenic shock by increasing the cardiac output and unloading the left ventricle. Nevertheless, the sucess of this technique is highly dependent of the different multidisciplinary teams, in the understanding of the physiological effects and possible complications associated with the different techniques and procedures.

Adult - Respiratory failure

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The ProtekDuo in ECMO configuration for ARDS secondary to COVID-19 - a systematic review

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Objectives: Assessment of the literature on the ProtekDuo cannula when used as venopulmonary (V-P) extracorporeal membrane oxygenation (ECMO) in ARDS secondary to COVID-19.

Methods: Systematic literature search in EMBASE, Medline (Pubmed) and NHS library using appropriate keywords as well as PICOS and PRISMA approach.

Results: We found 285 publications, of which 5 publications met the search criteria and were included in this review. A total of 194 patients with COVID-19 related ARDS had a ProtekDuo placed to establish veno-venous (V-V) ECMO and right ventricular (RV) support. Patients treated with the ProtekDuo cannula had survival rates between between the studies of 59 and 89%, with a significant survival compared to an invasive ventilation group or when compared to dual site V-V ECMO or other double lumen ECMO cannulas. One of the studies focused on extubation and early discontinuation of ventilator support, which the authors achieved in 100% of ProtekDuo patients. The incidence of acute kidney injury (AKI) and use of continuous renal replacement therapy (CRRT) was significantly reduced in the ProtekDuo versus other groups.

Conclusions: The ProtekDuo displayed lower mortality rates, AKI occurrence and CRRT need as compared to other respiratory support modalities and has shown to be a game changer for ECMO support in patients suffering from COVID-19 ARDS. Many authors suggested the ProtekDuo for first line use in these patients.

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Extracorporeal membrane oxygenation in adult burn care

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Objectives: We conducted a systematic review of the role of extracorporeal membrane oxygenation (ECMO) in adult patients with burn and smoke inhalation injury.

Methods: A literature search was addressed according to specific key words (burn, burn injury, major burns, inhalation injury and smoke inhalation). The review was based on the PICOS approach and the PRISMA flow chart.

Results: Twenty two articles out of 265 were considered suitable for the analysis. Eleven single case reports; two case reports with two patients each; one case reports with three patients; two case series with five patients each; four case series with six, eight, 11 and 14 patients; two retrospective reviews with 20 and 30 patients. Prospective randomised trials were not available. The total number of patients was 117. Age range was 19-69 years. Variable survival rates observed ranging between 16.67% and 80%. ECMO support duration and total body surface area burn (TBSA) were the key factors.

Conclusions: ECMO may have a role to play in adult patients sustaining burn and inhalation injuries despite the limited number of available studies. Venovenous ECMO seems to achieve better survival with outcomes comparable to non-burn patients. ECMO treatment may not be used as salvage treatment but remains an option if a positive outcome is considered a likely event.

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Veno-venous extracorporeal membrane oxygenation should be considered early in patients with traumatic brain injuries and severe respiratory failure

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Objectives: Veno-venous extracorporeal membrane oxygenation (VV ECMO) can support trauma patients with severe respiratory failure. Its use in traumatic brain injury (TBI) may raise concerns of worsening complications from intracranial bleeding. However, VV ECMO can rapidly correct hypoxemia and hypercarbia, possibly preventing secondary brain injury. We hypothesize that adult trauma patients with TBI on VV ECMO have comparable survival to trauma patients without TBI.

Methods: Our single center, retrospective cohort study included all trauma patients with and without a discharge diagnosis of TBI treated with VV ECMO over an 8-year period. Univariable analysis was performed. After testing for normality, significance was defined as a $P < 0.05$.

Results: Seventy-five trauma patients were treated with VV ECMO; 36 (48%) had TBI. Of those with TBI, 19 (53%) had a hemorrhagic component. Survival was similar between patients with and without a TBI (72% versus 64%, p=0.45). TBI survivors had a higher admission Glasgow Coma Scale (7 versus 3, p<0.001) than non-survivors. Though admission oxygen saturations were similar between TBI survivors and non-survivors (93% versus 95%, p=0.62), pre-ECMO oxygen saturations were higher in survivors (86% versus 77%, p=0.03). Evaluation of prognostic scoring systems on initial head CT demonstrated TBI VV ECMO survivors were more likely to have a Rotterdam score of 2 (62% versus 20%, p=0.03) and no survivors had a Marshall score ≥ 4. Twenty-nine (81%) patients had a repeat head CT on VV ECMO with one incidence of expanding hematoma and one new focus of bleeding. Neither patient with a new/worsening bleed received anticoagulation. Survivors demonstrated favorable neurologic outcomes both at discharge and outpatient follow-up, based on their mean Ranchos Los Amigos scale (6.5, SD 1.2), median Cerebral Performance Category (2, IQR 1-2), and median Glasgow Outcome Scale-Extended (7.5, IQR 7-8).

Conclusions: Adult trauma patients with TBI on VV ECMO have the same survival compared to trauma patients without TBI. They have good neurologic outcomes despite a low admission GCS. VV ECMO may minimize secondary brain injury and should not be withheld from patients with TBI.

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Omicron driven ECMO in a vaccinated critically ill patient

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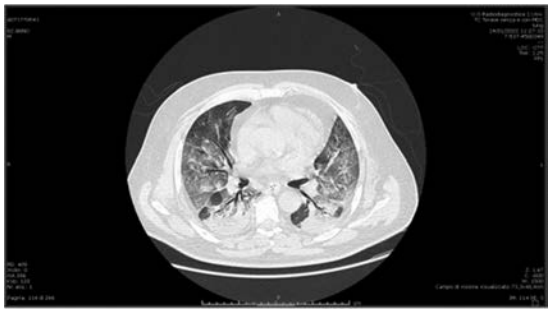
Objectives: Reporting a case of a COVID-19 vaccinated patient admitted to our intensive care unit

with severe acute respiratory failure due to SARS-CoV2 - Omicron variant, rapidly deteriorating requiring intubation, prone ventilation, and ECMO support.

Methods: A 62 years old Caucasian male was admitted in ICU for rapidly deranging respiratory failure and fever which occurred over the previous 24h. The patient received two doses of SARS-CoV2 vaccine (Oxford, AstraZeneca), the last one over five months before onset of symptoms. The patient was admitted to the intensive care unit (ICU) with tachypnea, low peripheral saturation (80%), elevated serum creatinine (2.4 mg/dl), and mild obesity (BMI 34,6). Pressure support ventilation trial (2 hours) failed carryng out to orotracheal intubation and protective ventilation.



Worsening of respiratory exchanges (5 th day from the admission) required a rescue prone ventilation cycle, in the meantime an indication was given to the placement of veno-venous ECMO. The cannulation site was femoro-femoral and the configuration used was V_{ivc}25-V_a21, according to the current ELSO nomenclature; ECMO flow was progressively increased until a peripheral saturation of 95% was obtained.

Results: The patient passed out after 2 month of extracorporeal support with no sign of recovery of pulmonary and renal function.

Conclusions: Unlike evidences showing a lower symptomatic engagement of the Omicron variant SARS-CoV2 positive patients, we have witnessed a rapid and massive pulmonary involvement. The short time that passed from the onset of symptoms and the rapid decay of respiratory function required rapid escalation of the intensity of care up to extracorporeal support. The patient showed previous pathologies that can lead to suspicion of a loss of immune coverage given by the vaccine, in addition to the long time elapsed since the last dose.

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Long-term functional outcome of severe COVID-19 pneumonia treated with venovenous extracorporeal membrane oxygenation support – learnings from a single centre

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Objectives: Implementation of venovenous extracorporeal membrane oxygenation (VVECMO) allowed survival of patients with severe respiratory failure associated with SARS-CoV-2 infection. However, VVECMO treatment is usually associated with long ICU stays, prolonged sedation, and neuromuscular blockage days. Functional disability, due to delirium and acquired muscle weakness, is frequently an inevitable burden causing long term disability. This study aims to analyse main characteristics of patients under ECMO due to COVID-19 pneumonia, their outcomes and functional status six months after ICU discharge.

Methods: Retrospective review of a prospectively collected database in an ECMO referral centre. All patients receiving VVECMO for SARS-CoV-2 infection were included. Epidemiological and clinical data were reviewed. Functional status at 6 months after ICU discharge was assessed with modified Rankin Scale (mRS).

Results: Ninety-three patients were included (29% female). Median age was 54±12 years, mean SOFA was 5.7±2.9, mean SAPS II was 35.6±13.6. Mean time from intubation to cannulation was 5±5.6 days in 91 patients; awake-ECMO was performed in 2 patients. Mean ECMO run duration was 33.1±30 days (longest ECMO run was 194 days). A period of awake-ECMO was performed on 36.5% of patients, during 16.4±21.2 days. ICU-acquired weakness was diagnosed on 64.5% of patients and delirium on 63.4%. Mortality was 24.7% (23 patients) with only 1 patient deceased in hospital after ICU discharge. At

6 months follow-up, all patients were still alive and most of them (65.1%) were independent on all daily activities (mRS ≤ 2).

Conclusions: Patients with severe COVID-19 treated with VVECMO support had very good functional outcomes at six-month follow-up. Despite long ICU length-of-stay, high incidence of delirium and acquired muscle weakness, full recovery at six-month post-ICU discharge was achievable in most patients

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Successful ECMO course in an Acquired Immune Deficiency Syndrome (AIDS) patient with ARDS complicated by pneumocystis jirovecii pneumonia and COVID-19: A unique case

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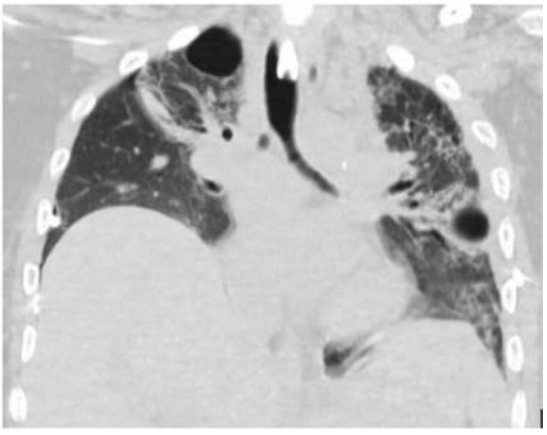
Objectives: Reviewing current literature and case reports of patients placed on Venous-Venous ECMO support for HIV and AIDS, with confection with Pneumocystis pneumonia and covid-19 pneumonia. The use of extracorporeal membrane oxygenation (ECMO) in patients who have acute respiratory distress syndrome has been shown to have very good outcomes. However, there is limited data to support the initiation of ECMO in patients who have human immunodeficiency virus infection with or without acquired immune deficiency syndrome.

Methods: We present a unique and challenging case of a 30 year old male, with no known past medical history, unvaccinated against covid-19, who presented with one week of progressive shortness of breath. On admission he was found with moderate bilateral infiltrates and was diagnosed with covid-19 pneumonia. Despite appropriate medical therapy, patient developed worsening hypoxic respiratory failure. Found to have elevated (1-3)-β-d-glucan and tested positive for HIV. CD4 count 11, HIV viral load 70,000. The patient remained severely hypoxemic despite mechanical ventilation, sedation, paralytics and proning. Venous venous extracorporeal membrane oxygenation was initiated. Considering his non improvement with variety of antivirals and antibiotics and with elevated (1-3)-β-d-glucan in the setting of AIDS he was treated for presumed Pneumocystis pneumonia. The patient tolerated proning while on VV ECMO and his course was complicated with bilateral pneumothorax necessitating chest tube placement.

Figure 1: CT chest with contrast approx 40 days into VV ECMO support



Results: The patient successfully completed 64 days on VV ECMO, where he was treated for PCP pneumonia, covid pneumonia, CMV viremia and tolerated initiation of anti-retroviral therapy. Patient was successfully decannulated, and ultimately discharged from the hospital.

Conclusions: VV-ECMO can be a beneficial intervention with successful outcomes in severely immunocomprimised patients with AIDS. This case highlights the importance of minimizing sedation and early mobilization on ECMO support.

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Echocardiographic findings in critically Ill patients with COVID-19 treated with and without extracorporeal membrane oxygenation

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Objectives: There is a paucity of data on echocardiographic findings in patients with COVID-19 supported with Venovenous Extracorporeal Membrane Oxygenation (VV ECMO). This study aimed to compare baseline echocardiographic characteristics of mechanically ventilated patients for acute respiratory distress syndrome (ARDS) due to COVID-19 infection with and without VV ECMO support and to describe the incidence of new echocardiographic abnormalities in these patients.

Methods: Single-center, retrospective cohort study of patients admitted from March 2020 to June 2021 with COVID-19 infection, that required mechanical ventilation, and had an available echocardiogram within

72 hours of admission. Follow-up echocardiograms during ICU stay were reviewed.

Results: A total of 242 patients were included in the study. One-hundred and forty-five (60%) patients were supported with VV ECMO. Median (IQR) PaO_2/FiO_2 was 76 (65–95) and 98 (85–140) in the VV ECMO and non-ECMO patients, respectively ($P = < 0.001$). On the admission echocardiograms, the prevalence of left ventricular (LV) systolic dysfunction (10% vs 15%, P= 0.31) and right ventricular (RV) systolic dysfunction (38% vs. 27%, $P = 0.27$) was not significantly different in the ECMO and non-ECMO groups. However, there was a higher proportion of acute cor pulmonale (41% vs. 26 %, $P = 0.02$) in the ECMO group. During their ICU stay, echocardiographic RV systolic function worsened in 44 (36%) patients in the ECMO group compared with six (10%) patients in the non-ECMO group ($P< 0.001$). The overall odds ratio for death for patients with worsening RV systolic function was 1.8 (95% confidence interval 0.95-3.37).

Conclusions: Echocardiographic findings suggested that the presence of RV systolic dysfunction in COVID-ECMO patients was comparable to the non-ECMO group on admission. However, a higher percentage of patients on ECMO developed worsening RV systolic function during follow-up.

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Successful Inter-Professional Team (IPT) collaboration in the care of peripartum women with COVID-19 on Extracorporeal Membrane Oxygenation (ECMO)

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Objectives: To describe the IPT collaborative approach for peripartum women with COVID-19 on ECMO and report the intervention outcomes.

Methods: A retrospective electronic health record review was performed from January 2020 through January 2022. All peripartum women on ECMO with COVID-19 admitted to the cardiothoracic intensive care unit (CTICU) were included. The IPT came together to coordinate peripartum care and delivery. An algorithm was created to outline the roles and workflow in the care of these patients. The outcomes evaluated included delivery method, timing, and location, maternal survival at discharge, maternal ICU length of stay (LOS), and neonatal survival

Results: Thirteen Peropartum women were placed on ECMO (5 antepartum and 8 postpartum, ages 27-42). None had been vaccinated against COVID-19. All received femoral vessel cannulation (11 venovenous and 2 venoarterial). Four patients underwent Caesarean-section delivery while on ECMO. Maternal survival to hospital discharge was 84.6%. All neonates survived with COVID-19 negative status.

Conclusions: The collaborative IPT approach with a structured algorithm facilitated survival outcomes. This report adds to the limited literature on peripartum. ECMO and provides insights to consider in planning for the care of these patients.

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Defining health states to assess the cost-effectiveness of interventions in laryngectomized patients

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Objectives: To assess the cost-effectiveness of heat and moisture exchangers (HMEs) for laryngectomized patients, cancer-based health states (i.e., disease free, recurrent cancer, and death) are commonly used in decision models. However, the effect of HMEs is not reflected in a change in cancer state, but rather in an improvement in health-related quality of life (HRQoL) due to reduced cough and sputum symptoms and impact. The aim of this study is to investigate whether the Cough and Sputum Assessment Questionnaire (CASA-Q) can be used to identify health states that distinguish in HRQoL, or utility, for cost-effectiveness models.

Methods: Patient-level data from a clinical study was used to determine whether the CASA-Q can inform health states that distinguish in HRQoL. The EuroQol-5-dimensions (EQ-5D) and CASA-Q were administered in 40 patients with three different measurement moments (i.e., 120 measurement moments). The cut-off scores were informed by literature. Correlations between the CASA-Q domains and EQ-5D were calculated to assess the level of convergence. One-way ANOVA was used to assess the magnitude of differences in the utility scores across the health states.

Results: The correlation between the EQ-5D and CASA-Q indicate a moderate level of convergence for the cough impact (r=0.32; p=0.0005), sputum symptoms

(r=0.46; p<0.0001), and sputum impact (r=0.59; p<0.0001) domains. The correlation between the cough symptoms domain is weak (r=0.20; p=0.03). Based on the sputum impact domain, three health states with their cut-offs were distinguished: no to mild sputum impact (SPUI=>94), moderate sputum impact (64<=SPUI<94), and severe sputum impact (SPUI<64). The utilities of these health states were 0.9183, 0.8009, and 0.6228, respectively. There was a statistically significant difference in utilities between health states as demonstrated by one-way ANOVA (F(1,118)=36.3, p<0.0001).

Conclusions: The sputum impact domain of the CASA-Q may be suitable to differentiate health states for cost-effectiveness models and capture improvements in HRQoL in laryngectomized patients. These health states may provide a more sensitive choice and complement the current available models.

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Prolonged unconsciousness in severe COVID-19 infection with veno-venous ECMO support

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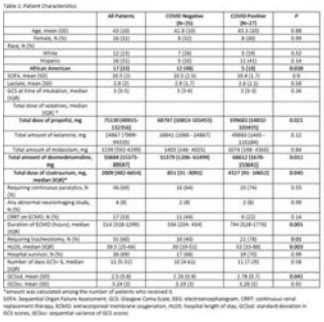
Objectives: Patients with severe COVID-19 infections have been shown to have prolonged periods of coma followed by meaningful neurological recovery. Therefore, neurological prognostication is challenging, particularly in those who require veno-venous extracorporeal membrane oxygenation (VV-ECMO) support. We hoped to evaluate which variables can be considered when trying to predict neurological recovery.

Methods: We conducted a case-control retrospective chart review of patients on VV-ECMO from March 2020 to January 2022. This time-frame was selected to limit the effect of post-pandemic changes in sedation practices. Our outcome was duration of unconsciousness, defined as days with GCS motor score <6. We first conducted a matched cohort analysis, comparing COVID and non-COVID patients. We then performed a Classification and Regression Tree (CART) analysis to determine the Relative Variable Importance (RVI) of clinical variables associated with duration of unconsciousness.

Results: Our matched analysis included 52 patients, 27 (52%) of whom had COVID-19. There were no significant differences in the baseline characteristics of the groups (Table 1). Patients with COVID-19 had a significantly longer median duration on ECMO (p<0.001) and hospital length of stay (p=0.003). The median duration of unconsciousness was similar between COVID-19 and non-COVID patients (p=0.58). The CART analysis results (Figure 1) showed that the most important variables to predict duration of unconsciousness were successive variations in GCS (RVI 100%) and GCS standard deviation (RVI 99%). COVID positivity only had a weak predictability (RVI 4%).



Conclusions: Our analysis has shown that in patients on VV-ECMO, those with COVID-19 spent a longer time on ECMO and in the hospital. While there was no significant difference in the duration of unconsciousness, we found that patients who had high fluctuations of GCS during ECMO had a shorter duration of coma.

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Development of a combined, highly integrated extracorporeal lung and kidney support device (RenOx): Evaluation of fibre configurations on gas exchange preservation

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Objectives: We aim to develop a novel artificial lung that integrates lung and kidney support in a single device by combining oxygenation and haemodialysis fibres in

the same housing. For this, we investigated how many oxygenation fibres can be replaced by haemodialysis fibres to maintain 90% of the oxygenator's gas exchange capacity and what influence fibre configuration has on this.

Methods: Fibre bundles consisted of stacked oxygenation fibre mats (Oxyplus™ 90/200,3M) placed perpendicularly and/or crossed in a 24° angle on top of each other. Bundles in perpendicular configuration had 50% of fibres closed ($Oxy50_P$), 25% fibres closed ($Oxy75_P$), or all fibres open ($Oxy100_P$). Bundles in crossed configuration had $^1/_3$ of fibres closed ($Oxy67_C$), or all fibres open ($Oxy100_C$). Closed fibres did not contribute to gas exchange, simulating haemodialysis fibres. Oxygen transfer was measured during blood tests performed according to ISO 7199: 2016.

Results: Results show that 25% of oxygenation fibre layers in perpendicular configuration could be closed keeping 90% of the oxygen exchange efficiency of our oxygenator. We found no statistically significant difference in oxygen transfer for bundles with 25% of perpendicular fibres closed and bundles with all fibres open. Moreover, up to 140 mL/min, these bundles were able to deliver oxygen above 55 mL_{Oxygen}/L_{Blood}. A higher number of fibres could be closed in perpendicular than in 24° angle causing a lower decrease in oxygen transfer. Below 140 mL/min, closing 33% of 24° angled fibres or 50% of perpendicular fibres resulted in an equal decrease in oxygen transfer by 20%.

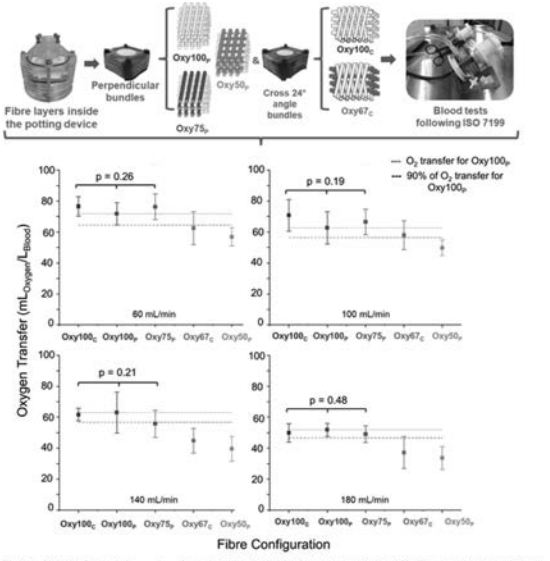

Figure: O_2 transfer (■ mL_{Oxygen}/L_{Blood}) ± standard deviation from the mean (n=10). There was no statistically significant difference in mean oxygen transfer for $Oxy75_P$ and the fully open oxygenator (ANOVA p>0.1)

Conclusions: Results show that 25% perpendicular oxygenation fibres can be replaced by haemodialysis fibres maintaining 90% of the oxygen exchange capacity of our oxygenator. This is one step towards combining pulmonary-renal support in one device.

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Lung and serum immune monitoring during acute lung injury supported with VV-ECMO – a malaria-ARDS case supporting feasibility

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Objectives: Feasibility study for immune monitoring of cell-associated markers in the BALF/blood in patients under VV-ECMO.

Methods: A 52-year-old male with malaria-ARDS required rapidly escalating support that culminated in a 16-day extracorporeal support run. Peripheral blood (PB) was obtained at 4 timepoints (TP) and BALF collected during bronchoscopy performed for clinical reasons at 3 timepoints (Figure 1). A further 2 TP were obtained at recovery (2 weeks post discharge, 10 months post-illness). A flow cytometry tube with 24 markers targeting T cells and innate lymphoid cells (ILC) was acquired with spectral flow cytometer (Aurora, Cytek) and analysed using FlowJo.

Results: During critical illness absolute lymphocyte count was always above 1000cells/uL (1470-3150). PD-1, a possible therapeutic target to modulate critical illness associated immune paralysis, was increased in PB on all lymphocyte subsets, only remitting in the last TP in T cells (from 63% to 34% in CD8 T cells, and 42.3 to 25.7% in CD4 T cells), but decreasing steadily since TP1 (31% in TP1 to 0.5% in TP6) in ILCs. PD-1 was found to be always very high in the BALF both in T-cells (85-100%) and ILC (12-38%). Conversely, the recent activation cell marker CD69 decreased consistently in the blood from the first TP onwards (CD8: 22 to 3.2%; CD4: 4.7 to 0.8%) despite peaks of inflammation associated with nosocomial infection. CD69+ expression in the BALF is known to reflect both cell activation and tissue residency. Nevertheless, there was a peak of CD69 expression homogenous in T cells in TP2 (63 vs 93%), coincident with an episode of *K. pneumoniae* VAP. Extracorporeal support did not alter PD-1 or CD69 expression in circulating lymphocytes.

Conclusions: The distinct kinetics of PD-1 levels according to cell subpopulation and location should be considered when repurposing drugs targeting this immune checkpoint. Immune monitoring of cell-associated

markers throughout critical illness is feasible and likely useful in the setting of chronic critical illness.

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Analysis of long run VV-ECMO runs based on variation in sweep gas flow: a case series

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Objectives: The average length of ECMO and the number of patients requiring prolonged ECMO support is increasing. For these patients requiring, it can be difficult to determine who will recover. The objective of this study is to determine if sweep gas flow (SGF) trajectory is a predictor of subsequent decannulation.

Methods: We conducted a retrospective review of patients requiring prolonged VV ECMO support, defined as greater than 12 days (average ECMO run per ELSO), at a tertiary academic medical center between January 2021 through March 2022. Demographic information, outcome and daily SGF was recorded. Analysis was limited to the first 11 days of support to eliminate the weaning phase from the data.

Results: 10 patients requiring ECMO support for 12 days or longer were identified. Six of the patients were male with a median age of 40.5 years (IQR: 32,48). All patients required ECMO for ARDS for a median duration of 27 days (IQR: 13, 49). Deceased patients required longer ECMO support than those that survived (32 days [IQR: 13, 49] vs 13 days [IQR: 12, 49]; p=0.011). The median SGF was higher in those that died compared to those that were decannulated (6 L/min [IQR: 4.3, 6.5] vs 4 L/min [IQR: 2.5, 5.0]; p<0.001). As SGF increased over time, the odds of decannulation decreased (OR: 0.38; 95% CI: 0.12-1.15), though the relationship was not statistically significant (p=0.087).

Conclusions: Patients who require prolonged ECMO support are more likely to die if SGF requirements remain high. When considering continued support vs withdraw, a decreasing or fluctuating SGF could imply recoverable disease.

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Purulent oxygenator - infected thrombosis causing venovenous extracorporeal membrane oxygenation dysfunction in a patient with chronic thromboembolic pulmonary hypertension

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Objectives: Infection and thrombosis are serious risks with extracorporeal life support. We report a unique case of a patient on VV-ECMO who developed severe bacteremia leading to gross purulence and thrombosis of the membrane oxygenator

Methods: A 41 year old female with history of asthma, HIV, bacteremia, and recent unsuccessful endovascular thrombectomy for acute on chronic thromboembolic pulmonary hypertension (CTEPH) presented with syncope and acute hypoxemia. CT scan confirmed an acute massive right main pulmonary artery thromboembolism on top of chronic clot burden. Echocardiography demonstrated right heart strain and pulmonary hypertension consistent with CTEPH. Due to clinical decompensation, she was intubated, cannulated for VA-ECMO, and transferred to our facility for further surgical intervention. Due to persistent bacteremia, her surgery was delayed. An attempt to decannulate her was unsuccessful due to hypoxia and she was re-cannulated for VV-ECMO with a single site dual lumen cannula. Five days later, a circuit exchange was performed due to oxygenator and circuit thrombosis. This was followed by septic shock due to Klebsiella bacteremia. Two days later, purulence was noted at the cannula along with pus-appearing material in the oxygenator.

Results: Given her continued state of septic shock and concern for incomplete resolution with antibiotics alone, she was decannulated from the single

cannula site and recannulated via femoral venous drainage cannula and a left subclavian venous return cannula. She subsequently had hemodynamic improvement, underwent successful pulmonary thromboendarterectomy, and was ultimately discharged home.

Conclusions: ECMO has risk of thrombosis and infection that can lead to gross purulence to the circuit. Vigilant sterile practices, early identification of clinical changes, and empiric antibiotics are essential in management of these patients. Additionally, circuit exchanges and cannula replacement may be necessary to obtain infection control.

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Subphenotypes of severe ARDS patients on vv-ECMO based on early trends of respiratory system compliance

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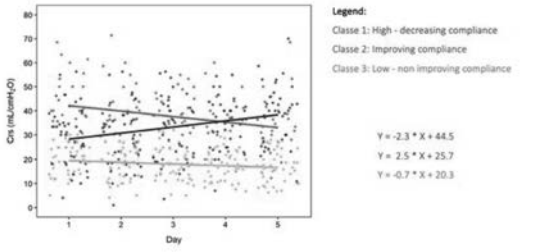
Objectives: Respiratory system compliance(Crs) could be an important prognostic factor in patients with the acute respiratory distress syndrome(ARDS) receiving veno-venous extracorporeal membrane oxygenation(vv-ECMO). We analyzed the correlation between trends of Crs during the first 5 days of ECMO and clinical outcome.

Methods: We conducted a single center observational cohort study of all consecutive adult patients treated with vv-ECMO for severe ARDS between 2012 and 2021. Exclusion criteria were death or switch to assisted ventilation before vv-ECMO day 5. We collected clinical and physiologic variables during the first 5 days of vv-ECMO support. A trajectory analysis model(Growth Mixture Model) was applied to identify subphenotypes of patients with homogeneous trends for Crs.

Results: 111 patients were enrolled and a growth mixture model with three classes yielded the lowest value for Bayesian Information Criteria(3761.8). Patients in the "High-decreasing compliance" class (n=25-23%) showed higher day 1 Crs (40[38-50]mL/cmH_2O), followed by a decreasing trend. "Improving compliance" class (n=39-35%) started by lower Crs values (31[19-39]mL/cmH_2O) and showed a clear improvement from day3. Finally, "Low-non-improving compliance" patients (n=47-42%) were characterized by low day 1 Crs (22[16-25]mL/cmH_2O) without subsequent improvement. Hospital mortality differed between classes (28% *vs.* 15% *vs.* 57%, p=0.0002). Multiple logistic regression model showed that subphenotype with "Low-non-improving compliance" independently predicted mortality, even after correction for clinical severity and etiology (Table 1).

Figure 1



This graph shows the average Crs trend estimated by the model for the three groups of patients (Classes) identified. The solid lines represent the trajectories derived from the Growth Mixture Model.

Parameters	OR	IC 95%	p
Univariate analysis for Prediction of mortality			
Age	1.05	1.00-1.09	0.02
Sex	0.79	0.35-1.78	0.56
BMI	0.99	0.93-1.05	0.71
Acute Illness:			
- Covid-19 vs Bacterial	2.71	1.06-6.95	0.04
- H1N1 vs Bacterial	0.43	0.11-1.69	0.23
- Others vs Bacterial	2.17	0.49-9.65	0.31
Pre ECMO Intubation days	1.21	1.07-1.38	0.004
SOFA	1.10	0.91-1.32	0.32
SAPSII	1.01	0.97-1.05	0.75
Resp	0.70	0.53-0.93	0.01
ECMO support days	1.03	1.00-1.05	0.04
Mechanical Ventilation days	0.99	0.98-1.01	0.65
ICU Length of Stay	0.99	0.97-1.01	0.28
Growth Mixture Model classes:			
- Improving Crs *vs* High-decreasing Crs	0.47	0.14-1.60	0.23
- Low-non improving Crs *vs* High-decreasing Crs	3.47	1.22-9.89	0.02
- Improving Cr vs Low-non improving Crs	0.14	0.05-0.38	0.0002

(continued)

(continued)

Parameters	OR	IC 95%	p
Mutivariate Stepwise analysis for independent predictors of mortality			
Age	1.06	1.01-1.11	0.01
SOFA	1.28	1.01-1.60	0.03
Improving Cr *vs* High-decreasing Crs	0.40	0.11-1.49	0.17
Low-non improving Crs *vs* High-decreasing Crs	5.00	1.61-15.51	0.005
Improving Cr vs Low-non improving Crs	0.08	0.02-0.27	<0.0001

Conclusions: In ARDS patients undergoing ECMO, trends of compliance over the first days of support could predict patient's outcome.

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Development of a machine learning prediction model for oxygenator replacement during veno-venous ECMO using electronic health records

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Objectives: Oxygenator exchanges need fit regularly performed during VV-ECMO treatment to avoid severe complications such as thrombosis. Currently, only individual clinical markers, such as D-Dimer or fibrinogen levels are used, and more sophisticated predictor models might be helpful. The aim fit study was to develop a prediction model for oxygenator replacement during VV-ECMO treatment using electronic health record (EHR) time series data.

Methods: We conducted a retrospective cohort study of VV-ECMO patients (01.01.2018-12.01.2022) in the ARDS and ECMO Centre Cologne-Merheim. Only patients with controllable documentation in the patient data management system on replacement events were included. Demographic data as well as time series data such as laboratory findings, vital signs and ECMO parameters were integrated into the model. Data processing involved outlier removal, reduction to daily data points, scaling, missing value handling, feature selection and further transformations. We used machine learning algorithms like extreme gradient boost to develop a prediction model fit of remaining useful lifetime (RUL) fit oxygenator. The performance fit model was evaluated using RMSE, R2 and mean SHAP values to reveal the feature importance.

Results: A total of 132 VV-ECMO patients (age (years) – mean: 53.7, SD:12.6; male: 98 (74.2%); mortality: 51 (38.6%); mean ICU stay length (days): 43.2 (IQR: 23.8-51.0)) were included in the study. In the total of 5705 treatment days fit cohort, 363 oxygenator exchanges were recorded. After processing 3152 daily datapoints with 74 parameters were analyzed. D-Dimers, ECMO duration and fibrinogen could be identified with the highest influences on the replacement. The RUL (0-100) prediction model had an RMSE of 23.6 and R2 of 0.2.

Conclusions: Our study demonstrates the partial feasibility of predicting oxygenator replacements during VV-ECMO treatment using EHR data. It could potentially be used to identify patients states at high risk for oxygenator replacements and guide the development of targeted prevention strategies. Further research is needed to validate the model in other clinical settings and to determine the optimal set of variables for predicting oxygenator exchanges in this population.

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Pneumothorax in patients with ARDS requiring V-V ECMO

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Objectives: Pneumothorax is a serious complication affecting outcome in patients with acute respiratory distress syndrome (ARDS) requiring invasive mechanical ventilation. In this study, we investigated the incidence and risk factors for pneumothorax in severe ARDS patients managed with VV-ECMO.

Methods: This is a multicenter, retrospective study of adult ARDS patients managed with V-V ECMO from January 2012 to December 2021. Patient characteristics (age, gender, BMI, comorbidities, SOFA score), etiology of ARDS, respiratory management (ventilator settings, neuromuscular blocking agents), corticosteroid use, and complications of pneumothorax were investigated.

Results: A total of 158 patients from three hospitals were identified, of which 123 (78%) were male. The median [quartile] age was 63 [52-60], BMI was 24.6 [22.1-28.9], and SOFA score at admission was 13 [12-15]. The most common comorbidities were hypertension (n=58, 37%), diabetes (n=40, 25%), and chronic respiratory diseases (n=32, 20%) (emphysema, n=13 (8%); bronchial asthma, n=8 (5%); interstitial pneumonia, n=11 (7%)). Nineteen patients (12%) had complicated with pneumothorax. The mortality rate at ICU discharge was significantly higher in patients with pneumothorax than in those without pneumothorax (78% vs. 33%,

p=0.005).The duration of ECMO (days) was significantly longer in the pneumothorax group (18 [15-28] vs. 10 [7-16], p = 0.006). Patients with pneumothorax had significantly higher rates of interstitial pneumonia as the underlying lung diseases (42% vs. 12%, p=0.02) and corticosteroid use before V-V ECMO (73% vs. 46%, p=0.03).

Conclusions: Pneumothorax complicated with ARDS requiring ECMO could contribute fit higher mortality rate. Interstitial pneumonia and corticosteroid use were associated with the occurrence of pneumothorax.

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Single centre, cross-sectional assessment of airway hemorrhage in a cohort of patients with COVID-19-associated ARDS under Venovenous extracorporeal membrane oxygenation

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Objectives: Airway hemorrhage (AH) frequently complicates extracorporeal membrane oxygenation (ECMO) treatment. Inflammation, coagulopathy and antithrombotic therapy are contributing factors. Patients with COVID-19-associated ARDS (CARDS) supported with ECMO present all these features. We aim to characterize the incidence and the clinical and prognostic impact of AH.

Methods: Review of a cohort of patients with CARDS treated with ECMO support at a single ECMO centre between March 2020-February 2022 (n=92). AH was defined as a clinically significant hemorrhage fit demanded interruption of anticoagulation, transfusional support or bronchoscopy. Univariate analysis was performed using GraphPadPrism®.

Results: One third (n= 31) of patients with CARDS treated with ECMO had clinically significant AH. Patients who developed AH had significantly longer ICU length-of-stay (LoS), ECMO run and invasive mechanical ventilation (IMV) duration. Significant differences in coagulation and inflammatory markers were detected between patients with early (<72h) versus late (>9 days) onset of AH (Table 1). Mortality at day 90, demographics, comorbidities, CT scan pattern and clinical severity indexes were similar between patients with and without AH (NAH).

Conclusions: In patients with severe CARDS treated with ECMO support, the occurrence of airway hemorrhage leads to clinically important morbidity but does not increase mortality. Distinct pathways may be involved in the development of early v. late AH.

Table 1. Results (IQR).

	Early AH	Late AH	NAH	*P*
Age	56 (47-57)	49 (40-57)	52 (39-60)	*NS*
ICU LoS (days)	36 (19-56)	46 (31-78)	31 (21-47)	*NS*
IMV (days)	34 (19-51)	35 (28-49)	22 (14-39)	*NS*
Fibrinogen	600 (420-764)	291 (216-495)	-	*0.04*
Platelet	256 (231-305)	133 (86-172)	-	*0.003*
C-RP (IQR)	9.3 (6-16)	4.3 (0.2-8)	-	*0.05*
Procalcitonin	0.64 (0.38-2.5)	0.12 (0.09-0.2)	-	*0.007*

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Differences in nosocomial infections in patients on VV-ECMO for COVID-19 and influenza

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Objectives: In COVID-19 associated acute respiratory distress syndrome (ARDS) requiring VV-ECMO, ventilator-associated-pneumonia (VAP), pulmonary aspergillosis and viral reactivations are observed frequently, but there is only little knowledge on incidence, onset and causative pathogens. This study analyzes frequency of VAP, pulmonary aspergillus infections, and viral reactivations in a large cohort of patients with ARDS treated with VV-ECMO due to either COVID-19 or Influenza.

Methods: Retrospective analysis of all consecutively patients at the University Hospital Regensburg requiring VV-ECMO due to COVID-19 (March 2020 and May 2022) or Influenza (May 2012 and December 2022). VAP was diagnosed according to current guidelines. Pulmonary Aspergillosis met criteria of probable COVID-associated Aspergillosis according to current guidelines.

Results: 147 patients (age (median [IQR]) 55.3 [48.7 – 61.7], SOFA at VV-ECMO initiation 9 [8 – 12], 23 [14 – 38] days on VV-ECMO) suffering from COVID-19 and 72 influenza patients (age 55.3 [46 – 61.3], SOFA at VV-ECMO initiation 13 [10 – 15], 16 [10 – 23] days on VV-ECMO) were included in the analysis. Pulmonary superinfections were more frequent in COVID-19 than in influenza (VAP: 61% vs. 39%, pulmonary Aspergillosis: 33% vs. 22%, CMV reactivation: 19% vs. 4%, HSV reactivation: 49% vs. 26%.) The first episode of VAP in COVID-19 and Influenza was detected 2 days [1 – 15] after and 1 day (-3 – 22) before ECMO initiation, respectively. First VAP-episode in COVID-19 were mainly caused by *Klebsiella spp*. (29%,), *Staphylococcus aureus* (27%) and *E. coli* (11%). Further VAP-episodes (30% in COVID-19) and relapses of VAP were mainly caused by *Klebsiella spp*. (53%, 64%, respectively). In Influenza, VAP was mainly caused by *Staphylococcus aureus* (28%) and *Streptococcus pneumoniae*(28%), further VAP episodes were not observed.

Conclusions: Superinfections were common in patients treated with VV-ECMO and occur more frequently in COVID-19 ARDS compared to Influenza. VAP occurs early and may significantly contribute to the need of VV-ECMO. Therefore, a meticulous routine microbiologic workup is advisable. The observed differences in the spectrum of secondary infectious agents in COVID-19 compared to Influenza are not understood yet.

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Long-term support of COVID-19 patients with veno-venous extracorporeal membrane oxygenation: Complications, predictors of mortality and long-term outcome

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Objectives: Treatment of severe respiratory distress syndrome (ARDS) due to COVID-19 by veno-venous extracorporeal membrane oxygenation (VV-ECMO) had a mortality of up to 70% in Germany. Many patients with COVID-19 need VV-ECMO support longer than 28 days (long-term VV-ECMO). Evidence on mortality, complications during intensive care, functional status after discharge and mortality-predictors for patients supported with long-term VV-ECMO is lacking.

Methods: Retrospective study of 137 consecutive patients treated with VV-ECMO for ARDS due to COVID-19 at University Hospital Regensburg from March 2020 to March 2022.

Results: 38% (n=52; 87% male) of patients needed long-term VV-ECMO support. In these, SOFA score (median [IQR]) at ECMO initiation was 9 [8-11], age 58.2 [50.6–62.5] years, PaO2/FiO2-ratio 67 [52-88] mmHg, $pCO_2$62 [52–74] mmHg, Murray-Score 3.3 [3.0-3.6] and PEEP 15 [13 – 16] cmH2O. Duration of long-term support was 45 [35-65] days. 26 (50%) patients were discharged from the ICU. Only one patient died after hospital discharge. At VV-ECMO initiation, baseline characteristics did not differ between deceased and survivors. Complications were frequent (acute kidney injury: 31/52, renal replacement therapy: 14/52, pulmonary embolism: 21/52, intracranial hemorrhage 8/52, major bleeding 34/52 and secondary sclerosing cholangitis: 5/52) and more frequent in the deceased. Karnofsky index (normal 100) after rehabilitation was 70 [57.5-82.5]. Twelve of the 18 patients discharged from rehabilitation had a satisfactory quality of life according to their own subjective assessment. Four patients required nursing support. Mortality-predictors within the first 30 days on VV-ECMO only observed in those who deceased later, were: Bilirubin >5mg/dl for > 7 days, pulmonary compliance <10ml/mbar for >14 days, and repeated serum concentrations of interleukin 8 >150ng/L.

Conclusions: Long-term extracorporeal lung support in patients with COVID-19 resulted in 50 % survival and subsequently lead to a satisfactory quality of life and functionality in the majority of patients. It should preferably be performed in experienced centers because of a high incidence of complications. Several findings during the early course were associated with late mortality but need validation in large prospective studies.

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VV-ECMO in critical COVID-19 obese patients

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Objectives: Obesity is a condition prone to pose difficulties to a successful extra-corporeal membrane oxygenation (ECMO) support. Not being a contraindication, it yields significant challenges to physicians and may interfere with patient's outcome. The number of obese patients

supported by ECMO has increased during COVID-19 pandemic due to severe illness in this population. We designed a retrospective study in order to identify prognostic factors for 180-day survival in critical COVID-19 obese patients in venovenous ECMO (VV-ECMO).

Methods: Single-center retrospective cohort of critical COVID-19 adult patients in VV-ECMO, obese and overweight (according to WHO classification), admitted in a tertiary hospital's ICU from April 1st 2020 to May 31th2022. Univariate logistic regression analysis was performed to assess 180-day mortality differences.

Results: The analysis included 41 patients. The median [interquartile range (IQR)] age was 55 (IQR 45-60) years and 70,7% were male. Median body mass index (BMI) was 36 (IQR 31-42,5) Kg/m^2; 39% of patients had a BMI ≥40 kg/m^2. The sampling had 3 (IQR 1,5-4) days of invasive ventilation prior to ECMO and 63,4% were weaned from ECMO-VV support after a median of 19 (IQR 10-34) days. The median ICU length of stay was 31,9 (IQR 17,5-44,5) days. The invasive ventilation period was 30 (IQR 19-49,5) days. The 60, 90 and 180-day mortalities were 41,5%. On the univariate logistic regression analysis we found that higher BMI was associated with higher 180-day survival (odds ratio [OR] 1,157 (1,038-1,291), p 0,009). Younger age, female patients, less invasive ventilation time prior to ECMO and fewer complications at time of ECMO cannulation were associated with higher 180-day survival [respectively, OR 0,858 (0,774-0,953), p 0,004; OR 0,074 (0,008-0,650), p 0,019; OR 0,612 (0,401-0,933), p 0.022; OR 0.13 (0,03-0,740), p 0,022)].

Conclusions: In this retrospective cohort of critical COVID-19 obese adult patients supported by VV-ECMO, a higher BMI, younger age and female patients were associated with higher 180-day survival. A shorter invasive ventilation time prior to ECMO and fewer complications at ECMO cannulation were also associated with increased survival.

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Lung re-transplantation for COVID-19 related respiratory failure: A case report

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Objectives: We would like to report a case in which a COVID-19 patient who was transferred to our hospital due to a lack of medical resources due to the COVID-19 outbreak in Daegu, South Korea, on February, 2020, underwent double lung transplantation after 110 days with VV-ECMO support and performed double lung re-transplantation 865 days after lung transplantation.

Methods: ECMO was performed on a total of 69 patients with COVID-19-related acute circulatory/respiratory failure from February 2020 to December 2022. Among them, 16 patients were registered for lung transplantation, and 5 out of 16 registered patients performed lung transplants. One in five people who performed lung transplantation performed re-transplantation on the 865thday after transplantation.

Results: A 52-year-old female patient was transferred to our hospital, and VV-ECMO was performed the next day. The double lung transplantation was performed 112 days after hospitalization and was discharged 238 days after surgery. 668 days after lung transplantation, home O_2 was applied as bronchitis obliterans syndrome, and her lung function deteriorated rapidly later, and re-transplantation was decided. In the patient's HLA test, HLA class I cPRA% was 32% and HLA class II cPRA% was 100%. Desensitization was performed six times plasmapheresis with administrating Bortezomib and immunoglobulin, and then re-transplantation was performed on the 865th day after lung transplantation. The patient has maintained her daily life without any special complications other than the occurrence of central DI after surgery. The pathological findings of the lung previously transplanted to the patient were acute rejection (ISHLT grade A2), chronic airway rejection (ISHLT grade C1, B0), and chronic vascular rejection (ISHLT grade D1).

Conclusions: The long term result of patients who performed lung transplantation with COVID 19 related respiratory failure is still unknown. Therefore, even patients who have undergone long-term VV-ECMO support due to COVID 19 related respiratory failure are expected to achieve good results if lung transplantation is needed by carefully approaching and treating with a multidisciplinary approach.

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Medical intensivist directed VV ECMO cannulation for the facilitation of tracheostomy in a patient with severe tracheal stenosis: A case report

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Objectives: We present a case report of medical intensivist driven ECMO program using ECMO as a pre-procedural tool to maintain oxygenation in a patient with critical tracheal stenosis during tracheostomy placement.

Methods: VV ECMO is primarily used to support patients when mechanical ventilation is unable to

provide adequate gas exchange. Alternatively, it has been used pre-procedurally when intubation is required in anticipation of a difficult airway. Described here is the first intensivist preformed awake VV ECMO cannulation to facilitate tracheostomy in a patient with severe tracheal stenosis.

Results: The patient is a 41-year-old female with the relevant background of COVID19 pneumonia status post tracheostomy and subsequently decannulated after prolonged intubation and ICU stay. As a result, the patient developed symptomatic tracheal stenosis and presented two years after her ICU stay for scheduled bronchoscopy and balloon dilation. However, the patient developed worsening stridor and shortness of breath requiring heliox and BPAP. After multidisciplinary discussion between the critical care team ENT teams, the decision was made to cannulate for VV ECMO as a pre-procedural maneuver to allow for oxygenation during open tracheostomy in the OR. Dexmedetomidine and local anesthesia were used for the procedure with the patient sitting at 30 degrees on non-invasive ventilation and heliox. The patient was cannulated with a 21F right internal jugular return cannula and 25F right common femoral drainage cannula by medical intensivists in the intensive care unit using ultrasound guidance. The patient went for operative tracheostomy the next day and was subsequently decannulated from ECMO the following day without complication. She was discharged home on trach collar.

Conclusions: Intensivist performed ECMO cannulation has been shown to be safe and effective. We anticipate the indications and use will continue to expand. This case is an example that intensivist driven pre-procedural ECMO is a viable extension of that practice.

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Non-Intensive care unit feasibility for ambulatory veno-venous extracorporeal membrane oxygenation patients

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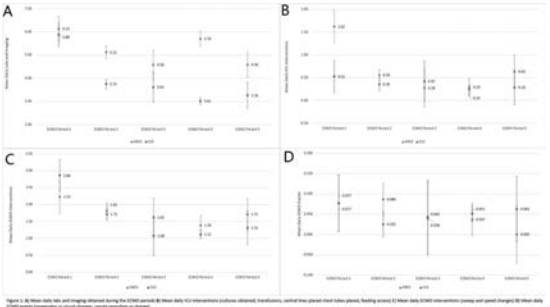
Objectives: Currently, veno-venous extracorporeal membrane oxygenation (VV-ECMO) support mandates intensive care unit (ICU) level care. However, patients who are stably supported and ambulatory may be suitable for lower acuity monitoring, and potentially discharge home. The purpose of this study was to evaluate daily interventions in ambulatory VV-ECMO patients.

Methods: A single-center, retrospective cohort study was performed on VV-ECMO patients who ambulated ≥100ft between 2014 and 2020. Patients were grouped as acute respiratory distress syndrome (ARDS) or Chronic Lung Disease (CLD). The frequency of daily interventions was collected and grouped as laboratory tests/imaging, ICU interventions (cultures obtained/transfusion/central line placement/chest tube placement/non-surgical feeding access), ECMO interventions (speed change ≥100rpm/sweep change), and ECMO events (oxygenator/circuit changes/cannula reposition/revision). The daily interventions were analyzed in discrete periods; (1) first 3 ECMO days, (2) days between first 3 and walking 100ft, (3) 3 days after walking 100ft, (4) days between walking and last 3, and (5) last 3 ECMO days.

Results: 28 ECMO runs were identified (14 ARDS and 14 CLD). CLD patients had a higher Respiratory ECMO Survival Prediction (RESP) score (p=0.002), longer duration of ECMO (p=0.05), and earlier liberation from the ventilator (p=0.01) than ARDS patients (Table). Laboratory/imaging data, ICU interventions and ECMO interventions were all most frequent during period 1 then subsequently decreased (Figure 1). After period 1, laboratory/imaging data was collected a mean 3.8 times/day (95%CI 3.7-3.9), while ICU interventions decreased to a mean of 0.35 times/day (95%CI 0.29-0.41). ECMO events were exceedingly uncommon, and after period 3, none were emergent. All 5 patients who died, had CLD with withdrawal of ECMO due to ineligibility for lung transplant.



	Overall (n=28)	ARDS (n=14)	CLD (n=14)	p-value
Age (y)	34 (IQR 25, 52)	34 (IQR 26, 50)	38 (IQR 26, 54)	0.51
Sex (Female)	10 (36%)	4 (29%)	6 (43%)	0.69
Pre-ECMO Ventilator Duration (d)	1 (IQR 0, 7)	1 (IQR 3, 7)	1 (IQR 0, 7)	0.50
RESP Score	0 (IQR -1, 4)	3 (IQR 1, 5)	-1 (IQR -2, 0)	0.002
Post-Cannulation Ventilator Duration (d)	13 (IQR 1, 29)	22 (IQR 12, 30)	1 (IQR 0, 16)	0.01
Time from cannulation to ambulation (d)	14 (IQR 5, 27)	15 (IQR 8, 23)	12 (IQR 2, 28)	0.63
Max distance ambulated on ECMO (ft)	600 (IQR 300, 731)	415 (IQR 281, 698)	615 (IQR 390, 785)	0.42
ECMO Duration (d)	32 (IQR 18, 76)	19 (IQR 13, 39)	47 (IQR 31, 88)	0.05
Survival to discharge/Lung transplant	23 (82%)	14 (100%)	9 (64%)	0.04

Conclusions: Patients stably supported on VV ECMO, particularly for CLD, are likely suitable for lower acuity care.

Conflict of interest: Aakash Shah and Bartley P. Griffith have consulted for Abiomed.

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Design and development of an oxygenator model for the use as a biohybrid lung

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Objectives: Conventional oxygenators provide lung support for a maximum of 30 days due to insufficient hemocompatibility of the gas exchange membranes. Membrane endothelialization can extend the application period and has been proven effective in small laboratory models. The Kolobow-designed spiral-coil oxygenator is particularly well suited for this purpose in combination with the spraying coating of endothelial cells. Thus, this work aims to design and fabricate a laboratory model of a spiral-coiled oxygenator and test it.

Methods: The work includes research on and procurement of suitable membranes and spacing materials, as well as the construction of housing and the design of appropriate seals and connections. Polydimethylsiloxane (PDMS) is used as a membrane material. 3D-air fabric and fiberglass sheets are used as a spacer on the gas side. Lastly, a final design is chosen for the laboratory model, which is 3D printed in-house and tested in vitro.

Results: The PDMS membrane of 50 µm thickness has sufficient strength for practical handling and processing. 3D air fabric and fiberglass sheet proved to have sufficient airflow and prevent inwards bulging. Nevertheless, deformations of the membrane envelope during assembly and by external pressure influences during operation are not optimal yet. The membrane envelope has a surface area of 0.2 m^2. The oxygenator is leak-proof up to a flow rate of 1000 ml/min. The priming volume reaches up to 350 ml. Pressure drop on the gas and liquid side is relatively low. The membrane envelope is subjected to a negative pressure of 100 mmHg to test the tightness of the envelope and there is no abrupt pressure loss during testing. Blood tests are performed for gas transfer and hemolysis.

Conclusions: An optimized oxygenator model for endothelialization via spraying is successfully designed, manufactured, and tested. It is cheap to manufacture, and the design allowed easy upscaling. Still, mechanical properties can be improved by further optimizing the spacer material in the blood and gas side. Here, the first step towards a non-microfluidic oxygenator laboratory model for endothelialization is achieved.

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Clinical characteristics, complications, and outcomes of severe COVID-19 ARDS patients supported by ECMO and triaged for lung transplantations

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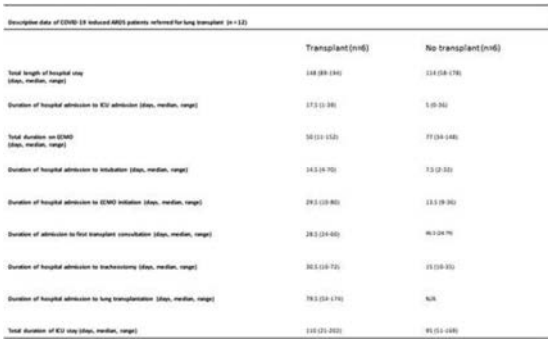
Objectives: More than 200 patients have benefited from lung transplantation who failed to recover from COVID-19-induced acute respiratory distress (ARDS) with conventional ventilatory support and/or extracorporeal membrane oxygenation support (ECMO) in USA. We aim to share our experience and lessons learned at our institute through this case series.

Methods: After IRB approval, we performed a retrospective chart review and identified 37 patients who received ECMO for COVID-19 induced ARDS between May 2020 through January 2022. Out of these, 12 received a formal consultation from the transplant

team. We studied patient characteristics, interventions during ECMO support, and evaluation outcomes.

Results:



	Transplant (n=6)	No transplant (n=6)
Total length of hospital stay (days, median, range)	148 (89-194)	114 (58-178)
Duration of hospital admission to ICU admission (days, median, range)	17.5 (1-34)	5 (0-26)
Total duration on ECMO (days, median, range)	50 (11-152)	77 (34-148)
Duration of hospital admission to intubation (days, median, range)	14.5 (4-70)	7.5 (2-32)
Duration of hospital admission to ECMO initiation (days, median, range)	29.5 (10-80)	13.5 (9-26)
Duration of admission to first transplant consultation (days, median, range)	29.5 (14-66)	46.5 (24-79)
Duration of hospital admission to tracheostomy (days, median, range)	30.5 (10-72)	15 (10-35)
Duration of hospital admission to lung transplantation (days, median, range)	79.5 (54-174)	N/A
Total duration of ICU stay (days, median, range)	110 (21-202)	85 (51-169)

Most of our patients had single organ failure i.e., lung, except for two who required dialysis after ECMO initiation. Six out of the 12 patients received bilateral lung transplant. One patient received the transplant before ECMO initiation. However, the patient required two runs of ECMO after the transplant due to postop complications from suspected COVID19 re-infection and deceased on postoperative day 101. All the patients after transplant had an expedited recovery except one who required prolonged hospitalization before starting physical therapy. The median length of hospital stay for the transplant group was 148 (89-194) days and for the non-transplant group was 114 (58-178) days. The 30-day survival rate was 100% for the transplant group. At a median follow-up of 207 (0-456) days after discharge, 5(83.3%) patients in the transplant group and 3(50%) patients in the non-transplant group were alive. In the non-transplant group, 4 patients received ECMO support for more than 75 days and at last follow-up 2 were alive and functioning well without needing new lungs. This asks for an objective prospective study to define the timeline of irreversibility of the lung injury.

Conclusions: Lung transplantation is a viable salvage option in patients with COVI-19 induced irreversible lung injury. However, the irreversibility of the lung injury and the timing of lung transplant remains to be determined case-by-case.

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The feasibility of hybrid ECMO in cardiopulmonary failure: A single-center experience

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Objectives: The hybrid extracorporeal membrane oxygenation (ECMO) has been used as rescue therapy for patients with both circulatory and respiratory failure. However, the feasibility of hybrid ECMO has not been evaluated due to the lack of reports about clinical results.

Methods: This study retrospectively analyzed a total of 952 adult ECMO cases from January 2011 to December 2019. Total 77 patients were treated with hybrid ECMO. The cohort was divided into cardiac support group (I) and pulmonary support group (II) and the feasibility of hybrid ECMO was assessed.

Results: Among the total 78 patients with hybrid ECMO, group I and II had 31 and 47 patients, respectively. The mean duration of ECMO was 3.7±5.5 days. TThe initial mode of ECMO was veno-arterial (VA) ECMO in 40 patients (51.3%), veno-venous (VV) ECMO in 30 (23.4%) patients and veno-arteriovenous (VAV) ECMO in 8 (10.2 %) patients. The rate of ECMO weaning and in-hospital discharge were 55.1% (43/78), 39.7% (31/78), respectively. The rate of ECMO weaning in group I and II were 58.1% (18/31), 52.2% (24/46) (p=0.465), the rate of in-hospital discharge in group I and II were 41.9% (13/31), 37.0% (18/46)(p=0.425), in group I and II were 41.9% (13/31), 32.6% (15/46)(p=0.404), and 5 years survival were in group I and II were 38.7% (12/31), 26.1.0% (12/46)(p=0.241).

Conclusions: The survival rate of patients with hybrid ECMO was relatively lower than the reported survival rate of simple ECMO support. However, considering that selected patients have a cardio-pulmonary failure, it is considered worthy to perform as rescue therapy.

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ECMO-COVID offer and global mortality: Where does Portugal stand?

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Objectives: To evaluate the ECMO offer during the COVID pandemic in the different European countries

Methods: We colected COVID and demographic data from Worldometer and the national ECMO runs from the EuroELSO platform.

Results: Europe presented a broad offer of ECMO. If during the first wave the Health System's resources were not prepared to accommodate the high number of patients, during the following two years ECMO

demonstrated to be a useful tool in the treatment of COVID pneumonia. However, across different European countries the use of ECMO was very different. In Portugal ECMO was used in 336 patients, in a universe of 5,557,941 COVID cases within a total population of 10,140,570 individuals. Of these, 336 were placed on extracorporeal circulation, which corresponds to 60.5 cases per million positive cases and 33.1 per 1 million individuals. The average number of patients placed on extracorporeal membrane oxygenation (ECMO) per million positive cases was 39 amongst the surveyed countries. Portugal was the 4th country with the most patients of ECMO per million cases (1st is Belgium with 106.5; Estonia 106.1; and Austria 68.5) and per million inhabitants (33.1), after Estonia (49.2), Austria (43.2) and Belgium (42.6). The mortality rate of COVID patients in Portugal is 0.46%. It is lower than the average of the countries under analysis (0.56%). When analyzing the frequency of cases concerning the mortality rate, there is seemingly an increase in the mortality rate with a decrease in the number of cases. The significant differences in the mortality rate between different countries can be explained by several other factors: different criteria for the main diagnosis of death; capacity of the different countries regarding the population's access to vaccination and the different access to health care.

Conclusions: ECMO-COVID offer was very different across countries. In Portugal, the offer was amongst the greatest in Europe, not compromising the overall response to the global COVID population.

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Early prone positioning under VV-ECMO in SARS- CoV-2-induced acute respiratory distress syndrome - a retrospective cohort study

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Objectives: The effectiveness of prone positioning (PP) under VV-ECMO for severe COVID-19 still be unclear. Until now, PP under VV-ECMO was often performed as the trump card for refractory hypoxemia and weaning off ECMO. On the other hand, PP has the effect of promoting homogenization of Lung aeration and leading to prevention of VILI. Combine use of early prone positioning together VV-ECMO may have synergy effects of ultra-lung protective strategy. In this study, we analyzed early PP cases under VV-ECMO for severe COVID-19 in our hospital and examined their efficacy and feasibility.

Methods: We performed a retrospective study of patients with SARS-CoV-2-induced ARDS submitted to early PP during VV-ECMO. During VV-ECMO, PP was considered in case of "Type-H transition in imaging findings (CT / LUS)" and cases that the physician deemed necessary. The lung aeration is evaluated by LUS before and after each PP. If there is a finding that the dorsal collapsed lung is improved through PP, it is implemented as effective, and it continued.

Results: From April 2021 to August 2021, there were a total of 10 early PP cases under ECMO, and the age was (average) 56 years. ECMO was implanted with P/F 98 and Murray score 3.3 points, and PP was started 14 hours after the ECMO implantation. The average PP duration is 17.4 hours and PP performed 5.8 times per patient. Comparing blood gas and respiratory mechanics before and after PP showed a significant difference in PaCO2 (before: 46 ± 8 vs after: 42 ± 9, $p = 0.02$). Finally, there were 10 ECMO successful weaning (100%) and 8 surviving discharges (80%). No major complications were observed.

Conclusions: Early PP under VV-ECMO for severe COVID-19 can be safely performed, and it is suggested that the synergy effect of ultra-lung protective strategy may be associated with a reduction of hospital mortality.

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Experience achieved after implementation of the Veno-Venous ExtraCorporeal Membrane Oxygenation(ECMO) retrieval program in the region of Madrid (Spain). Hospital Universitario 12 de Octubre

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Objectives: The objetive of this study is to describe the cases trasferred to an ECMO referral´s centre (Hospital Universitario 12 de Octubre, Madrid (Spain)), to investigate characteristics before ECMO and while the patient was on ECMO, to analyse the presence or not of complications secondary to transfer and cannulation and finally to analyse the ICU outcome.

Methods: This is a Prospective study done from November 1st, 2020 to December 31st, 2022. The cases were accepted either for emergency ECMO cannulation in the hospital of origin and retrieval or for conventional

transfer. We analysed basic decriptive variables such as male proportion, age, IMC and etiology of ARDS and variables before ECMO such as prone position, duration of non-invasive ventilation, invasive ventilation and ICU leght of stay before ECMO. We recorded ELSO, SOFA and APACHE Severity Scores. We also analysed several variables on ECMO: if prone position on ECMO was done, median days of ECMO and succesfull weaning from ECMO. We also recorded whether there were complications or not in the transfer and cannulation. Finally ICU survival was examined.

Results: 31 cases were accepted. 22 (71 %) were male. 29 cases were accepted for emergency ECMO cannulation. Median age was 47 years and IMC 31.1. The etiology of SDRA was COVID 19 infection in 23 cases (74% cases). Lenght of non invasive and invasive ventilation before ECMO were 4 days and 3 days respectively and lenght of ICU admission before ECMO was 2 days. Prone position was 1 day and 2 prone sessions were done before ECMO. Severity scores: APACHE 10 , SOFA 4 , ELSO 3 . On ECMO Prone position was done on 15 cases(48.4%) . Median days on ECMO were 13.5 days. Succesfull weaning from ECMO were achieved on 20 cases(61%), 2 cases remain on ECMO. No complications were seen on transfer or cannulation. ICU Survivors were 16(51.6%).

Conclusions: After 2 years of experience on ECMO retrieval in the region of Madrid ECMO availability was achieved. Our results are similar than ELSO mortality.

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Experiences and views of MDT health care professionals regarding the end of life care and withdrawal of VV-ECMO across the UK ECMO network

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Objectives: ECMO is a rescue therapy for respiratory failure, however the mortality within this population remains high and caring for a dying patient on ECMO can be distressing with the discontinuation of ECMO when deemed futile challenging. With the rapid development of this new technology health care professionals are becoming increasingly confronted with unique and complex ethical situations for which traditional ethics cannot easily be applied and there is limited evidence on the best approach. Therefore, this study aims to elicit experiences and views of the MDT healthcare professionals delivering EOLC and withdrawal of care to patients with severe respiratory failure requiring VV-ECMO support across the UK ECMO network to further identify the issues and challenges experienced.

Methods: Twelve participants were recruited from the MDT health care professionals across the UK ECMO network. Semi-structured interviews were conducted via MS teams and the resulting data analysed using thematic analysis.

Results: Multiple themes were identified, but the overarching theme was the challenges and difficulties of delivering EOLC in the "awake" ECMO patient. There were further themes and sub-themes; Difficulties in decision making due to uncertainty and benefits of consistent MDT shared decisions; difficulties in gaining acceptance of withdrawal from families due to breakdown in trust from misunderstanding and lack of continuity; Importance of communication to ensure information giving and early expectation setting; Variable Palliative care involvement often felt to be late and underutilised; Significant impact on staff from traumatic experiences with a high emotional burden due to a relatable patient population.

Conclusions: This is a qualitative study exploring the experiences and views of healthcare professionals delivering EOLC and withdrawal in VV-ECMO patients. The "awake" ECMO was identified to be overwhelmingly the most difficult and challenging aspect of participants previous experiences. Further work is required to develop a standardised practice approach to these challenging situations.

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Delivery on ECMO during COVID: a case report

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Objectives: Despite their rarity, there are a few worldwide reports of delivery during ECMO. Due to the overall scarcity and heterogeneity, these cases pose a challenge to the multidisciplinary team of professionals.

Methods: We present the only hitherto known case of a pregnant woman infected with SARS-COV2 that gave birth during a ECMO run. A 32-year-old woman at 38 weeks of pregnancy arrived at our hospital with a recorded history of cough and dyspnoea. A subsequent PCR test registered her as positive for SARS-COV2. Due to the aggravation of her respiratory state and insufficient improvements with mechanical ventilation, VV-ECMO therapy was induced with close monitoring of

the status of the foetus by the obstetric and neonatal teams.

Results: When the patient contracted pre-eclampsia at 39 weeks, the decision was taken to deliver the baby during the 8th day of ECMO. The procedure was uneventful and ECMO was maintained for more 15 days after delivery with minor occurrences, resulting in a total ECMO run time of 23 days. The patient stayed in ICU 30 days and was transferred home in day 40. The baby course was similarly uneventful.

Conclusions: This case will be compared with other cases of delivery during ECMO with the aim of discussing peculiarities and similarities shared with other diseases.

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Extracorporeal membrane oxygenation for airway emergencies

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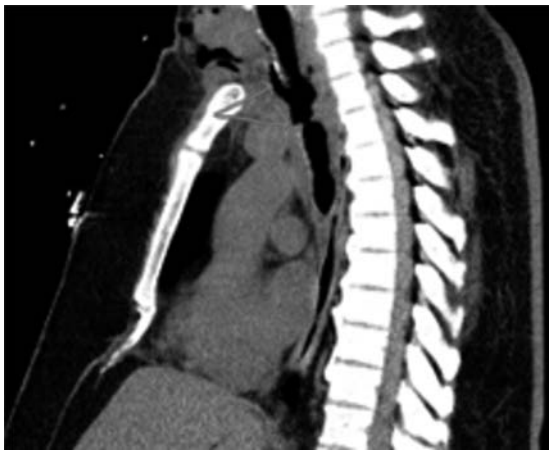
Objectives: Extracorporeal membrane oxygenation (ECMO) is well established in cardiorespiratory failure. Here we report the use of ECMO in an airway emergency to provide respiratory support.

Methods: Informed consent was obtained from patient at the time of admission.

Results: A 48-year-old with COVID-19 requiring venovenous ECMO (VVECMO) for 32 days and tracheostomy for 47 days had developed tracheal stenosis three months after tracheostomy removal, and undergone tracheal resection and reconstruction. He presented two weeks later with acute dyspnea, bloody drainage and a bulge in his neck with coughing. A computerized tomography (CT) of the cervical spine and chest showed dehiscence of the tracheal wound and a gap in the trachea. He was managed with High Flow Nasal Canula and supported on VVECMO support using 25 Fr. right femoral drainage cannula and 23 Fr. left IJ return cannula. A covered stent was placed, neck wound was irrigated and debrided. Patient was decannulated after 10 days on ECMO. Future therapeutic considerations include mediastinal tracheostomy, aortic homograft interposition of the disrupted segment of trachea with stent placement and permanent self-expandable stent with internal silicone stent.



Conclusions: ECMO is increasingly used in complex thoracic surgery as well as in the perioperative period as salvage support. One of the areas where it has shown promising results is traumatic main bronchial rupture, airway tumor leading to severe airway stenosis, and other complex airway problems. The ease of cannulation, the technological advances and growing confidence in the management of ECMO patients are the main reasons for the expansion of ECMO use beyond conventional indications. The case described above is an example of the use of ECMO in the perioperative management of impending respiratory failure due to airway obstruction or disconnection.

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Right ventricular status in patients with VV-ECMO and its prognostic significance –the Mayo Clinic experience

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Objectives: Extracorporeal membrane oxygenation(ECMO) is used to support patients with refractory hypoxemia and avoid Ventilator-induced Lung Injury. Several patients develop right ventricular(RV) failure while on ECMO. Venovenous-ECMO (VV-ECMO)'s effect on RV function is increasingly reported, but the association's nature is not well defined. We aim to explore the effects of VV-ECMO over time on RV size and function and understand prognostic implications.

Methods: We conducted a retrospective IRB-approved study from January-2018 to June-2022 and enrolled all

patients from Mayo Clinic Florida, and Rochester campuses admitted with respiratory failure and placed on VV-ECMO. Data was collected via chart review. Qualitative echocardiographic parameters from the published report were used to represent RV function. Chi-square tests were employed to compare categorical variables, and multinomial logistic regression was used to understand the relation between ECMO and RV function. Statistical analysis was performed using R statistical software (version 4.2.2).

Results: Our study cohort consisted of 70 patients, of which 70% were males and 83% were Caucasians. The mean age was 48(±14) years. The most common admission diagnosis was pneumonia(85%). In a comparison of RV size and RV function, RV dilatation was noted in 21%, 70%, 85%, and 95% of patients with absent, mild, moderate, and severe RV dysfunction ($p<0.001$). In a multinomial regression analysis, ECMO flow (OR 1.3-2.6) was directly associated with RV size. Similarly, ECMO flows (OR 1.1-1.8) and ECMO duration (OR 1.01-1.03) were inversely associated with RV function. Mortality increased from 38 to 85% in patients when RV size increased ($p< 0.05$) and from 37 to 75% when RV function worsened ($p< 0.05$).

Conclusions: RV size and function worsened in patients on VV-ECMO and are associated with poor survival. Prospective trials assessing RV function at pre-specified intervals are needed to establish causality.

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Unique vascular complication following extended VV-ECMO support

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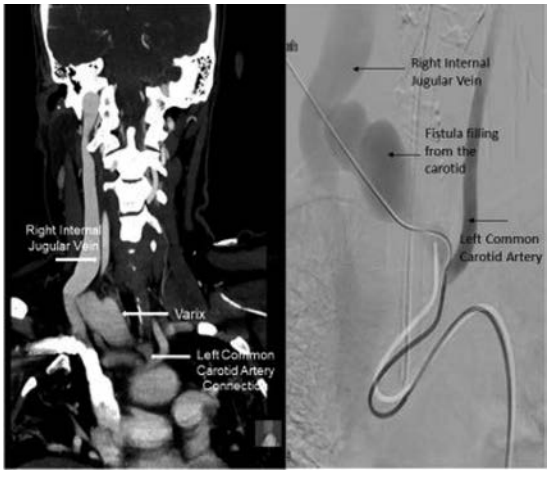
Objectives: To present an unusual complication related to prolonged ECMO support in a patient with COVID-19 induced acute respiratory syndrome (ARDS).

Methods: Clinical chart review of the care process after obtaining the informed consent from the patient.

Results: A 48-year-old female with COVID-19 infection during second wave of pandemic in August 2021 progressed to severe ARDS. She was put on VV-ECMO support after failing conventional therapy for refractory hypoxemia. Her cannulation configuration included a 25 F venous drainage cannula in the right femoral vein and a 21 F venous return cannula in the right Internal Jugular (IJ) vein. Cannulations were performed using the 'Seldinger technique' under USG guidance, and no difficulties or complications were reported. Her hospital course was notable for delirium, and intermittent bleeding from the cannula sites. After 80 days of support, she showed adequate respiratory improvement which allowed ECMO decannulation. She continued to show improvement, and was eventually discharged after 102 days of total hospital stay. During her 6 weeks follow-up clinic visit a palpable thrill was noted at the jugular ECMO cannula site. A CT angiogram of the neck demonstrated a large venous varix connecting the right IJ and the left common carotid artery with filling from the left common carotid artery. ECMO cannulation site complications such as aneurysm, clots, infections and stenosis are well known. What was unusual in this case is the nature of the aneurysm given that there were no arterial procedures performed on the left side of the neck. She was managed by an 'Amplatzer plug' to the carotid artery at the level of the connection to the varix without any complications.



Conclusions: Longer duration of ECMO support needs careful follow-up for timely recognition and management of vascular complications.

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Determinants of death in patients with COVID-19 pneumonia treated with venovenous extracorporeal membrane oxygenation support

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Objectives: Death from SARS-CoV-2 pneumonia resulted from progressive respiratory failure in most patients. Whenever accessible, venovenous extracorporeal membrane oxygenation (VVECMO) was implemented to rescue patients with refractory hypoxemia. Reported mortality in this population reached values from 20 to 50 percent, but the direct causes of death were not so widely acknowledged. The aim of our study was to characterize mortality in patients treated with VVECMO support.

Methods: Retrospective review of a prospectively collected database in an ECMO referral centre. All patients with diagnosis of SARS-CoV-2 infection treated with VVECMO support were included. Survivors and non-survivors were compared using *t*-student and χ^2methods. A Cox regression analysis was performed to identify predictors of mortality at admission.

Results: Ninety-three patients were included (29% female). Median age was 54±12 years, mean SOFA was 5.7±2.9 and SAPS II was 35.6±13.6. Hospital mortality was 24.7%. Main causes of death were septic shock in 39.1% (9 patients), irreversible lung fibrosis 30.4% (7 patients) and catastrophic hemorrhage in 4.3% (4 patients). End-of-life care measures (withdrawal or withholding) were adopted in 65.2% of non-survivals. Patients who died were older (55 vs 48 years, $p<0.05$), had longer disease course (19 vs 15.3 days, $p<0.05$), longer invasive mechanical ventilation course before cannulation (8.5 vs 5 days, $p<0.05$), lower static lung compliance (25.5 vs 31.8 mL/cmH2O, $p<0.05$) and were ventilated with lower PEEP (8 vs 10 cmH2O, $p<0.05$) on cannulation. On a Cox-regression model, only prone ventilation before cannulation (HR 9,7; CI 95% 1,4-68,6; $p<0.05$) and SAPS II (HR 1.04; CI 95% 1,001-1,083; $p<0.05$) predicted mortality.

Conclusions: Mortality in patients with severe SARS-CoV-2 pneumonia treated with VVECMO was exceedingly low in our study, when compared with other series. Only one-third died from progressive lung disease, which suggests that protocol improvement can further reduce mortality.

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The use of venovenous extracorporeal membrane oxygenation in COVID-19: An updated systematic review and meta-analysis of clinical outcomes

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Objectives: The objective of this study is to assess the clinical benefits and potential risks of using venovenous extracorporeal membrane oxygenation (VV ECMO) as a treatment for COVID-19 patients with severe respiratory failure.

Methods: Relevant studies were identified through searches of electronic databases, including PubMed, EMBASE, and the Cochrane Library, from January 2020 to December 2022. We included observational studies on adult patients who received venovenous (VV) ECMO support for COVID-19-induced ARDS. The primary outcome was in-hospital mortality, 3-month mortality, and complications associated with VV ECMO. Statistical analysis was performed using R version 4.0.3 and the metafor and meta packages.

Results: The final analysis included 39 studies comprising 10,702 patients. In-hospital mortality for adults receiving ECMO was 34.2% (95% CI: 28.5% - 40.3%; I2 = 93%), while the 3-month mortality rate was 50.2% (95% CI: 44.4% - 56.0%; I2 = 51%). Bleeding requiring transfusion occurred in 33.7% of patients (95% CI, 23.9 - 45.1; I2 = 96%). The pooled estimates for other complications were as follows: overall thromboembolic events 40.9% (95% CI, 24.8 - 59.3; I2 = 97%), stroke 8.7% (95% CI, 5.7 - 13.2; I2 = 72%), deep vein thrombosis 15.4% (95% CI, 9.7 - 23.6; I2 = 80%), pulmonary embolism 15.6% (95% CI, 9.3 - 25.1; I2 = 92%), gastrointestinal haemorrhage 8.1% (95% CI, 5.5 - 11.8; I2 = 56%), and the need for any renal replacement therapy in 38.0% of patients (95% CI, 31.6 - 44.8; I2 = 84%). Bacterial pneumonia occurred in 46.4% of patients (95% CI, 32.5 – 61.0; I2 = 96%).

Conclusions: Venovenous extracorporeal membrane oxygenation (VV ECMO) may be an effective treatment option for COVID-19 patients with severe respiratory failure. The use of VV ECMO was associated with reduced in-hospital and 3-month mortality. However, bleeding is a common complication that should be closely monitored. Further research is needed to determine the optimal use of VV ECMO in this patient population and to identify factors that may predict a favourable response to treatment.

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Gender differences in COVID-19 patients supported with extracorporeal membrane oxygenation (EuroECMO-COVID): Pathways, complications, outcomes and follow up

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Objectives: Gender differences is increasingly recognized as a critical determinant of health and disease, particularly relevant to the COVID-19 pandemic caused by the SARS-CoV2. Epidemiological data and observational reports from the recent COVID-19 pandemic have consistently shown, since the beginning, that males are more likely to exhibit enhanced disease severity and mortality than females. On the other hand, the persistence of symptoms over a long period of time after infection, a condition known as long COVID, is more common in women. The aims of this study are to investigate the gender differences associated with in -hospital variables and outcomes in patients who received ECMO during the COVID-19 pandemic and to describe the 6-months follow up after ECMO initiation

Methods: EuroECMO COVID is a prospective, multi-center, observational study developed by the European Extracorporeal Life Support Organization. This study was based on data from patients aged ≥16 years who received ECMO support for refractory COVID-19 during the first wave pandemic (from March 1 to September 13, 2020) at 133 centers in 21 countries. The analysis investigates associations between patient and management-related variables as patient demographics (obesity, smoking habits), underlying disease especially cardiovascular comorbidities (arterial hypertension, diabetes, renal insufficiency), pre ECMO status, ECMO settings and complications, and in-hospital deaths.

Results: Between March 1 and September 13, 2020, 1215 patients of whom 78% men (942) and 22% women (267) were included in the study. Cardiovascular disease is more prevalent in males and most of the deceased patients were elderly (age ≥60 years), obese and with at least one complication The gender disparity is consistent in most of the countries involved in the EuroECMO-COVID Study and men consistently demonstrate an increased mortality across age-groups on a global level.

Conclusions: Men and women present significant differences regarding COVID-19 that can be partly explained by known genetic, hormonal, physiological and other gender variations. Such differences should be considered in the treatment and follow-up of patients with COVID-19. Moreover, they could represent an important step for formulation of different tailored health policies.

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Extracorporeal membrane oxygenation in massive pulmonary hemorrhage secondary to arteriovenous malformation

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Objectives: We report a case of a 63-year-old man with severe pulmonary hemorrhage secondary to

arteriovenous malformation and ventilatory failure due to reduced alveolar diffusion and airway obstruction. Bronchoscopy revealed high flow active bleeding and clots obstructing the orotracheal tube and bronchial tree, refractory to local therapeutic measures. The patient was successfully treated with veno-venous extracorporeal membrane oxygenation (ECMO) for 12 days, during which he underwent two unsuccessful angiographic arterial embolizations, ultimately requiring right inferior pulmonary lobectomy. The discussion includes diagnosis, management and outcome of patients with massive hemoptysis.

Methods: Data were collected from the patient's electronic medical record.

Results: Veno-venous ECMO was used safely and successfully without systemic anticoagulation in a case of massive hemoptysis as bridge therapy to definitive treatment.

Conclusions: In cases of massive hemoptysis, maintenance of airway patency and bleeding control should be carried out simultaneously. Treatment often includes bronchoscopy, angiographic arterial embolization, and, in the case of refractory bleeding, surgery. Veno-venous ECMO provides short term stabilization in pulmonary hemorrhage with refractory hypoxemic respiratory failure that is limiting a definitive intervention to achieve hemostasis.

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VV-ECMO decannulation under anticoagulation: Our strategy

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Objectives: to analyze and report the results of a decannulation strategy designed to reduce the incidence of cannula-related thrombosis.

Methods: observational prospective study at a tertiary hospital mixed intensive care unit. Intensivists were asked to fill a questionnaire whenever they decannulated a patient. We collected data regarding patient demographics, anticoagulation interruption before the procedure, manual compression after cannula removal, and procedural complications, such as haemorrhage or echographic evidence of venous thrombosis.

Results: we collected data from 19 patients, 20 ECMO runs and 42 cannulas (3 patients with more than one ECMO run and/or configuration), during a 12 month period. Median age was 43 years old (minimum-maximum 24-68), median APACHE II score was 12 (4-25) and median ECMO support duration was 9 (1-26) days. Anticoagulation was stopped in 19% of cannulas removed, mostly for reasons other than decannulation itself; median delay between anticoagulation suspension and cannula removal was 48 (2-96) hours. Sixty-nine percent of cannulas were removed without significant manual compression being applied. When pressure was applied, it was done so for a median of 5 (3-20) minutes.

Nineteen cannulation sites had ultrasound signs of thrombosis (45,2 %), with a non-statistically different incidence in patients who stopped anticoagulation and those who did not (75% and 43,3%, respectively; p-value 0,06; chi-square test). In one cannulation site thrombosis could not be evaluated by ultrasound. Around one third of observed thrombi were non-occlusive (36,8%), and rate of therapeutic anticoagulation after ECMO decannulation was 45,0%.

No hemorrhagic complications were noted. One case of massive pulmonary embolism with obstructive shock was observed after thrombus' migration a few hours after decannulation, in a patient under anticoagulation.

Conclusions: although the study sample is small and results aren't statistically significant, this data suggests that anticoagulation continuation at decannulation appears to be a safe strategy and may be related to less thrombosis. Further conclusions could be withdrawn from a bigger cohort and, ideally, a randomized trial.

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Extracorporeal membrane oxygenation instead of invasive ventilation in patients with COVID-19 acute respiratory distress syndrome (ARDS) and pneumomediastinum: A cohort trial

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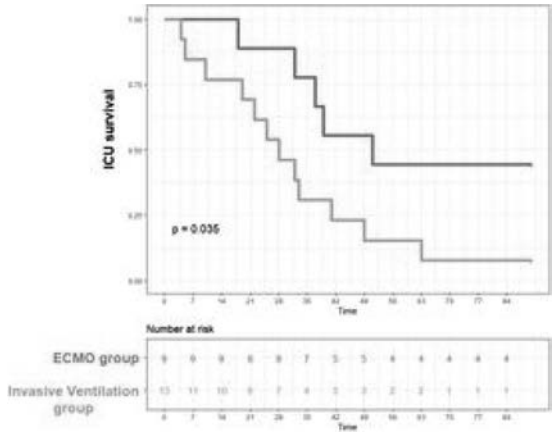
Objectives: In patients with severe respiratory failure, invasive ventilation may deteriorate the pneumomediastinum and hypoxia. This study aimed to compare the mortality and the complications of the patients with coronavirus disease 2019 (COVID–19) related severe ARDS treated with invasive ventilation or veno-venous ECMO (VV-ECMO) to avoid intubation. We hypothesized that VV-ECMO support without prior intubation is a feasible alternative strategy to invasive ventilation.

Methods: This retrospective study evaluated patients with COVID–19 related severe respiratory failure and

radiological evidence of pneumomediastinum. The primary outcome was intensive care unit (ICU) survival at 90 days.

Results: Out of 347 patients with COVID–19 disease treated in our unit, 22 patients developed spontaneous pneumomediastinum associated with deterioration of respiratory function. In 13 patients (59%), invasive ventilation was chosen as initial respiratory support; in 9 patients (41%), VV-ECMO was chosen as initial respiratory support. The median age of the patients in the invasive ventilation group was 62 years (IQR: 49-69) compared to 53 years (IQR: 46-62) in ECMO group (P=0.31). No statistically significant difference in SAPS II score between the groups was observed (39.7 (IQR: 33.2−45.3) vs. 28.9 (IQR:28.4−34.6), P=0.06). No elevated fluid balance within the first 4 days was observed in the ECMO group compared to the invasive ventilation group (162 mL (IQR: -366−2000) vs. 3905 mL (IQR: 2068−6192), P=0.07). VV-ECMO as the initial strategy for supporting patients with severe respiratory failure and pneumomediastinum, was associated with lower 90 days mortality (HR: 0.33 95%−CI: 0.11−0.97, P= 0.04) compared to patients treated with invasive ventilation (Figure).



Conclusions: VV-ECMO can be an alternative strategy to invasive ventilation for treating patients with severe respiratory failure and spontaneous pneumomediastinum.

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Interhospital ECMO transport during Covid-19 pandemic: A clinical experince

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Objectives: During COVID pandemic, ECMO support for the patients with ARDS have saved many lives. Although its an important and effective treatment modality, management of ECMO could be done in a few specialized centers. In this study, we share our in- and out-of-city ECMO transport experience of the patients with COVID-ARDS.

Methods: A total of 75 patients (57% male- 43 %female) were included in this study. The decision ECMO support, initiation at referral hospital, and transport process of all of the patients to our centre were performed by our mobile ECMO team. All transports were done by land ambulance

Results: Mean age of the patients was 43.4±11.5 years. Mean intubation period before ECMO support was 8.5 ±8.3 days. We transferred 14 patients from the centers within the city and 12 patients from the centers outside the city to our hospital. Mean distance between our center and the referral center was 36,2 kms (max 269-min 1). We did not experience any major complication during transport. A total of 30 patients (38,6 %) were weaned from ECMO and discharged from hospital.

Conclusions: ECMO support is an advanced treatment modality for pulmonary failure patients. The decision of initiation, cannulation, transport and management should be performed by experienced centers to achive acceptable results.

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Prolonged oxygenator usage for VV ECMO for COVID ARDS: A clinical experience

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Objectives: Its known that with the prolonged use of ECMO, because of the thrombogenic activations -minor/majorclot formations may ocur at the oxygenator and eventually it fails to function properly. Physicians take some precautions to prevent or postpone this process but usually exchange the circuit. In this study we share our follow up strategy and prolonged oxygenator use for the COVID-ARDS patients.

Methods: A total of 68 patients who were followed more than 7 days were included in this study. Sorin/LivaNova oxygenators and VV-ECMO circuit were used for all of the patients. Bivaluridin infusion was used for routine anticoagulation protocol.

Results: Mean age of the patients was 44.1 ±12.2 years. The patients were followed for a total of 2705 days with a total of 103 oxygenators [mean 26.2 ±18.3(104-7) days for per oxygenator] Mean duration of ECMO support was 40.3 ±24.4 days . The oxygenator use per patient was 1.5 ±0.89. There was no major hypoxic period experience for the patients. Survival rate was 43.2 %.

Conclusions: With using bivaluridin for anticoagulation, daily washing of oxygenators and close follow up methods we can protect the oxygenators and use them for longer periods safely like in our experience which can save us from serious additional costs and interventions.

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A systematic review of the use of CytoSorb© Hemoadsorption in patients undergoing veno-venous ECMO support for severe acute respiratory distress syndrome

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Objectives: Acute respiratory distress syndrome (ARDS) often results in high mortality and morbidity. Hemoadsorption therapy, such as CytoSorb©, is being increasingly used to target the underlying hyper-inflammation that occurs with ARDS. This review aims to evaluate the available data on the use of CytoSorb in combination with veno-venous extracorporeal membrane oxygenation (V-V ECMO) in severe ARDS cases, and to assess its effects on inflammatory, laboratory, and clinical parameters, as well as on patient outcomes.

Methods: A systematic literature review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Whenever possible, an analysis of changes in relevant biomarkers and clinical parameters was performed.

Results: CytoSorb© therapy was associated with significant reductions in circulating levels of C-reactive protein and interleukin-6 ($p = 0.039$ and $p = 0.049$, respectively), as well as an increase in PaO2/FiO2 levels ($p = 0.028$). There was also a trend towards reduced norepinephrine dosage ($p = 0.067$). Mortality rates in patients treated with CytoSorb©tended to be lower than in the control groups, but these studies had high heterogeneity and low power. In an exploratory analysis of 90-day mortality in COVID-19 patients receiving V-V ECMO, the therapy was associated with a reduced risk of death.

Conclusions: Overall, the reviewed data suggests that CytoSorb© therapy can effectively reduce inflammation and potentially improve survival in ARDS patients treated with V-V ECMO. Therefore, early initiation of CytoSorb©in conjunction with ECMO may offer a promising approach to enhance lung rest and promote recovery in patients with severe ARDS. A randomised trial is warranted to confirm our findings.

Conflict of interest: C.R., T.K. and J.S. are employed at CytoSorbents Europe. A.A. and F.P. have received speaking honoraria from CytoSorbents Europe. L.C.N.: lecture/consulting honoraria and research support from CytoSorbents, lecture honoraria from Abbott and Maquet, and lecture/proctoring/consulting honoraria and research funding from Abiomed. Other relationships beyond the topic of this work exist.

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Outcomes and mortality in a newly implemented ECMO center in Northeast Brazil during pandemic

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Objectives: To evaluate the outcomes and risk factors associated with mortality of patients cannulated on ECMO in the context of covid infection during the pandemics in a newly implemented ECMO center

Methods: This was a unicentric observational retrospective study performed at Real Hospital Português, in Recife, state of Pernambuco, Brazil. All consecutive patients with laboratory confirmed SARS-CoV-2 infection cannulated for VV-ECMO or VA-ECMO for severe ARDS from march 2020 to december 2021 were included retrospectively. Patients recieving ECMO for isolated refratory cardiogenic shock were excluded. Descriptive statistics and association tests were used to analyze characteristics, management and patient outcomes during that period.

Results: In our cohort of 47 ECMO for covid associated ARDS (CARDS), 39 patients (83%) were admitted by our emergency department. 8 patients (17%) had been transferred from other hospitals as soons as they had been cannulated. 32 patients (68%) were male, median age was 50 years (18-69). Mean body mass index was 31 (21,4-46,3). 37 patients (78%) had at least 1 comorbidity. Major bleeding occurred in 34 (72%) patients. Venous thromboembolism and hemolysis ocurred in 19 (40%) and 13 (23%) patients, respectively. When we compared treatments before ECMO initiation (imunoglobulin, tocilizuman, nitric oxide, neuromuscular blockade and

proning), proning was associated with better survival (RR 0,67 IC 0,46-0,97 p 0,029). The mean duration in mechanical ventilation until ECMO cannulation was 9,69 days and mean time in ECMO was 23 days. The 90-day mortality was approximately 72%.

Conclusions: The only variable associated with a better chance of survival was proning before ECMO. Our mortality (72%) is higher than reported from a recent meta-analysis of 1986 ECMO patients implanted during the first pandemic year(37,1%). However it is similar to a German populational registry of covid patients receiving VV-ECMO (73%). Althought it's impossible to make causal inferences with such a design and sample sizes, we believe that describing the experience of smaller and newly implemented ECMO centers serves as motivation to improve quality and also to plan for future episodes of pressure on health system.

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Continuous Renal Replacement Therapy (CRRT) worsens the outcomes in patients receiving veno-venous extracorporeal membrane oxygenation

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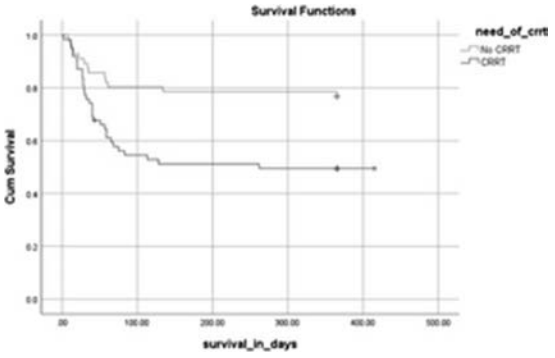
Objectives: 1. To study the baseline characteristics of patients receiving VVECMO alone and concurrent VVECMO and CRRRT. 2. To compare the clinical outcomes and survival in patients receiving VVECMO and simultaneous VVECMO and CRRT.

Methods: A retrospective observational study was carried out at Mayo clinic Rochester and Florida. All adult patients who were placed on VV ECMO between January 2019 to March 2022 were included. The study population was classified into two groups: VVECMO with CRRT and VVECMO alone. Demographic data, baseline clinical characteristics, treatments administered, laboratory parameters, mechanical ventilator and ECMO data and survival outcome were collected and analyzed.

Results: Total patients -118 { concurrent CRRT -62 (53%)}

The pre-ECMO clinical status and lab parameters were comparable between the groups. The 30-day mortality (7% vs 24%, p=0.02), duration of ICU stay (32 days vs 45 days, p=0.02) and hospital stay (42 days vs 53 days, p=0.03) were higher in CRRT group. The survival difference is shown in the figure.



Conclusions: Patients with pre-existing cardio-respiratory or kidney disease are more likely to require CRRT on VVECMO. Patient receiving concurrent CRRT while on VVECMO have longer length of ICU stay, hospitalization and have decreased survival.

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Analgosedation of patients with severe COVID-19 associated respiratory failure supported with extracorporeal membrane oxygenation: A retrospective, single-center analysis

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Objectives: Analgosedation of patients with severe respiratory failure due to coronavirus disease 2019 (COVID-19) proved to be challenging. Patients supported with

	Total (n=118)	VVECMO(n=56)	VVECMO+CRRT(n=62)	p-value
Age, median(IQR)	53(46-62)	52(45.75-60)	54(46.5-63)	0.38
BMI,median(IQR)	29.68(25.54-36.04)	31.5(27.4-36.08)	30.35(25.18-36.28)	0.4
Gender (male),n(%)	76(64.4)	32(57.14)	44(71)	0.11
Immunocompromised,n(%)	35(29.66	16(28.57)	16(30.65)	0.8
Obesity,n(%)	44(37.29)	21(37.5)	21(37.1)	0.96
Pre-existing cardiac condition,n(%)	39(33.05)	13(23.21)	13(41.94)	**0.03**
Pre-existing respiratory condition, n(%)	13(11.02)	2(3.57)	11(17.74)	**0.01**
Pre-existing renal insufficiency, n(%)	16(13.56)	1(1.79)	15(24.19)	**0.00023**

venovenous extracorporeal membrane oxygenation (VV ECMO) seemed to require analgosedative drugs in high doses. This study reviews analgosedation practices in patients with COVID-19 associated severe respiratory failure supported with VV ECMO.

Methods: This is a retrospective, single-center registry study including all patients with COVID-19 associated severe respiratory failure that were supported with VV ECMO at our center. All sedative and analgetic drugs administered intravenously or via inhalation to patients for at least two hours were recorded and analyzed.

Results: Between March 2020 and January 2022, 88 patients with COVID-19 associated severe respiratory failure were supported with VV ECMO at our center. Propofol and sufentanil were used most frequently for analgosedation in this cohort. Both drugs were co-administered following treatment standards established prior to the emergence of COVID-19 at our center. Sedative and analgetic drugs were switched to alternative regimens after a median time of 3 and 12.5 days. Alternative regimens included Isofluran, alpha-2-agonists (clonidine or dextomidine) or esketamine. Alpha-2-agonists were initiated at a median time of 2 days after starting VV ECMO support. Benzodiazepines were used primarily as last resort treatment option for sedation at our center. During the four waves of the pandemic experienced at our center, we experienced an increased average number of drugs needed for analgosedation.

Conclusions: Analgosedation in critically ill COVID-19 patients supported with ECMO is challenging. It remains unclear, whether the standard analgosedation regimen with sufentanil and propofol established at our center prior to the COVID-19 pandemic is optimal for this patient cohort. Further studies are needed to determine optimal and long term safe analgosedation regimens in critically ill patients supported by VV ECMO. Furthermore, changes experienced during the course of the pandemic need to be scrutinized in comparison to other cohorts.

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Successful VV-ECMO weaning from pulmonary involvement of anaplastic large T-cell lymphoma

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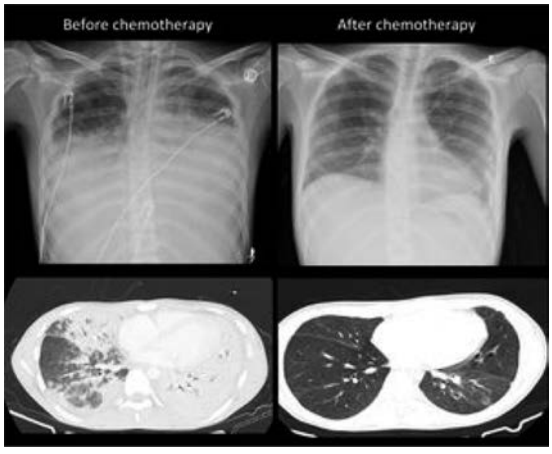
Objectives: To highlight that venovenous extracorporeal membrane oxygenation (VV-ECMO) is an adequate life-support option for patients with hematologic malignancies and severe acute respiratory failure (ARF) as a bridge to appropriate cancer treatment.

Methods: A 19-year-old male was admitted to a secondary hospital with a 10-day history of pleuritic chest pain, cough, fever, anorexia, and unquantified weight loss. He presented bilateral retroauricular adenopathies and CT scan revealed bilateral lung infiltrates, hepatosplenomegaly, and multiple adenopathies. He developed progressive ARF, refractory to high-flow nasal cannula (4 days) and invasive mechanical ventilation (2 days), with Murray score 3.0, which prompted rescue by our team on VV-ECMO support.

Results: Distributive shock emerged, complicating VV-ECMO run and imposing differential diagnosis between septic shock and cytokine storm. After hematology consultation, bone marrow and lymph node biopsies were performed and established the diagnosis of ALK-positive anaplastic large T-cell lymphoma. Chemotherapy with CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisolone) was promptly initiated, allowing rapid resolution of shock, within hours, and growing tidal volumes on ventilation. No infection was documented. The patient was successfully weaned after 38 days. The most relevant complications included ICU-acquired weakness with diaphragmatic dysfunction, heparin-induced thrombocytopenia, bleeding from tracheostomy stoma, and membrane lung dysfunction which motivated 2 circuit changes. He was transferred to the Hematology ward and discharged home after 52 days. Two months later, he was readmitted due to disease progression with pulmonary involvement and severe ARF, motivating a second VV-ECMO run. After emergent rescue chemotherapy with brentuximab vedotin plus ESHAP chemotherapy (etopodide, methylprednisolone, cytarabine, cisplatine), he was successfully weaned in 11 days and discharged home after 28 days of hospital stay.



Conclusions: This case report reinforces the most recent evidence suggesting a mortality benefit with ECMO support in some patients with hematologic malignancies and ARF, particularly in young patients with lymphoma. Also, it is the first known report of a patient successfully weaned by ECMO due to pulmonary involvement of anaplastic large T-cell lymphoma.

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Membrane dysfunction in patients with severe COVID-19 treated with venovenous extracorporeal membrane oxygenation – analysis from a pooled data from a single centre

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Objectives: It is well known that severe COVID-19 is associated with complex immunological and inflammatory dysregulation. Both these physiopathological events translate to a high risk of major thrombotic or hemorrhagic events. In patients treated with venovenous extracorporeal membrane oxygenation (VVECMO), membrane dysfunction might affect systemic oxygenation and limit its duration-expectancy. This study aimed to assess the possible causes of extracorporeal membrane failure in COVID-19 patients and its impact on outcome.

Methods: Retrospective, single-center, observational case-control study involving adult COVID-19 patients admitted to an ECMO referral centre in a tertiary university hospital. All patients required VVECMO for acute respiratory failure, including 48 cases who needed one or more extracorporeal membrane exchanges and 45 controls (no membrane exchange). These two groups were compared for demographic characteristics, severity of the disease using validated scores (SAPS II and SOFA), duration of ECMO run, coagulation assessment, cumulative anticoagulation dose, associated complications, and outcomes (ICU and hospital mortality).

Results: Most patients were males (71.0%) and younger than 50 years (79.5%). Median ECMO run duration was significantly longer in the case group (35.0 vs 14.0 days, p <0.001), as well as ICU length-of-stay (45.5 vs 28 days, p <0.001). Membrane exchange tended to be associated with sepsis (56% vs 33%, p=0.037), major hemorrhage (58% vs 43%, p=0.022), heparin-induced thrombocytopenia (25% vs 9%, p=0.054), higher D-dimer title (17.36 ng/dL vs 7.5 ng/dL, p=0.07) and lower platelet counts (133.000/μL vs 154.000/μL). Median SAPS II (32.0 vs 33.0, p=0.20) and the mortality (27% vs 24%, p >0.99) were similar between these groups.

Conclusions: In patients with SARS-CoV-2 pneumonia and severe hypoxemia treated with VVECMO support the emergence of infection, coagulopathy and inflammation were associated with high risk of membrane dysfunction. No impact on mortality could be confirmed from these data. Anticoagulation monitoring and dosing strategies should be reinforced to promote membrane protection.

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SARS-CoV2 infection after vaccination in patients requiring extracorporeal life support: An analysis from the EuroECMO-COVID study group

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Objectives: At the beginning of the pandemic, it was believed that severe SARS-CoV2 infection would induce lifelong immunity and that reinfections would be unlikely. However, several cases of reinfection were documented in previously infected patient and the waning humoral immunity has raised significant concerns. Accordingly, long-term and durable vaccine-induce antibody protection against infection have also become a challenge, as several breakthroughs of COVID-19 have been identified in individuals partially or fully vaccinated. This study describes the incidence, the characteristics of severe COVID-19 infections requiring ECMO occurred after vaccination and the presence of side effects related to the vaccine.

Methods: EuroECMO COVID is a prospective, multicenter, observational study, developed by the EuroELSO, based on data from patients aged ≥16 years who received ECMO support for refractory COVID-19 during the pandemic in 204 centers. The analysis investigates the survival of vaccinated patient, the associations between management-related variables, the incidence of vaccination during the different pandemic phases, the type of vaccines and the possible side effects.

Results: Immunosuppressed patients are susceptible to reinfection even after being naturally infected or receiving a full vaccination. Ineffective antibody production, due to relatively ineffective vaccines, inadequate number of doses or the time after vaccination are involved in the pathogenesis of post-vaccination infections. This population was found to have a partial immunity due to an inadequate number of doses and an overlapped time from vaccination and SARS-CoV2 incubation with PCR results after being vaccinated. Several manifestations of SARS-CoV2 infection are similar to vaccine-induce side effects and mild symptoms can be presented both as an adverse reaction after vaccination and a result of infection. In this subgroup no side effects were attributable to the vaccine.

Conclusions: Vaccination does not entirely prevent SARS-CoV2 but will lead to less morbidity and mortality, as demonstrated by less need of ICU and ECMO care. In addition, the partial immunity for inadequate doses of vaccine or through the evolution of new variants demonstrated the importance of further analysis to differentiate the possible causes of waning humoral immunity.

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Outcomes of severely ill Covid-19 patients retrieved on ECMO: Single institution experience

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Objectives: Extracorporeal membrane oxygenation has been widely used in patients with severe respiratory failure due to Covid-19 infection. ECMO was initiated at ECMO center or implantation performed in regional hospitals and patients transferred to ECMO center for further treatment. The aim of the study was to evaluate characteristics and outcomes of patients retrieved with ECMO versus thoseimplanted in our institution.

Methods: Retrospective, single center study. Data of all Covid-19 patients, supported with ECMO from 2020.04.01 to 2022.06.01 in our institution were evaluated. Data of patients retrieved on ECMO to our hospital were compared with data of patients when ECMO support was initiated at our institution.

Results: During Covid-19 pandemic 54 patients with severe respiratory failure were supported with ECMO. Out of them 24(44.4%) patients were retrieved on ECMO. In all patient VV configuration was used. There were no significant differences of preoperative characteristics between retrieved vs institutionally cannulated patients (mean age 44 ± 16 vs 45 ± 12 years, pre-ECMO arterial pO2 62 ± 16 vs 66 ± 14 mmHg, pre-ECMO mechanical ventilation 2.1 vs 2.2 days). The overall survival to hospital discharge was 32%, 33% in patients retrieved with ECMO vs 30% in the group of patients with ECMO implantation on site.

Conclusions: Patient characteristics and hospital survival of patients who were retrieved with implanted ECMO to our ECMO center were comparable to those patients with ECMO implantation on site.

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Zero Recirculation (REC) and Cardiac Output (CO) in VV ECMO patients

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Objectives: Two major factors that influence the level of recirculation at VV ECMO are the position of the cannulas and the patient's hemodynamic. Low CO will limit amount of oxygenated blood entering the heart, as it will recirculate regardless position of cannulas. Thus, absence of recirculation suggests that CO is higher than ECMO flow. The animal experimental data with direct CO measurements showed that REC remain zero at good canula position until the ECMO flow reaches ≈60-70% of CO value [1]. The purpose of this study was to examine the frequency and the flow range of zero recirculation observed in a large clinical data.

Methods: The ELSA monitor (Transonic Systems Inc., Ithaca NY, USA) was used to measure recirculation via the ultrasound dilution method. Two flow-dilution sensors were located on the arterial and venous blood lines. Injection of 10-20ml of isotonic saline were administrated after the pump and before oxygenator. Total data archive of 4724 REC measurements was retrospectively examined (Table 1).

Results: Table 1. Recirculation measurement results.

Conclusions: Zero recirculation phenomena was observed in nearly 40% of the cases including high end of ECMO flow. This provides the opportunity to estimate CO as equal or higher than 1.3*ECMO flow. High recirculation or increase of REC during ECMO procedure may suggest a low or decreased CO due to hypovolemia or heart failure that may need to be addressed.1. Russ, M. et al. ASAIO J 2022, 68, 721-729

Conflict of interest: I am employee of Transonic Systems inc.

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Two-year outcome of extracorporeal membrane oxygenation in COVID-19 related severe respiratory failure

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Objectives: We sought to evaluate 2-year outcome of V-V ECMO support for COVID-19 related severe respiratory failure in our center.

Methods: Retrospective analysis of 41 consecutive patients (73% male, mean age 51.6±14.2 years, mean BMI 35.1±12.5 kg/m2) with critical hypoxemic and/or hypercapnic refractory respiratory failure (mean P/F ratio 67.9±14.3 mmHg, mean pCO2 77.6.0±185.7 mmHg, Murray Score 3.71±0.4) on V-V ECMO support from October 2020 to January 2022

Results: With mean support duration of 234.4±63.2 hours, 29 patients (70.7%) were successfully weaned off. Finally, 19 of them (46.3%) were discharged home with good neurological outcome (CPC 1,2). During follow-up, 30-day, 6-, 12-, and 24 -month survival rate was 61.3%, 46.2%, 41.9%, and 41,9% respectively. In survivor group shorter symptoms onset to respiratory failure time (4±4.7 vs. 7±6.7 days, p=0.04), higher P/F ration (86±41.5 vs. 65±37.5 mmHg, p=0.04) and norepinephrine support (0.03±0.06 vs. 0.09±0.12 ug/kg/min, p=0.04), and lower IL-6 level (12.3±7.5 vs. 25.9±8.8 ng/l, p=0.03) p=0.01) were analysed before cannulation. Mean in-ICU stay and in-hospital stay in survivors' groups reached 32.5±27.7 days and 42.6±35.8 days, respectively. All long-term survivors (17 patients) complained about slight functional health limitation only with normal 6MWT (542.6± 89.2 min), near to normal spirometry parameters (FEV/VC 87±7.4%, DLCO 63.1±13.7%, KCO 82.,1±19.4%) and minimal neurological disability (CPC 1-2)

			REC -zero		REC not zero		
Population	Patients	Meas	Meas	Average flow (range), ml/min	Meas	Average flow (range), ml/min	Average REC (range),%
Adult	461	4587	1693	3080 (904-6127)	2894	3840 (1120-7960)	20 (5-68)
Pediatric, neonatal	24	137	77	540 (210-1100)	60	580 (170-1180)	29 (6-67)
Total	485	4724	1770	2990 210-6127)	2954	3470 (170 -7960)	20 (5-68)

Conclusions: 2-year outcome of V-V ECMO support in COVID-19 severe respiratory failure is acceptable even in the scope of low-volume ECMO centre. Reported functional status of long-term survivors was good despite the complicated and prolonged in-hospital stay. *Supported by MH CZ – DRO (FNOl, 00098892*

Adult - Other

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Minimally invasive versus conventional sternotomy for aortic valve replacement: A systematic review and meta-analysis

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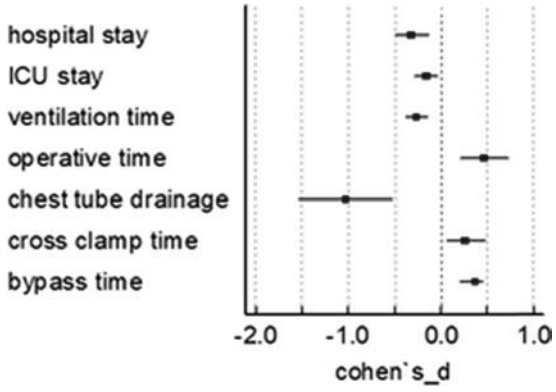
Objectives: We aimed to compare the safety and outcomes of the minimally invasive approaches versus conventional sternotomy procedure for aortic valve replacement

Methods: We conducted a PRISMA-compliant systematic review and meta-analysis. We ran an electronic search of PubMed, Cochrane CENTRAL, Scopus, and Web of Science to identify the relevant published studies. Data were extracted and pooled as standardized mean difference (SMD) or risk ratio (RR) using StataMP version 17 for macOS.

Results: Forty-one studies with a total of 15,065 patients were included in this meta-analysis (minimally invasive approaches n=7231 vs. conventional sternotomy n=7834). The pooled effect size showed that minimally invasive approaches had lower mortality rate (RR 0.76, 95%CI [0.59 to 0.99]), intensive care unit and hospital stays (SMD -0.16 and -0.31, respectively), ventilation time (SMD -0.26, 95%CI [-0.38 to -0.15]), 24-h chest tube drainage (SMD -1.03, 95%CI [-1.53 to -0.53]), RBCs transfusion (RR 0.81, 95%CI [0.70 to 0.93]), wound infection (RR 0.66, 95%CI [0.47 to 0.92]) and acute renal failure (RR 0.65, 95%CI [0.46 to 0.93]) However, minimally invasive approaches had longer operative time, cross clamp, and bypass times (SMD 0.47, 95%CI [0.22 to 0.72], SMD 0.27, 95%CI [0.07 to 0.48], and SMD 0.37, 95%CI [0.20 to 0.45], respectively). There were no differences between the two groups in blood loss, endocarditis, cardiac tamponade, stroke, arrhythmias, pneumonia, pneumothorax, bleeding reoperation, tracheostomy, hemodialysis, or myocardial infarction, (all P>0.05).



Conclusions: Current evidence showed higher safety and better operative outcomes with minimally invasive aortic valve replacement compared to the conventional approach. Future RCTs with long term follow up are recommended

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Rehabilitation in patients bridging to lung transplantation with extracorporeal membrane oxygenation - a UK centre experience

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Objectives: Bridging to lung transplantation (BTT) with extracorporeal membrane oxygenation (ECMO) is historically underutilised. Rehabilitation is associated with reduced post-operative length stay. This service evaluation reviews physiotherapy practice at a single UK centre.

Methods: Data were retrospectively collected from records for patients receiving ECMO BTT at Royal Brompton and Harefield hospitals from 2011 to 2022. Data were analysed for demographics, ECMO configuration and mobility interventions.

Results: Clinical characteristics are illustrated in Table 1. Of the 46 patients receiving ECMO, 40 (87%) were awake, 31 (77.5%) engaged in 186 active rehabilitation sessions. An ICU mobility scale (IMS) score ≥3, sitting over the edge of the bed was achieved by 24 (77.4%) patients on 133 (71.5%) of the mobility sessions. IMS ≥ 8, ambulating away from the bedspace was achieved in 6 patients (25%). Of the awake patients, 33 (82.5%) were self-ventilating and 7 (17.5%) had a tracheostomy. Time to commence rehabilitation ranged between 0 and 22 days, with a median time of 2 (±4.5) days. Patients were mobilised irrespective of

ECMO configuration and cannulation site with no adverse events.

Table 1. Clinical characteristics of patients undergoing ECMO BTT

Characteristics (n=46)	Range (mean ± SD) Group and Number			
Age (years)	19 – 66 (35.7 ± 11.9)			
Male	26 (56.5%)			
BMI (kg/m²)	16 - 30.1 (21.4 ± 3.2)			
Underlying disease	CF: 32 (70%)	ILD: 10 (22%)	BE: 2 (4%)	Other: 2 (4%)
ECMO configuration (n=54*)	VV 43 (80%)	VA: 6 (11%)	VV-V: 4 (7%)	VV-A: 1 (2%)
ECMO Cannulation sites utilised (n=54*)	Fem Fem: 27 (50%)	Jugular (co-axial): 13 (24%)	Fem Jug: 11 (20%)	Central: 3 (6%)
Time on ECMO (days)	1 – 57 (8 ± 10)ª			

Key: BMI = body mass index; CF = cystic fibrosis; ILD = interstitial lung disease; BE = bronchiectasis; ECMO = extracorporeal membrane oxygenation; VV = venovenous; VV-V= venovenovenous VA= venoarterial VV-A = venovenoarterial
*8 patients had ECMO upgraded during BTT; ªmedian ± IQR

Conclusions: Early awakening and effective management of delirium, anxiety and pain facilitated feasible and safe rehabilitation. Patients were mobilised on differing levels of ventilatory and ECMO support with varying cannulation sites. The approach to mobilisation and staffing required fluctuated based on these factors, however did not prevent rehabilitation. Rehabilitating this population was labour intensive and required highly skilled physiotherapists, an engaged multidisciplinary ECMO team and a culture of prioritising early rehabilitation. Rehabilitation is critical for successful BTT with physical therapy amongst the most effective treatments to regain muscle strength and overall condition. In our institution, embedding physiotherapists into the multidisciplinary ECMO team is considered essential care.

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Feasibility and efficacy of high flow normothermic regional perfusion for donation after circulatory death

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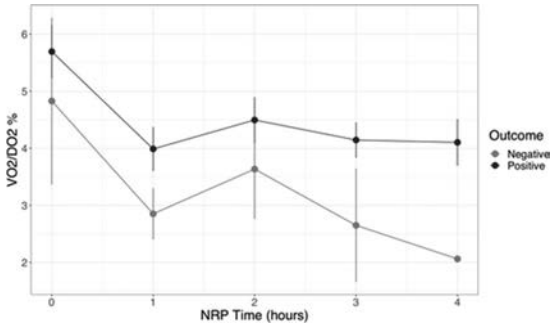
Objectives: Normothermic regional perfusion (NRP) was developed to allow i*n-situ* perfusion and evaluation of abdominal organs to facilitate graft assessment and recovery in donation after circulatory death (DCD). Current recommendations indicate maintaining a flow>1.7 l/min regardless of the donor body surface area (BSA). The objective of this study was to evaluate the feasibility and efficacy of NRP with high target flow.

Methods: Since the start of the DCD program at Turin University Hospital, NRP was conducted maintaining a target flow of 50% of the predicted cardiac output based on BSA. The outcome of NRP was defined based on the viability of the liver grafts.

Results: The target flow was maintained in all donors and no difference was found in donor characteristics between the outcome groups (Table 1).

	Negative Outcome (n=7)	Positive Outcome (n=20)	p
Functional warm ischemia time (min) DCD III	47 [44;55]	44 [39;49.8]	0.53
Asystolic time (min) DCD III	30 [28;33]	30 [28.25;31]	1
Mean Blood Flow (l/min)	3.09 [2.87; 4.05]	3.00 [2.64;3.27]	0.24
Lactate start DCD (mmol/l)	11.8 [10.4;13]	10.0 [8.85;11.7]	0.19

No difference was found at each time point in the ability of NRP to maintain an adequate oxygen delivery (DO2) but, since the positive outcome group showed an increased VO2 in the first 2 hours of NRP, the percentage of VO2 to the available DO2 was higher in the positive outcome group (p=0.007, figure 1). Moreover, the positive outcome group showed a higher ability to clear lactate (p<0.001).



Conclusions: High flow NRP was feasible in all donors and indicates that a different baseline function or more severe ischemic injury may be the cause of liver graft nonfunction in DCD.

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Bivalirudin during extracorporeal support – a retrospective case series

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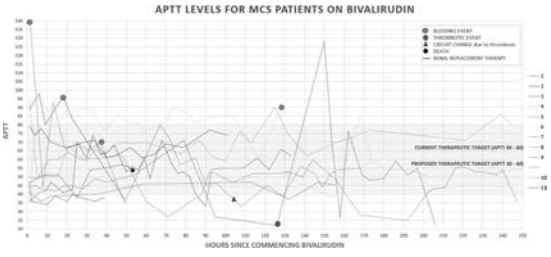
Objectives: Extracorporeal membrane oxygenation (ECMO) and mechanical circulatory support (MCS) are frequently complicated by thrombotic or bleeding

Patient	Dose (mcg/kg/hr)	aPTT range	Median aPTT [IQR]	Duration (hours)	No. Infusion interruptions	No. Dose changes	PRCs (units)	Platelets (units)	RRT req'd.
1	0.02-0.05	36-74	55 [49-62]	136	0	8	0	0	Y
2	0.007-0.05	34-46	38 [36-38]	53	0	6	0	0	Y
3	0.2	83-98	89 [83-95]	25	1	0	0	0	N
4	0.1-0.23	50-94	70 [63-74]	250	0	12	0	0	Y
5	0.03-0.25	33-144	54 [44-65]	182	0	17	10	1	N
6	0.05-0.13	38-95	60 [51-84]	307	2	8	6	0	N
7	0.08-0.17	22-128	47 [27-51]	205	0	12	7	3	Y
8	0.05	26-45	45 [39-46]	181	5	0	1	0	Y
9	0.01-0.02	38-57	52 [51-55]	62	0	3	5	6	Y
10	0.02-0.17	25-64	50 [36-54]	298	3	8	15	4	Y
11	0.15	61-79	69 [67-71]	108	0	0	3	0	N

complications. Bivalirudin may be a safe alternative to unfractionated heparin in such patients, however optimal anticoagulation targets are unclear. A conservative APTT target (40–60s) may offer similar efficacy to current, more intensive protocols (60-80s).

Methods: Retrospective audit of 11 patients who received Bivalirudin at our tertiary ECMO/MCS centre since 2013 (table). Duration of Bivalirudin therapy, median dose, dose changes, serial APTT measurements, requirement for RRT or blood products, and major bleeding or thrombotic episodes were reported.

Results: Major bleeding occurred in 3 patients with supratherapeutic Bivalirudin anticoagulation (APTT 70–140s) (graph). Major thrombotic events occurred twice in 2 patients (APTT <40s). One major bleeding event occurred in the conventional target range for APTT (60–80s); no bleeding or thrombotic events were recorded in the conservative APTT range (40–60s). 7 patients underwent RRT; 1 patient died, unrelated to anticoagulation.



Conclusions: Bivalirudin anticoagulation is feasible in MCS patients, including those receiving RRT (n=7). A conservative APTT range (40-60s) may be optimal but requires prospective, high-quality validation.

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Achieving individualized protein targets improves nitrogen balance for patients on venovenous extracorporeal membrane oxygenation

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Objectives: Research has shown that adults on venovenous extracorporeal membrane oxygenation (VV ECMO) have high protein requirements which vary over ECMO duration. The purpose of this study was to investigate the impact of protein delivery on nitrogen balance (NB) and assess protein dosing targets for patients on VV ECMO.

Methods: Previously reported datasets on NB in adults on VV ECMO were aggregated. This data included patient age, weight, ideal body weight (IBW), body mass index (BMI), mortality, nutrition infusion on the day of NB study, 24-hr urine urea nitrogen, and NB results. Protein targets are assessed at 2 g/kg/d actual weight for patients with BMI <30kg/m^2, and ≥2.5 g/kg IBW for BMI ≥30kg/m^2, then individualized based on NB results to target -4 to +4 g/day. Median NB for patients receiving <80% of their goal protein and those receiving ≥80% goal protein was compared using Mann-Whitney U. Linear regression was used to evaluate associations between NB and proportion of protein goal received, and weight-based protein intake as g/kg/d actual weight in non-obese and g/kg IBW/d in obese patients.

Results: A total of 123 NB studies in 59 patients were included for analysis, 50 studies in 30 obese and 73 studies in 29 non-obese patients. Overall, the cohort was 59% male, in-hospital mortality was 8%, and patients received 100% (90%, 100%) goal energy and 93% (79%, 100%) goal protein on NB study days. NB results were significantly improved when patients received ≥80% of their prescribed protein (-1.82 g/day (-7.43, 3.77 g/day) vs -6.39 g/day (-12.5, -0.46 g/day), p= 0.009). Correlation between proportion of target protein received and NB approached statistical significance (r = 0.18, p = 0.053). On sub-analysis, significant correlations between weight-based protein dosing and NB weren't observed in obese (r= 0.1729, p= 0.23) and non-obese patients (r= 0.09, p= 0.43).

Conclusions: Protein needs vary considerably during VV ECMO and prescriptions should be individualized, ideally using nitrogen balance results. Achievement of at least 80% of prescribed protein is associated with improved nitrogen balance.

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A single centre, retrospective review of the provision and frequency of physiotherapy interventions delivered to patients receiving V-V and V-A ECMO

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Objectives: The UK Physiotherapy ECMO network consensus agreement for best practice for adult patients on V-V ECMO recommend physiotherapists should be involved with patients receiving ECMO from admission, providing assessment, respiratory and rehabilitation treatments. To review the type and frequency of physiotherapy interventions delivered to patients receiving V-V and V-A ECMO in a large tertiary centre in the UK. To compare the treatments delivered against the UK Physiotherapy ECMO network consensus agreement.

Methods: Electronic patient notes were retrospectively screened between January 2020 and October 2022. The following data was extracted: age, gender, type of ECMO, cannulation site, ECMO duration, sedation duration, type and frequency of physiotherapy interventions delivered.

Results: Thirty-three patients were identified as receiving ECMO during this period. Median age was 46 (13-68) years; 20 (60%) were male; 15 (45%) underwent V-V ECMO; 18 (55%) V-A ECMO; 23 (70%) had bi-femoral cannulation sites. Median ECMO duration was 6 (1-53) days. Median duration of sedation 12 (1-62) days. A total of 97 physiotherapy treatment sessions were undertaken during the data collection period, with a median of 2 (0-16) sessions per patient. The most applied intervention was passive range of movement exercises (n=67) followed by manual techniques for airway clearance (n=13) and active exercises in the bed once the patient was awake (n=11) Four (12%) patients were off sedation during their ECMO run and alert enough to engage in active rehabilitation. One patient undertook sitting over the edge of the bed whilst on ECMO. Bed exercises and in-bed cycle ergometry were the predominant choices of active rehabilitation in our patient cohort whilst receiving ECMO.

Conclusions: The provision of physiotherapy services in our centre reflected the UK Physiotherapy ECMO network consensus agreement for best practice for the physiotherapy management of adult patients on V-V ECMO, providing both respiratory and rehabilitative physiotherapy interventions to patients whilst receiving ECMO. This included the provision of early active rehabilitation as sedation levels permitted. Further exploration of the barriers impacting on higher levels of physical activity with ECMO patients is recommended.

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Actual cost estimation of extracorporeal cardio-pulmonary resuscitation (ACE-ECPR Study): a time-driven activity-based costing study

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Objectives: Determining the actual cost of extracorporeal resuscitation (E-CPR) is essential to understand the main determinants of the costs of this complex and resource-intensive intervention.

Methods: We performed a time-driven activity-based costing study from July 2020-June 2021 in a quaternary care ICU in Australia. The ICU provides round-the-clock E-CPR service for out-of-hospital (OHCA) and in-hospital cardiac arrest (IHCA). E-CPR care cycle was defined from the initiation of E-CPR in the hospital to either discharge or death of the patient. Detailed process maps with discrete steps and probabilistic

decision nodes accounting for the complex patient trajectories were developed. Direct observations and database reviews provided time estimates. Using the time estimates and costs per minute for all clinical and non-clinical resources, we calculated the total direct costs. The total direct costs were combined with indirect costs to determine the total cost of E-CPR. Ethics approval was obtained before commencement of the study.

Results: We developed 13 process maps with 141 discrete processes and 26 probabilistic nodes. During the observation period, ten E-CPR care cycles were observed, and a minimum of three observations were obtained per process (other then those where the probability of occurring was <30%). The in-hospital mortality was 70% and mean(95% CI) ICU and hospital duration were 6.2(4.56-7.83) and 11.6(7.88-15.38) days, respectively. The mean(95% CI) in-hospital cost of an E-CPR care cycle was AUD 107,804(AUD 94,856-119,907) [€ 48,564(€42,731-54,016)]. Initiation of ECMO and ECMO management constituted 18% of costs. The ICU management (35%) and surgical costs (20%) were the major cost determinants. The patients with IHCA had higher mean costs than those with OHCA (AUD 115,209 vs 89,448) and this was mainly due to the increased survival and ICU length of stay of IHCA patients. The cost for each E-CPR survivor was AUD 194,923(AUD 169,818-221,642).

Conclusions: The cost of an E-CPR care cycle was more than AUD 100,000, and in survivors, almost AUD 200,000. IHCA was more expensive likely due to greater survival. Most costs were derived from ICU and surgery after initiating E-CPR.

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Incidence of heparin resistance and heparin failure in patients receiving extracorporeal membrane oxygenation – an exploratory retrospective analysis

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Objectives: Unfractionated heparin (UFH) remains the anticoagulation of choice at most centres for patients receiving extracorporeal membrane oxygenation (ECMO). One disadvantage of UFH relies on its individual dosing requirement to achieve target values. In this context heparin resistance has been described, defined as doses exceeding 35,000 IU UFH/d. However, the incidence of heparin resistance and its association with thromboembolic complications despite anticoagulation within target ranges remains unknown.

Methods: This retrospective study included adults receiving venovenous (VV) and venoarterial (VA) ECMO, or extracorporeal CO_2-removal ($ECCO_2R$) between 2010 and May 2022. The primary outcome was the incidence of heparin resistance (>35,000 IU of UFH/d). Secondary outcomes were heparin failure (thromboembolic complications despite anticoagulation within target ranges) and survival. A multivariable poisson regression model was fitted to analyse the effect of heparin resistance, COVID-19 and ECMO type on the incidence rate of thromboembolic events.

Results: Of 197 included patients, 33 (16.8%) had heparin resistance. Patients with COVID-19 (n=51) had a higher rate of heparin resistance compared to non-COVID-19 patients (37% vs. 9.6%, P<0.001). Thromboembolic complications occurred at a rate of 5.89/100 ECMO days. There was a significant effect of COVID-19 (incidence rate ratio (IRR) 2.12, 95% confidence interval (CI) 1.4 to 3.3, P<0.001) and ECMO type (VA ECMO: IRR 2.35; 95% CI 1.43 to 3.87, P<0.001; $ECCO_2R$: IRR 2.63, 95% CI 1.37 to 4.9, P=0.003; reference VV ECMO) on incidence rate of thromboembolic events, but not of heparin resistance (IRR 1.11, 95% CI 0.7 to 1.76, P=0.7). ECMO duration was longer (25d (IQR 11-33) vs. 8d (IQR 4-18), P<0.001) in patients with heparin resistance, but hospital survival did not differ (23 (70%) vs. 91 (57%), P=0.2).

Conclusions: The study revealed a high incidence of heparin failure in ECMO patients, especially in those with COVID-19. Heparin resistance had no effect on the incidence rate of thromboembolic events, whereas our data suggest an increased risk in patients with COVID-19, VA ECMO and $ECCO_2R$.

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Neuropsychiatric sequelae do not depend on ECMO support nor on levels of consciousness during ECMO support

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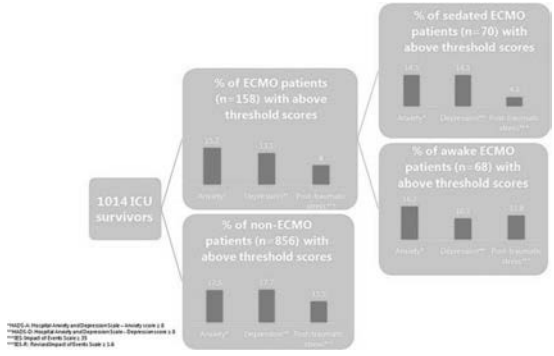
Objectives: We analyzed the impact of ECMO support and levels of consciousness during ECMO support on

self-reported neuropsychiatric symptoms in intensive care (ICU) survivors after one year.

Methods: We included consecutive ICU survivors who responded to the Hospital Anxiety and Depression Scale (HADS) and Impact of Event Scale (IES) questionnaire one year after ICU admission between 2013 – 2021. This cohort was restricted to ECMO recipients and general ICU patients who would have been eligible for ECMO , i.e., with comparable disease severity and without contra-indications for ECMO. Multivariable regression analyses were used to study the association between ECMO support and degree of neuropsychiatric symptoms. Models were adjusted for baseline confounders (sex, age, admission indication, Sequential Organ Failure Assessment (SOFA) on day 1, and Acute Physiology And Chronic Health Evaluation (APACHE) IV score. Among ECMO recipients, the association between awake ECMO (Richmond Agitation – Sedation Scale (RASS) between -1 and +3 ≥ 6 hours) and outcomes was studied.

Results:



Out of 2,531 respondents, 1,014 (158 ECMO and 856 non-ECMO) remained after restriction. After adjustment for baseline confounders, ECMO was not associated with higher levels of anxiety and depression (HADS ≥ 8) and post-traumatic stress (IES ≥ 35 or revised-IES ≥ 1.6) (OR [95%CI]) 0.83 [0.50; 1.40], 0.89 [0.52; 1.52], 0.66 [0.35; 1.24] , respectively). Patients who had been (partially) awake during ECMO support (n=68, 49%), versus those who had been continously sedated (n=70, 51%), did not suffer from higher levels of anxiety (n=11 (16.2%) vs n=10 (14.3%), p=0.73), depression (n=7 (10.3%) vs n=10 (14.3%), p=0.50) or post-traumatic stress (n=8 (11.8%) vs n=3 (4.3%), p=0.11).

Conclusions: Our findings support previous conclusions that ECMO support should not be withheld for risks of neuropsychiatric symptoms. Furthermore, awake ECMO appears safe in those that tolerate it.

Conflict of interest: Primary source of funding: Stichting Gezondheidszorg Spaarneland (SGS) Fund, Zilveren Kruis Achmea D.W. Donker from the institutional research cooperation of the Cardiovascular and Respiratory physiology group of the University of Twente with Maquet Critical Care AB, Solna, Sweden and Sonion Nederland BV, Hoofddorp, The Netherlands (no personal honoraria received). C. Meuwese received research funding from "Stichting Gezondheidszorg Spaarneland (SGS)" Fund the "Hartstichting".

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Combining information technology and human research efforts to lessen personnel burden and costs One success story

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Objectives: Develop a coding system to extract EHR data and establish research validity to lessen need for manual data extraction

Methods: As part of a data collection project for COVID + patients requiring ICU care, we established data elements able to be extracted from the Epic electronic health record (EHR). Collaboration between Information Technology (IT), research and clinical personnel established where data elements were located within the EHR and what data could be extracted with minimal manual assistance and uploaded to a research database. Coding was developed using Structured Query Language (SQL) with best practices (includes indexes, execution plans, optimized range keys, avoiding large reads inside read-write transactions as instructed by the Epic consultant). Accuracy of extracted data was evaluated by manual validation of data against Epic records via random selection of patient data within the cohort.

Results: From July-December 2022, coding was developed which extracted over 130 fields of data from 3093 COVID patients across 5 INOVA ICU sites (demographic, physiologic, lab, interventions, outcome). Prior efforts at data extraction of these elements from research personnel (ZS) who previously performed this task noted an average of 4 hours/patient to complete coded fields. Coded data was also noted to be more accurate when accessed by the same personnel to

manually extracted fields. Assuming 4 hrs/pt, manual extraction would require 12,372 hours, which equates to over 6 full time human research personnel. Data coding required 446 hours. Coded data extraction can be almost immediate once fields requested are established, decreasing personnel costs and effort significantly.

Conclusions: Reduction in need for manual data collection using automated coding extraction can reduce costs, personnel time and enhance research efforts. Sharing coding mapping to other EPIC sites or use of similar methods may improve timeliness of ongoing data extraction and will be useful to develop early-warning and patient-centered care algorithms to improve care.

Conflict of interest: Consultant, Innovative ECMO Concepts Consultant, Entegrion Consultant, Medtronic

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An open-source real-time data acquisition and analysis system for ECMO devices

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Objectives: Develop an open-source automated data acquisition tool for real-time monitoring of patients receiving extracorporeal membrane oxygenation (ECMO) treatment in the intensive care unit. Furthermore, interoperability should be ensured to integrate the data into a patient data management system or registries such as the ELSO Registry.

Methods: An automated data acquisition and monitoring tool (ECMO Reader) was created using Python 3.10 and a single-board computer (Raspberry Pi 4B). The software was developed to read data in real-time from Getinge CardioHelp and Rotaflow I and II ECMO devices. The received data is transferred to a single-board computer via a universal serial bus (USB) cable and stored locally.

Results: ECMO Reader is a cost-effective data acquisition and monitoring system for Getinge ECMO devices. After a cable connection, the software provides a visualisation of the received data in real-time and it allows treatment histories to be displayed over particular time spans to identify trends better. A detailed digital documentation of an ECMO treatment, with details of the configuration of the cannulas, recording of complications, and transportation can be achieved. The data is stored locally in a structured fashion in multiple files (vitals data, treatment events, system events, medical-administrative documentation) that allows further detailed post-treatment analysis. An intuitive graphical user interface (GUI) facilitates easy use and offers an alternative to paper-based treatment documentation. The use of Python as a programming language and standard libraries allows easy code maintenance and expandability.

Conclusions: ECMO Reader is the first open-source software tool designed for automated data acquisition and monitoring of ECMO treatment data. The software offers a possibility to reduce the administrative burden on hospital staff during treatment and will potentially allow early recognition of complications related to ECMO treatment before their onset. The event-annotated vitals data will potentially offer possibilities for improving patient care during ECMO treatments.

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Physical outcomes and hospital length of stay of patients receiving ECMO in a large tertiary UK centre

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Objectives: To examine the physical outcomes and hospital length of stay (LOS) of patients receiving ECMO in a large tertiary intensive care unit (ICU) in the UK

Methods: Retrospective review of patients requiring ECMO between January 2020 and October 2022. Data was extracted for: age, gender, ECMO modality and duration, sedation duration, ICU mobility score (ICUMS) at ICU and hospital discharge, ICU and hospital LOS.

Results: Thirty-three patients were identified: 11 (33%) died prior to hospital discharge, and 4 (12%) transferred to another centre for ongoing management. Eighteen patients were included in the final analysis: 12 (67%) male, median age 50.5 (29-68) years; 9 (50%) V-V ECMO; 9 (50%) V-A ECMO; median ECMO duration 7 (3-42) days and median sedation duration 14.5 (4-32) days. Median ECMO duration was 7 days for both ECMO groups, with longer duration of sedation in the V-V ECMO group: 15 vs 11 days. Physical outcomes were identical for both groups at ICU and hospital discharge (ICUMS 4 and 10 respectively). ICU and hospital LOS were longer for the V-A ECMO group: 36 vs 23 and 51 vs 34 days respectively. Fourteen (78%) patients remained sedated for the duration of their

ECMO run, compared with 4 (22%) who were awake whilst on ECMO. Awake patients had longer ECMO duration, (19.5 vs 6 days) ICU, (46 vs 21 days) and hospital LOS (51.5 vs 32.5 days) compared to sedated patients. Physical outcomes were better for awake patients at ICU discharge, but worse at hospital discharge than those remaining sedated.

Conclusions: Patients surviving ECMO within our organisation achieved good physical outcomes at ICU and hospital discharge. There was no difference in physical outcomes between patients based on ECMO modality, but LOS was longer for V-A ECMO. Awake ECMO patients had longer LOS and worse physical outcome at hospital discharge than those sedated on ECMO. These results should be interpreted with caution due to the small number of patients, warranting further exploration and comparison to other centres

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Veno-arterial extracorporeal membrane oxygenation as a bridge to redo cardiac surgery for inoperable patients: A case series

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Objectives: Patients presenting at the emergency department with non-ischemic cardiogenic shock (CS) have high risk mortality and it's even higher when they need a redo cardiac surgery. The aim of this study is to present early outcomes in patients with previous cardiac valve surgery presenting CS that has been resuscitated with VA-ECMO-therapy as bridge to successful redo cardiac operation

Methods: A retrospective case series was conducted on three patients with non-ischemic CS.Demographic variables and risk scores were calculated at admission and before intervention. High-definition videos were recorded during procedures. VA-ECMO was established as a bridge therapy to definitive surgical treatment. When recovered from CS patients were taken to definitive redo cardiac operation. Intraoperative and postoperative variables including major cardiovascular and neurological events were collected. Follow up period was 6 months after surgery.

Results: We describe three cases presenting CS and previous cardiac surgery. Step by step details of surgical technique is registered as well as hemodynamic condition before and during ECMO for each patient. First patient is a 57-year-old morbidly obese man in CS with bio-prosthetic aortic valve severe stenosis who collapsed during coronary angiography. A femoral VA-ECMO was initiated bridge to second redo AVR.VA-ECMO was sustained for 4 days and then VV-ECMO was required for 13 days for complete recovery. A second case is a 39-year-old man with medical history of mitral endocarditis, admitted in sepsis, CS and Mechanical-prosthetic mitral valve severe regurgitation due to dehiscence. Femoral VA-ECMO and IABP bridge to third redo mechanical mitral valve replacement (MVR) was successful performed. Weaning off circulatory support was achieved after surgery. The third case is a 21-year-old female with CS and bio-prosthetic mitral valve severe stenosis. Femoral VA-ECMO was initiated bridge to CS recovery. She underwent a successful third redo MVR operation and 4 days later ECMO therapy was discontinued. No deaths or neurological events were presented.

Conclusions: According to this experience, patients with CS due to dysfunctional prosthetic aortic/mitral valve might survive a redo cardiac operation using VA-ECMO therapy for optimization of hemodynamic status. This approach should contribute to reducing operative mortality in these high-risk patients.

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Early involvement of the specialist and supportive palliative care team for ECMO patients in a specialist cardio-thoracic transplant centre

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Objectives: Extracorporeal Membrane Oxygenation (ECMO) is associated with significant morbidity and mortality. Early referral to specialist supportive and palliative care teams (SSPCT) may benefit patients and their relatives. The aim of the Quality Improvement Project (QIP) was to determine the type of support required by ECMO patients and their relatives, collecting feedback from both families and ECMO Intensive Care Unit (ICU) nurses to inform future practice.

Methods: The QIP retrospectively analysed data from adult patients from October 2021 to October 2022. Information was gained from the patient data management programme. ECMO ICU nurses referred every

patient on ECMO therapy initiation to the SSPCT after gaining either patient or the next of kin's consent. The SSPCT completed an initial holistic assessment, providing weekly contacts and referring to other members of the multidisciplinary team when appropriate. A qualitative survey was sent to relatives and ECMO ICU nurses six weeks after ECMO discontinuation.

Results: Of the 47 patients eligible for analysis, four declined SSPCT input and four patients died before being seen with 247 reviews being delivered by the SSPCT. In total 91.5% of patients (43) were supported with Venoarterial (VA) ECMO and 8.5% (4) with Venovenous (VV) ECMO. The mortality rate was 42.5%. The findings revealed 74.5% of support needed was psychological; supporting young children 44.7%; facilitating end-of-life care discussions 34%; welfare advice 38.3%; spiritual support 29.8%. Relatives rated the overall experience positively, defining regular contacts with the SSPCT helpful. ECMO ICU nurses perceived early integration of the SSPCT positive and beneficial.

Conclusions: The study reflects the need for early SSPCT involvement for ECMO patients including psychological interventions, supporting young children, facilitating end-of-life care discussions, referring to the welfare team and addressing spiritual needs. Surveying both relatives and staff demonstrates a positive impact on both patient care and their relatives, enabling better communication and coordination of care. Suggestions were made to expand the service to all patients on mechanical life support.

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Nutrition delivery and its influence on outcomes for adult patients on venovenous extracorporeal membrane oxygenation

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Objectives: Over and underfeeding are associated with negative outcomes during critical illness. The purpose of this retrospective study was to assess the impact of nutrition delivery on outcomes for patients on VV ECMO.

Methods: Adults who received VV-ECMO between 8/2017 and 6/2020 were included. Data collected included age, sex, height, weight, ideal body weight (IBW), body mass index, sequential organ failure assessment score, respiratory ECMO survival prediction score, energy and protein goals, and all sources of nutrition intake. Nutrition intake data were collected for the first 14-days of ECMO, or until death, decannulation, or transition to an oral diet. Patients on ECMO £3 days or who received oral diets within 3-days of cannulation were excluded. Outcomes of interest included mortality and duration of VV-ECMO. For analysis, patients were divided into obese and non-obese groups and sub-divided based on energy or protein delivery <60% of goal, 60-80% of goal and ³80% of goal. Association between nutrition delivery, ECMO duration and mortality were assessed using the Kruksall-Wallis and Fischer's exact tests.

Results: A total of 2044 nutrition days in 178 patients were included for analysis. Obese patients (n=89) received 23.7 kcal/kg (20.5, 26.4 kcal/kg) and 1.7 g Pro/kg IBW (1.5, 2 g/kg IBW) or 81.4% (67%, 99%) and 62.2% (52%, 73%) of respective targets. Patients who received ³2 g Pro/kg IBW had significantly shorter duration of ECMO (p=0.037), however no association was observed with mortality (p=0.59). Energy delivery was not significantly associated with duration of VV-ECMO (p = 0.81) or mortality (p=0.87). Non-obese patients (n=89) received 83% (61.3, 96.7%) of energy and 67.4% (48, 79.4%) of protein targets for a delivery of 18.5 kcal/kg (14.1, 21.7 kcal/kg) and 1.4 g Pro/kg (1, 1.7 g Pro/kg). No significant associations were identified on univariate analysis. However, after excluding 4 underweight patients, a potential trend towards reduced mortality with increased protein delivery was noted (p=0.28).

Conclusions: High protein targets for patients on VV-ECMO may positively influence outcomes, while optimal energy targets continue to require investigation.

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The characteristics and clinical outcomes of patients acquiring infections during Extracorporeal Membrane Oxygenation (ECMO) run

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Objectives: To evaluate the incidence, risk factors, and clinical outcomes of bloodstream infection(BSI) in ECMO patients who cannulated in-house versus outside the hospital.

Methods: A retrospective chart review was performed on patients receiving ECMO treatment from January 1st, 2019, to December 31st, 2022. The incidence of BSI was calculated by the ECMO run time, patient body mass index(BMI),

ECMO retrieval location, gender, and age group. The clinical characteristics of patients with and without BSI while on ECMO were described.

Results: Among 604 ECMO patients, 83(14%), 37(10%) veno-arterial(VA), and 45(20%) veno-venous (VV) developed at least one BSI while receiving ECMO. There were 39 (21%) out of 187 cannulated at the outside hospital (OSH), 6(12%) out of 52 in the emergency department(ED), 22(14%) out of 158 in the cardiothoracic intensive care unit(CTICU), 11(11%) out of 103 in other ICU/floors, and 5 (5%) out of 104 in the operating room(OR). The average ECMO run time with and without infection was 632 hours for patients cannulated at OSH, 264 hours for the CTICU group, 284 hours for other ICU and floor, 179 hours for OR, and 84 hours for ED. Overall, ECMO runs with BSI averaged 938 ECMO hours compared to 264 hours for the group without BSI. The OSH ECMO retrieval has the highest BSI rate, with an average of 1175 ECMO run hours vs. 493 hours for the non-infected group. ECMO retrieval in OR has the lowest BSI rate with an average of 1506 hours ECMO run time vs. 112 hours ECMO run time for the non-infected group

Conclusions: This single-center report analyzes the concern for procedure-acquired BSUIs based on the location of ECMO retrieval. The results showed no significant impact on whether the patient was cannulated at OSH, CTICU, other ICU, non-ICU settings, OR, or ED. The most impactful factor in BSI's occurrence was the total ECMO run time. Further subgroup analysis would provide risk stratification, which will serve for case selection and decision-making, ultimately developing effective infection prevention strategies to improve patient outcomes.

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Simulation training for inter-hospital ECMO transport team

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Objectives: Inter-hospital ECMO transports are complex and carry a high risk of complications. (1) To ensure safety during inter-hospital ECMO transports it is vital that the transport team regularly trains in an environment similar to that on transport. In our program the transport team is composed of an ECMO specialist physician, an ECMO specialist nurse with ECLS priming skills, and a cannulating surgeon. Thus, any problem or emergency of the ECMO circuit/machine during transport has to be solved by these three individuals, making the situation more vulnerable than any emergency occurring in the ECMO intensive care unit.

Methods: Our transport team members simulate in an inter-hospital transport environment at a minimum once annually. These simulation exercises take place at the airport with the aircraft ambulance inside a hangar with the mobile intensive care unit (MICU; bus) in place. The MICU usually transports the team and ECMO patient from airport to hospital. The scenario is set up inside the aircraft cabin, while loading/unloading the patient, or inside the MICU. The transport stretcher is set up with a mannequin, attached to a monitor, ventilator and an ECMO circuit. All equipment used during transport is included.

Results: Team members are exposed to scenarios where they train in a confined space inside the aircraft, MICU or during patient transfer between transport vehicles. They are required to solve any emergency, e.g., prime rescue equipment packed inside the transport luggage. Accessing the right bag is vital and therefore all team members need to be familiar with the transport equipment. The ECMO specialist physician acts as team leader and must allocate and prioritize the tasks. All team members have practiced all elements of emergencies during conventional in-house water drills at least once a month. Thus, tasks such as priming, connecting, de-airing the circuit, are familiar procedures for all team members. These simulations offer the team members a new level of training with scenarios in an environment that is realistic to inter-hospital ECMO transports.

Conclusions: Inter-hospital ECMO transports should be performed by experienced team members. In our program the transports are carried out by a maximum of four staff. This low number of team members, (2) together with the constantly changing environment during the transport makes it more vulnerable in the case of an adverse event. Therefore, it is imperative that team members are offered regular team training in a realistic environment.

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Simulation training in implementing a new transport mode for inter-hospital ECMO transports

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Objectives: As part of the implementation of the hospital's new intensive care helicopter for our ECMO transport services, it became apparent that the transport team had to be offered training in how to work in this new environment. The helicopter allows a fast patient transport from one hospital's helicopter pad to another without the need of hazardous transfers between ambulances, etc. which presents a high-risk situation during inter-hospital ECMO transport. However, working in a helicopter is unlike working in an ambulance or an aircraft, and troubleshooting in this environment can be challenging. Communication between team members requires headsets, the helicopter's motion differs from other transport vehicles, and space is limited. Another restraining factor are the survival suits required when flying over open water.

Methods: As the helicopter is based approximately 40 km from the hospital and frequently utilized by other hospital transport resources, it was not feasible to use the helicopter for simulation exercise. The simulation team set up a mockup of the helicopter in our unit using a small space approximately the same size as the helicopter cabin. In this space our transport stretcher with a mannequin attached to monitoring, ventilator and ECMO circuit, four seats and the transport equipment were placed. The team members had "headsets", the light was dimmed, and prerecorded helicopter sound was played via loudspeakers inside the small space.

Results: Each team was composed of groups of three, mimicking the constellation during transport: one ECMO specialist physician, one ECMO specialist nurse, and one cannulating surgeon. In total 12 transport team members attended the training over two days. The team entered the mock helicopter, and the simulation instructors staged a scenario for each team. The inactive team acted as observer during the scenario. After the scenario, the instructors led a short debriefing. Several questions emerged and the team that already had simulated transports in the helicopter could share their experiences, an exchange of information could take place. The team members expressed that the training had been rewarding and necessary for the implementation of the new transport mode. It also became apparent to them that they will face new challenges with this new transport mode and that training together as a team made them better prepared for this.

Conclusions: Inter-hospital ECMO transports counts as a high-risk procedure and although our program has performed over 1350 inter-hospital ECMO transports, team training in new environment is essential when introducing a new transport mode, in this case an intensive care helicopter. It is feasible to set up training with limited resources and yet make it authentic for the team members.

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ECMO rescue: Our experience

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Objectives: Since the beginning, ECMO therapy was only available on a few selected highly specialized medical centres. Because of this, it is common practice to rescue patients in cardiac and/or pulmonary support of ECMO therapy from secondary hospitals to our tertiary centre.

Methods: We carried out a statistical analysis of our ECMO database between 2010 and 2022 with concerns pertaining to our land-based and airborne rescues and the associated events.

Results: Since 2010 to 2022 we have performed 70 ECMO rescues with 4 of them being airborne. There were 5 VA-ECMOs and 65 VV-ECMOs. There were no major complications reported in association with the rescues. Based in our 12 years experience, changes in the methodology were made, allowing us to save time, improve safety after offer a better differencial diagnosis and care for the ECMO patient.

Conclusions: We present our accrued experience in land and airborne rescues, our pitfalls and our learnings. In regards to the results obtained, we thus consider the rescue ECMO of the patients to be a safe and feasible operation when performed by a properly trained multidisciplinary team.

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Could out-of-centre initiation of extracorporeal membrane oxygenation with mobile equipment improve outcome and prognosis in COVID-19 patients? A retrospective study from the ECMO centre Regensburg

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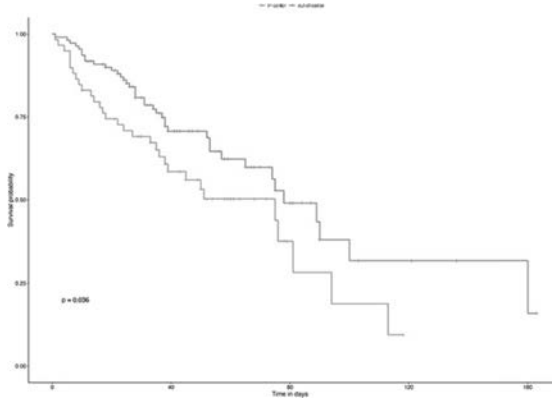
Objectives: Besides in-centre ECMO care, the certificated ECMO centre of the University Hospital Regensburg

(UKR) offers out-of-centre ECMO initiation with mobile equipment. During the pandemic situation, this treatment was especially meant for patients with critical cardiopulmonary failure in remote hospitals who present themselves as too unstable for inter-hospital transfer. We evaluated if treatment with out-of-centre ECMO initiation could benefit patients' outcome, by comparing this group with a group of COVID-19 patients who received ECMO therapy at the UKR by in-hospital initiation.

Methods: Retrospective single-centre study including 169 patients who received ECMO due to COVID-19-induced cardiopulmonary failure between March 2020 till March 2022. Patients' population was separated into two groups according to the location of ECMO initiation, out-of-centre or in-centre, and into two subgroups by the used ECMO mode, venovenous (VV) or venoarterial (VA). We compared demographics, treatment duration, adverse events and patient's outcome. The primary endpoint of the investigation was patients' survival to hospital discharge rate or death on ECMO or after ECMO explant.

Results: Regarding the total study population, 98 (58.0%) of the 169 patients could be discharged from the UKR. Before initiation of ECMO therapy and with regard to complications during the course of intensive care, such as renal failure requiring dialysis or bleeding, there were no relevant differences between the two groups and subgroups. The out-of-centre group showed a significantly higher survival rate with 70 (63.6%) survivors out of 110 externally cannulated patients.



Conclusions: In the study population, external ECMO cannulation was beneficial in terms of survival, although the reasons did not show significant differences between the groups. A possible approach for the good overall survival of the study groups in international comparison could be the existing centre expertise.

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Multidisciplinary approach to bridge a critically ill patient affected by Acute Heart Failure. Unconventional use of prolonged ambulatory Intra-Aortic Balloon Pump. Our experience

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Objectives: Heart Failure guidelines recommend that patient with acute heart failure (AHF) are supported by a multidisciplinary dedicated team to enhance better outcomes.(1)It has been reported that the use of Intra-Aortic Balloon Pump (IABP) helps bridging patients to heart transplantation(2).Our aim is to describe how nonconventional prolonged use of ambulatory IABP and multidisciplinary approach favor optimal conditions to patient's recovery.

Methods: A literature review was conducted together with a retrospective review of the patient electronic medical record. A descriptive analysis is presented. A 53 years-old woman,B Rh-was admitted for cardiogenic shock due to myocardial infarction with severe cachexia and sarcopenia associated to heart-failure. The use of left ventricular assist device was excluded due to a lack of family support post discharge. A femoral IABP was initially inserted and replaced by a right axillary IABP to promote mobility.

Results: As a result of the multidisciplinary care plan the patient achieved an acceptable level of muscle trophism favored by the use of ambulatory IABP. 35 days of femoral IABP,110 days axillary ambulatory IABP. No IABP infection. Regression of cachexia and sarcopenia. No delirium events(pain control,adequate hydratation,regulation of sleep-awake cycle).Close monitoring of vital signs,intake and output,laboratory results and SVO2 level. Daily dietician support. Daily physical therapy-sessions (average ambulatory distance covered 853 feet).Dedicated nurses and the physical-therapists,tailored care plan.

Conclusions: In August 2022, after 145 days of IABP support, the patient received a new heart on optimum conditions. The unconventional use of axillary IABP for 110 days, together with a strict physical therapy program and prevention complication plan helped the patient maintaining the activity of daily living,thus reversing

cardiac cachexia and sarcopenia. A tailored cardiac rehabilitation together with synergic effort and expertise of a multidisciplinary team has had a significant impact to successfully bridge our patient to heart transplant.

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Characterizing electroencephalographic abnormalities in patients receiving extracorporeal membrane oxygenation support

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Objectives: Acute neurological complications, such as ischemic stroke, intracranial hemorrhage, and seizures, are major drivers of poor outcomes in patients receiving support through extracorporeal membrane oxygenation (ECMO). Reliable clinical examinations and neuroimaging studies can be difficult to obtain in critically-ill patients who are often deeply-sedated, thus warranting the evaluation of non-invasive methods for detecting neurological abnormalities. The aim of this study was to characterize and correlate electroencephalography (EEG) findings with prognostic measures, including survival and acute cerebral complications in adult patients receiving ECMO support.

Methods: This was a retrospective, single-center study of adult patients who received any duration of EEG monitoring while on ECMO between 2020-2022. EEG reports, CT/MRI results, and other notes were reviewed to assess outcome measures. Mann–Whitney U and Chi-squared tests were performed for continuous and categorical variables respectively, with $p < 0.05$ considered statistically significant. All data was analyzed using Stata 17.

Results: Of 255 patients receiving ECMO support, 38 (68.4% male, 31.5% female) had continuous EEG for at least 24 hours and were eligible for analysis. Of the 38 patients, 30 (79%) were on VV-ECMO while 8 (21%) were on VA-ECMO. The mean age was 52.7 (range 20-73) years. Neuroimaging and EEG abnormalities are presented in Table 1. EEG abnormalities were common and occurred in 36.8% of patients. No patient was found to have electrographic seizures.

Table 1.

	Died (n = 26)	Discharged Alive (n = 12)	Total
Any acute neuroimaging abnormality (%)	12 (46.2%)	5 (41.7%)	17 (44.7%)
Hemorrhage (%)	4 (15.4%)	2 (16.7%)	6 (15.7%)
Hypoxic-Ischemic injury (%)	3 (11.5%)	1 (8.3%)	4 (10.5%)
Ischemic Stroke (%)	5 (19.2%)	1 (8.3%)	6 (15.7%)
Other (%)	0 (0%)	1 (8.3%)	1 (2.6%)
Any EEG abnormality (%)	8 (30.8%)	6 (50.0%)	14 (36.8%)
Periodic discharges (%)	4 (15.4%)	1 (8.3%)	5 (13.1%)
Epileptiform discharges (%)	4 (15.4%)	3 (25.0%)	7 (18.4%)
Rhythmic activity (%)	5 (19.2%)	3 (25.0%)	8 (21%)
Electrographic seizures (%)	0 (0%)	0 (0%)	0 (0%)

Conclusions: Epileptiform abnormalities on EEG were common in patients receiving ECMO support, although frank electrographic seizures were not seen. There were no significant associations between the presence of EEG abnormalities and outcome variables. Further work using a larger patient sample and looking at functional outcome measures are required.

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A collaborative palliative care and intensive care support service for ECMO patients and their families

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Objectives: An early integrated Specialist Palliative Care (SPC) support service was established for all ECMO patients and families in the Adult Intensive Care Unit (AICU) in a Specialist Heart & Lung Hospital during the Covid-19 pandemic. The pandemic added further complexity to the morbidity and mortality faced by this patient group: uncertainty around treatments/ timelines, limited hospital visitation/ communication, little time to adjust to psychosocial burden of sudden critical illness.

Our aim was to evaluate the feasibility of delivering this novel service and to assess the impact on families and AICU staff.

Methods: Retrospective data were collected through note review of all ECMO patients in the 3 months period prior to commencement of the new SPC service. Prospective data were collected over the initial 4 months of the new SPC service. Descriptive statistics were used to describe the feasibility of the service, defined as the proportion of patients referred to SPC team and time to SPC referral. Anonymous family and AICU staff feedback were collected.

Results: 28 ECMO patients were included in the prospective evaluation and results compared with baseline data from 24 ECMO patients. Referrals to SPC increased from 30% to 100%. Average time between starting ECMO and SPC referral decreased to 0.8 days vs 28 days at baseline. Average duration of SPC contact for those who died was 45 days vs 18 days at baseline. Feedback: 10/10 families and 15/20 AICU staff found service beneficial. The main themes identified were information, psychosocial and spiritual needs, holding uncertainty and end of life discussions. Total of 30 referrals to wider AICU MDT made to support with these needs

Conclusions: Preliminary data suggests early integration of SPC within AICU facilitates effective communication and relationship building with ECMO families to alleviate distress and burden, including in the context of ECMO withdrawal when there is no chance of recovery. This collaborative approach allowed for sharing of expertise and colleague support.

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Anticoagulation in ECMO patients: Management in a portuguese center

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Objectives: To describe the anticoagulation protocol in use in a portuguese ECMO center and preliminary results in terms of hemorrhagic complications in 4 years of protocol use.

Methods: All patients on ECMO at our center are eligible for anticoagulation unless there is any contraindication assessed by the team. We use an UFH (unfractioned heparin) protocol implemented in 2017. Patients receive an initial UFH bolus of 50-100 U/Kg at the cannulation time and then, an UFH infusion rate of 20-50 U/Kg/h. The aPTT target is defined as 1,5-2,5 of its baseline value (50-60 seconds). Afterwards, the whole blood aPTT is checked every 4 hours with a point-of-care device (Werfen Hemochron®), and the UFH dosing is adjusted according to the aPTT result and a modified weight-based heparin nomogram. After 3 on target aPTT results (consecutives), the aPTT measures are performed every 8 hours. In addition, anti-FXa is monitored once a day when aPTT is on target. If necessary, the aPTT target may be adjusted according to the anti-FXa level (goal level is 0,3-0,5 IU/ml for VV-ECMO). We analyzed anonymized data from patients who have been under VV-ECMO support in our unit (2019-2022), performing a preliminary analysis of demographic data and hemorrhagic complications and comparing them with ELSO ECLS International Complication Trend Report (October, 2022).

Results: ELSO ECLS Report (adult respiratory) describes in 2019-2021 a total of 22 915 VV-ECMO runs. Central Nervous System hemorrhage and pulmonary hemorrhage occurred in an average of 12,5% of the runs. We look over 163 patients who have been submitted to VV-ECMO support in our center in these 4 years, with an average of 10,4% of the same hemorrhagic complications.

Conclusions: In order to have better outcomes anticoagulation protocols should be monitored. This submission demands to present our anticoagulation protocol and to work as a bottom line to scrutinize data about ECMO complications.

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Classifying fidelity for ECMO simulators and simulations: an overview of existing physical and computational ECMO simulators

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Objectives: High-volume ECMO centers have better clinical outcomes than low-volume centers due to higher clinical exposure. Simulation-based training (SBT) can be an alternative for these centers to reach similar experience levels. SBT not only improves education of the individual caregiver but also improves multidisciplinary ECMO teams. However, ECMO simulators and/or simulations (Sims) differ on realism and functions, making each of these simulators useful for different purposes. Classifying Sims is often subjective and left to the individual user and/or creator. This scoping review aims to present a structured and objective way to classify available Sims.

Methods: Physical and/or computational Sims with public information in English were screened for eligibility. Overall fidelity was established by taking the median of definition-based fidelity, derived from

Table. Overall fidelity classification of ECMO simulators based on definition-based, component, and customization fidelity

Overall fidelity	Definition-based fidelity			Component fidelity			Customization fidelity		
	Low	Mid	High	Low	Mid	High	Low	Mid	High
Low, n = 10	8 (80%)	2 (20%)	0 (0%)	7 (70%)	3 (30%)	0 (0%)	10 (100%)	0 (0%)	0 (0%)
Mid, n = 16	2 (13%)	9 (56%)	5 (31%)	2 (12,5%)	14 (87,5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
High, n = 0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Parameters of classification	- Conceptual fidelity - Functional fidelity - Physical fidelity - Psychological fidelity			- Diagnostics - Circuit priming - Circuit monitoring - Cannulation - Connection ECMO / oxygenator - Gas exchange - Hemodynamics - Weaning - Decannulation - (Clinical) scenarios			- Visual representation of patient - Computational and/or Physical Simulation - Sex - Age - Size (body height) - Race - Disease and/or anatomy - BMI / Fat percentage		

literature, and combining this with the median of our newly established component fidelity and customization fidelity. Component fidelity was based on the main elements of ECMO support while customization fidelity was based on main parameters to (re)create a unique patient, see table. Sims were subsequently classified as being low-, mid-, or high-fidelity.

Results: Universal definitions for SBT were applied to Sims. According to our objective classification method, 10 (38%) low, 16 (62%) mid and no high-fidelity Sims exist. Most (54%) Sims are lacking customization options for patient-specific modelling.

Conclusions: Overall fidelity of available Sims were objectively classified based on definition-based, component, and customization fidelity. No high-fidelity Sims currently exists, urging for development of a high-fidelity simulator to improve ECMO-team training and improve patient outcomes. With our method, future Sims can be classified more objectively allowing for users and researchers to compare accordingly.

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Extracorporeal life support in thoracic emergencies - a narrative review of current evidence

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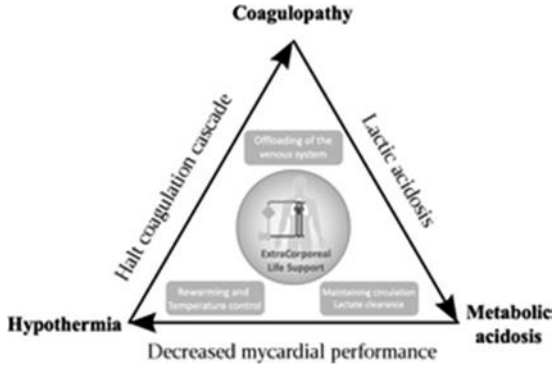
Objectives: Resuscitative therapies for respiratory and cardiac failure are lifesaving and extended by using extracorporeal life support (ECLS) as mechanical circulatory support (MSC). This review informs the debate to identify the life-threatening thoracic emergencies in which patients may be cannulated for ECLS support.

Methods: An advanced search was performed in PubMed, Google Scholar and references query, assessed in Kune 2022, identified 761 records. Among them, 74 publications in English were included in the current narrative review.

Results: ECLS in as additional tool for organ support in life-threatening thoracic emergencies. It provides bridging to recovery or to decision about destination as definitive therapy, intervention, or surgery. Non-traumatic emergencies include mediastinal mass, acute lung injury, aspiration, embolisms, acute and chronic heart failure. However, based on the current evidence, trauma, and especially blunt thoracic trauma, is one of the main indications for ECLS use in thoracic emergencies, among others in chest wall fractures, blunt and penetrating lung injuries. ECLS use is always individualized to patient's needs, injury pattern and kind of organ failure, circulatory arrest inclusive, depending on if respiratory or cardiac and circulatory support is needed. Further, ECLS offers the possibility for fast volume resuscitation and rewarming, thus preventing the lethal of trauma: hypothermia, hypoperfusion and acidosis. Anti-coagulation may be omitted for some hours or days.

Interdisciplinary cooperation between intensivists, surgeons, anesthesiologists, emergency medical services, and appropriately organized and trained staff, equipment resources and logistical planning are essential for successful outcomes.



Conclusions: ECLS use in selected life-threatening thoracic emergencies is increasing. The summarized findings appeal to policymakers, and we hope that our summary of recommendations may impact clinical practice and research.

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Caloric and protein intake and duration of venous-venous ECMO in covid patients in a newly implemented regional ECMO center in Brazil

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Objectives: To assess protein and energy intake and duration of venous-venous ECMO in critically ill patients with covid-19

Methods: We conducted a retrospective observational analysis on the intensive care units of a large tertiary private teaching Hospital. Adult patients admitted to intensive care unit (ICU) with laboratory confirmed SARS-CoV-2 (RT-PCR), cannulated on venous-venous ECMO and on exclusive enteral feeding were included. Data between march 2020 and june 2021 were collected. Weight and height data were acquired at the time of admission in ICU. Body mass index (BMI) was subsequently calculated. We obtained delivery and adequacy of nutrition data from a enteral nutrition form routinely filled out by nutritionists during hospitalization. Other data were obtained from electronic medical record. For statistical analysis of the data, we used SPSS version 13.0.

Results: This cohort included 39 patients. 27 (69.2%) were men, mean age was 50 (± 12) years and 11 (28,2%) had more than 60 years. The more prevalent comorbidities were obesity in 22 (56%), hypertension in 20 (51,3%) and diabetes in 6 (15,4%) patients. The mean time on ECMO was 24.7 ± 15.2 days. 29 patients (74%) died. Regarding nutritional support, the average protein intake was 0,9 ± 0.4 g/kg/day and calories 13.9 ± 5.2 cal/kg/day. No statistically significant association was observed between the nutritional intake and the duration on ECMO and clinical outcomes of patients.

Conclusions: There was a high mortality in our cohort. Center's inexperience may have played a role in these results, in addition to other factors. We observed a high prevalence of obesity. Neither energy nor protein intake were associated with the duration of ECMO and clinical outcomes. These results are similar to other recent observational studies where an insufficient energy and protein intake did not affected mortality or other outcomes. Our small sample and study design prevents a definitive conclusion on the subject. Thus, we propose further studies to elucidate the role of adequate nutrional strategies to improve outcomes and reabilitation of patients on ECMO.

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Risk factors for major neurological events in patients under venovenous extracorporeal membrane oxygenation – single centre study

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Objectives: Inflammation and antithrombotic therapy during venovenous extracorporeal membrane oxygenation (VVECMO) might contribute to increases the occurrence of major thrombotic or hemorrhagic events involving the central nervous system (CNS). Data about its epidemiology, pathophysiology and risk factors is still scarce.

Methods: Single center, observational study of patients under VVECMO treated from 2017 to 2022 in a large ECMO referral centre. Major neurological events (NE) were defined as CNS ischemia or hemorrhage resulting in death or severe disability. Potential risk factors were evaluated. Statistical analysis was performed using STATA 15.1.

Results: Two hundred-twenty-four patients were included (67.4% male). Mean age was 47±13 years, SAPS II was 40±14. Major NE were documented in 32 patients (incidence of 14%). NE patients had a higher mean SAPS II [NE group: 51±19 vs. non-NE group: 38±13 (*p<0.0001*)] and a lower hemoglobin level at cannulation [NE group: 9.8±1.9 vs. non-NE group: 11.3±2.3 g/dL (*p<0,0001*)]. The presence of hiperlactacidaemia (OR 2.32, 95% CI [1.02, 5.30]) and continuous renal replacement therapy (CRTT) (OR 3.45, 95% CI [1.61, 7.45]) were also associated with increased risk for major NE. Importantly, CO_2 variation (ΔCO_2) immediately after cannulation was associated with neurological complications (non-NE group: ΔCO2=-12 (95% CI [-15 to -9]) vs. NE group: ΔCO_2 = -21 [-30 to -12], p=0.02), particularly if $PaCO_2$ decreased more than 50% (OR 3.0, p=0.04). In a multiple regression model, SAPS II (OR: 1.1, *p<0.01*), hemoglobin level (OR 0.75, *p=0.01*) and deltaCO_2 higher than 50% from pre-ECMO level (OR: 3.8, *p=0.03*) were consistently associated with major NE.

Conclusions: Understanding the etiology and potential risk factors for the occurrence of CNS hemorrhage or thrombosis in patients under VVECMO is determinant to implement preventive measures.

Pediatric - Cardiac failure

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The criteria affecting survival rates of pediatric extracorporeal membrane oxygenation: Single center experience

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Objectives: Extracorporeal membrane oxygenation provides respiratory and hemodynamic support to critically ill patients. Our aim is to identify the factors associated with survival in pediatric population with extracorporeal membrane oxygenation support.

Methods: From April 2015 to October 2018, 101 consecutive pediatric and neonatal patients receiving venoarterial and venovenous extracorporeal membrane oxygenation support were enrolled in this study. Data was collected on demographic information, primary underlying diagnosis, duration of extracorporeal membrane oxygenation support, intensive care unit and hospital stay, all echocardiographic findings and serum markers, usage of inotropic support and inhaled nitric oxide treatment, date of decannulation and discharge from hospital.

Results: All of the pre- and post-extracorporeal membrane oxygenation blood assay results and clinical data were recorded and the correlation between results and survival rates were evaluated. Use of inotrope support, elevated lactate, creatinine, low protein/albumin ratio, low pH prior to cannulation were all significantly associated with survival prior to hospital discharge. During extracorporeal membrane oxygenation support, elevated lactate and creatinine, low protein/albumin ratio, low pH were, again, significantly associated with death; higher weight, age, gender, body surface area, genetic disorders, prematurity were not statistically significant about association with death. Active cardiopulmonary resuscitation during cannulation was significantly high in non-survivor group but was not statistically significant.

Conclusions: Extracorporeal membrane oxygenation support is widely used to improve survival in pediatric population but carries high morbidity and mortality. Factors affecting survival and poor outcomes should be identified with larger population studies. According to our study, factors such as inotrope support, elevated lactate and creatinine levels, low protein/albumin ratio, low pH prior to cannulation were all significantly associated with poor outcomes.

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The use of extracorporeal membrane oxygenation after arterial switch operation in neonates with d-transposition of the great arteries, an ELSO registry report

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Objectives: To determine risk factors and outcomes for neonates with transposition of the great arteries (dTGA) who are supported with Extracorporeal membrane oxygenation (ECMO) postoperatively.

Methods: Retrospective analysis of neonates with dTGA from 2000 – 2020 captured in the ELSO registry after approval of the ELSO scientific committee. All neonates with concomitant congenital diaphragmetic hernia,

single ventricle palliation, shunts and AVSDs were excluded. Data is presented as median and inerquartile range (IQR). Chi square and Mann Whitney U tests were used to compare survivors and non survivors. Forward multivariable logistic regression with a model including gender, age, birthweight, weight, ECLS arrest, duration of ECMO and presence of any complications was used to determine predictors for survival. A p-value <0,05 was considered statistically significant.

Results: Five-hundred-twenty-eight patients were postoperatively supported by V-A ECMO. There were 332 males and 190 females with a median age of 10 days (IQR 6-18) and weight of 3,3 (IQR 3,0-3,8) Kg. Two-hundred-forty-two (46%) neonates had dTGA with IVS and 286 (54%) d-TGA with VSD. Indications for ECMO were low cardiac output in 342 (65%) neonates, failure to separate from cardiopulmonary bypass (CPB) in 248 (47%), hypoxia in 13 (3%) and/or pulmonary hypertension in 36 (7%). One-hundred and eleven children (21%) suffered a cardiac arrest pre-ECLS and 25 (5%) were actively resuscitated during ECMO cannulation (ECPR). Two-hundred-forty (44%) patients died. Median duration of mechanical ventilation was 395 (IQR 225-696) hours, median duration of ECMO support was 95 (IQR 64-164) hours and median hospital lenght of stay was 29 (IQR 18-51) days. Lower birthweight (p=0,05), lower weight at time of surgery, TGA-VSD, infection and the need for renal replacement therapy (all p=<0,01) were significantly associated with mortality in univariate analyses. Shorter duration of ECMO, the absence of complications and higher birthweight were most predictive of survival in the multivariate model.

Conclusions: Mortality is high (44%) in children with dTGA who are supported with ECMO postoperatively. Shorter ECMO duration, absence of complications and higher birthweight are predictors of survival in this group.

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The use of pre-operative extracorporeal membrane oxygenation in neonates with d-transposition of the great arteries, an ELSO registry report

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Objectives: To determine whether there is a difference in outcomes between neonates with d-TGA operated while on ECMO compared to neonates operated after weaning from ECMO.

Methods: A retrospective analysis of neonates with dTGA from 2000 – 2020 captured in the ELSO registry was performed after approval of the ELSO scientific committee. We excluded all neonates with concomitant congenital diaphragmatic hernia, AVSD or who required single ventricle palliation or a shunt as main procedure. Data is presented as median with interquartile range (IQR) because of skewed distribution. The two groups were compared using a Mann Whitney U and a Chi square test. A p-value <0,05 was considered statistically significant.

Results: Hundred-and-twenty children with dTGA received preoperative ECMO support. There were 82 males and 35 females with a median age of 6 days (IQR 2-20) and median weight of 3,5 (IQR 3,0-3,9) Kg at the time of cannulation. Seventy-three (61%) neonates had dTGA with an intact ventricular septum (TGA-IVS) and 47 (39%) dTGA with a ventricle septal defect-(VSD). Seventy-five (63%) children received their corrective surgery while on ECMO and 45 (37%) children were weaned off ECMO before corrective surgery was performed. Groups were similar in terms of gender weight, age, TGA type, indications and pre-ECLS arrest. There were no statistically significant differences in mortality 38% versus 35% (p= 0,73), duration of ECMO support 77 versus 89 hours (p= 0,84), duration of mechanical ventilation 363 versus 301 hours (p= 0,16) or hospital length of stay 24 versus 25 days (p= 0,39) respectively.

Conclusions: Almost two-thirds of neonates with dTGA receiving ECMO prior to ASO are operated while on ECMO. We could not identify a difference in outcomes between neonates operated on ECMO and those who are weaned off prior to corrective surgery with an overall survival of 64%.

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ECMO in acute fulminant myocarditis in pediatrics

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Objectives: To describe our experience in ECMO for acute myocarditis

Methods: Descriptive, retrospective study (2018-2022) of a cohort of 8 patients < 16 years with acute myocarditis who were assisted on ECMO.

Results: 8 patients were collected, (6 females), with a mean age 7'8 years [range 0'1-13'8]. In 7/8, the reason for cannulation was hemodynamic instability refractory to medical treatment, with a mean inotropic score of 70 [range 10-122]. Sixty-two percent presented cardiorespiratory arrest prior to cannulation and 2 of them needed ECRP. The mean pre-cannulation troponin level was 1498 ng/ml [range 89-6212]. Primary transport was performed in 4 patients. ECMO was peripheral veno-arterial in 100%, jugulo-carotid in 2/8 and femoro-femoral in 6/8. All patients underwent atrioseptostomy. They received treatment with levosimendan, immunoglobulins, corticoids and carnitine. In 4 acute infectious etiology was confirmed (parvovirus, influenza and SARS-CoV2), another one was due to PIMS-TS and in 3 no etiology was found. Six patients underwent myocardial biopsy and 5 of them showed inflammatory infiltrates. The mean time on ECMO was 8 days [range 3-14], 2 of them requiring 2 ECMO courses. The mean length of PICU stay was 21 days [range 10-50]. Two were transferred to a heart transplant center. The main complications were arterial hypertension (88%), bleeding (63%), neurological (50%), arrhythmias (38%), coagulopathy (38%) and infectious (38%). One patient required renal replacement therapy. 1 patient died, 2 had moderate neurological sequels.

Conclusions: ECMO is a therapeutic option in patients with fulminant myocarditis refractory to medical treatment and may help improve their prognosis.

Pediatric - Difficult cases

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Bilateral lung transplantation as salvage therapy for bleomycin induced lung injury

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Objectives: Bleomycin is a mainstay of treatment for a variety of highly curable diseases, such as lymphoma and testicular cancer. However, bleomycin is associated with a dose-limiting pulmonary toxicity, which may occur in 2–42% of patients, with a mortality rate of 1–5%. In the lungs, free radicals and cytokines cause endothelial damage, stimulating a cascade of inflammatory markers, fibroblast activation, and collagen deposition. Interstitial pneumonitis, which can progress to pulmonary fibrosis, is the most common form of bleomycin pulmonary toxicity.

Methods: A two year review of all hemato-oncology patients supported by ECMO and received bleomycin prior to respiratory failure, at the largest tertiary center in Israel.

Results: Hereby, we present a 14 years old boy that was diagnosed with high risk metastatic testicular embryonal carcinoma. After radical left orchiectomy, he received full systemic chemotherapy including high dose bleomycin. During his last treatment cycle, he developed gradual respiratory failure with bilateral pneumothoraxes and suffered from severe diffuse bilateral airspace opacities. His lung function deteriorated with progressive refractory air leak and hypoxemia, and he ultimately required the initiation of veno-venous ECMO. He was treated with both immunomodulatory treatment as well as anti-fibrotic treatment which did not suffice and the patient develop a progressive, fibrotic lung disease. Nevertheless, after 3.5 months without clinical improvement he underwent bilateral lung transplantation. The patient is now 1.5 years post-transplant and has regained full functional status.

Conclusions: Bleomycin toxicity may be a transient condition under supportive therapy, however, some patients develop sever progressive fibrotic lung disease. The presented patient received full immunomodulatory treatment as well as anti-fibrotic treatment, nevertheless suffered from irreversible end stage lung disease which required 3.5 months of ECMO support followed by bilateral lung transplantation. Although a recent history of malignancy is usually a contraindication for transplant, the extremely favorable prognosis of metastatic germ cell tumor should not preclude transplantation unequivocally.

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ECMO as a bridge to pneumonectomy in a pediatric patient with necrotizing pneumonia: Stretching the boundaries

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Objectives: Necrotizing pneumonia (NP) can destroy lung parenchyma and result in an intractable air leak, leading to the need for prolonged ECMO support, discussions of transplant (TX) or withdrawal of support.

Methods: A 14-year-old male on VV ECMO with left lung NP (Legionella and subsequent MRSA) developed recurrent left-sided pneumothoraces, renal failure and intercurrent systemic infections from infected parenchyma leading to multi-organ failure. He remained neurologically intact. VV support could intermittently be weaned but not to decannulation. After 2.5 months of VV ECMO and lack of team and family consensus on further care options, he was accepted at our institution for a second opinion and consultation on endobronchial valve candidacy for his recurrent pneumothoraces as an option for lung recruitment. Imaging, bronchoscopies, and collaboration between pediatric and adult ICU, ECMO, Surgery, and Pulmonary teams concluded that endobronchial valves would not be useful, as parenchymal damage was too widespread and severe.

Results: As he was not a lung transplant candidate, pneumonectomy was the only viable option for potential survival. To establish that adequate gas exchange could be attained via the remaining functional lung, a trial of single-lung ventilation and weaning of VV support occurred. A sweep gas-clamp trial for over twelve hours on non-toxic ventilator settings with adequate gas exchange was able to be attained. Thus, a unilateral pneumonectomy was performed, with continued VV support to ensure low airway pressures during initial recovery. Although pulmonary function improved, the patient eventually succumbed to fungemia and refractory multi-organ failure.

Conclusions: This case illustrates that timely referral to centers with access to pediatric and adult services may provide options which are rarely considered or available during pediatric ECMO support. Further, considering that pediatric lung transplant results in a relatively short functional lifespan of 5-10 years, other options should be considered. Unilateral pneumonectomy during VV ECMO can be done safely and may allow recovery-obviating or delaying the need for lung transplant or allowing rehabilitation for patients who are initially deemed unsuitable transplant candidates.

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Bronchial artery embolization for a cystic fibrosis patient with hemorrhagic shock on VV-ECMO in the PICU: A case report

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Objectives: Bleeding in anticoagulated ECMO patients may occur in association with procedures performed, but specific patient populations have risks which may not be well appreciated. A minority (1%) of Cystic Fibrosis (CF) patients develop massive hemoptysis from bronchial artery changes which can be fatal.

Methods: An 18-year-old CF patient presented with MRSA pneumonia, bacteremia, ARDS and septic shock. Despite hemodynamic improvement, worsening ARDS occurred, and she was cannulated on to VV ECMO. Percutaneous tracheostomy was performed three weeks later with anticoagulation withheld per protocol. Massive hemoptysis occurred several hours later, with significant desaturations despite maximal ECMO support. Bronchoscopy did not identify any active bleeding site; during bag-valve-masking of patient, tension pneumothorax developed, requiring urgent chest tube placement. In addition to air, >1L/hr of blood was drained from the chest tube. Massive transfusion and antifibrinolytics were administered; hemodynamic compromise required vasoactive infusions. The tenuous state of the patient led to urgent open thoracotomy in the operating suite, where blood causing tamponade physiology was removed but no specific site of bleeding was found. Vasoactives were weaned with adequate support maintained via VV ECMO. Anticoagulation was withheld for several days until heparin was re-initiated with an anti-Xa goal of 0.2-0.35. A week later, sudden massive hemoptysis recurred, with bronchoscopy localizing it this time to the right lung. Angiography was undertaken urgently by Interventional Radiology, and right bronchial artery bleeding was identified and embolized. No further bleeding events occurred, the patient tolerated anticoagulation with bivalirudin when restarted, and she was weaned off ECLS support five weeks after cannulation. She was discharged to rehab then to home without need for mechanical ventilatory support or consideration for lung transplant.

Results: n/a

Conclusions: In ECMO patients with CF and hemoptysis, bronchial artery bleeding should be considered. Embolization can be lifesaving and safely performed during ECMO support.

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Excellent outcome after two periods of extracorporeal membrane oxygenation following severe SIRS reaction after total cavo-pulmonary connection

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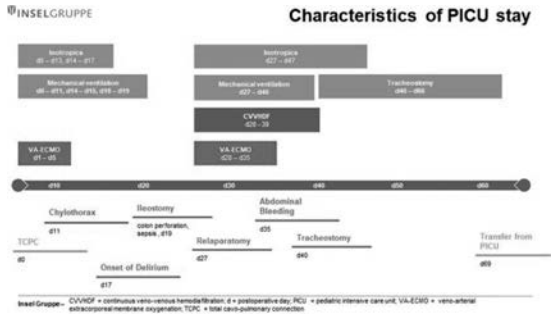
Objectives: We present a case of a 3-year-old girl with pulmonary atresia with intact ventricular septum (PA/IVS) who showed a favorable outcome after major

complications following severe SIRS reaction after total cavo-pulmonary connection (TCPC). The patient underwent veno-arterial extracorporeal membrane oxygenation (VA-ECMO) twice for low cardiac output (LCO). Further complications included acute renal failure, colon perforation and sepsis.

Methods: We reviewed the electronic patient charts including discharge letters and diagnostic reports of the hospital stay and the follow up visits.

Results: Following Glenn anastomosis three years previously, our patient was scheduled for elective completion of Fontan circulation for PA/IVS. TCPC was performed following standard protocol using an 18mm conduit, extracorporeal circulation time was 82 minutes. Postoperatively the patient developed a severe SIRS reaction with LCO refractory inotropic therapy. During the stay at our pediatric intensive care unit (PICU) she underwent VA-ECMO twice: day 1 after surgery (d1) until d5 with central arterial and femoral venous cannulation, second from d28 to d35, after colon perforation with sepsis and need of ileostomy, using cervical and femoral access. Further complications included acute renal failure with continuous veno-venous hemodiafiltration (CVVHDF), abdominal bleeding, prolonged mechanical ventilation and tracheostomy, delirium and mild neuropsychologic impairment. Total length of hospital stay was 86 days, length of PICU stay 69 days. At time of discharge echocardiography showed good results and kidney function was normalized. Six months later the patient was clinically fine and did not show any neurologic impairment.



Conclusions: We demonstrate a rare case of a girl who survived devastating complications following a severe SIRS reaction after TCPC with a very favorable outcome. In our knowledge it is the first report of two successful periods of VA-ECMO in a patient following TCPC.

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Use of methylene blue in refractory vasoplegia after heart transplant in pediatric patient

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Objectives: We present challenges in management of refractory vasoplegia post heart transplant in paediatric patients requiring ECMO support and administration of Methylene Blue.

Methods: An 11-year-old boy with history of dilated cardiomyopathy requiring ECMO and left ventricular assist device (LVAD) underwent orthotopic heart transplant. There was significant postoperative bleeding which was managed with multiple transfusions of blood and blood products. Despite rapid volume replacement, the child was requiring high dose continuous infusions of vasopressors including Noradrenaline and maximal Vasopressin. Due to continued haemodynamic instability, the patient was cannulated to central veno-arterial (V-A) ECMO. Following institution of full ECMO, there was still profound vasoplegia. This was noted despite good ECMO flow, fluid resuscitation and continuing maximal vasopressors. Steroids were also given with minimal effect on blood pressure. In light of the persistent vasoplegia, the use of methylene blue was discussed.

Results: A single dose of 27.5mg Methylthionium Chloride IV in 50ml 5% dextrose was given with subsequent improvement of blood pressure. Methylthionium Chloride is a salt, used as a thiazide dye and or a medication. Methylene Blue is used as a medication to treat methemoglobinemia, which can arise from ingestion of certain pharmaceuticals or toxins. There is data to show that Methylene Blue consistently increases blood pressure in people with vasoplegic shock as the patient discussed. Following administration, the chest could safely be explored and bleeding points were identified and addressed. The patient was then fully supported on full V-A ECMO and vasopressors weaned off rapidly.

Conclusions: This report demonstrates a rare use of methylene blue in a child with refractory vasoplegia despite full flows on ECMO. We concluded that giving of MB helped stabilise this patient while waiting for

chest re-exploration. There are a number of reports that detail the use of MB for this purpose in adults, but very little data is available in paediatrics.

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ECMO for the immunocompromised pediatric patient: Our experience

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Objectives: To present a series of immunosuppressed patients (oncohematological disease, congenital immunosuppression, hematopoietic stem cell (HSCT), and solid organ transplant) assisted on ECMO.

Methods: Descriptive, retrospective study (2011-2020) of a cohort of 9 immunosuppressed patients, supported on ECMO. Medical records were reviewed and demographic, clinical, and analytical variables were collected.

Results: In our series of 9 patients, 5 were male, the median age was 8 years [RIC 3-11 years]. Considering the underlying disease, 6 were oncologic, 1 liver transplant and 2 with congenital immunodeficiency after HSCT. 4 were under active chemotherapy (median 6 days after the last cycle [RIC 5-188]). 6 were admitted due to acute respiratory failure, 3 due to hemodynamic instability (3/9), (one septic shock). The median PEEP was 12 [RIC 9-15] and FiO2 100% (81-100%). 78% (6) required vasoactive drugs (median inotropic score 35 [RIC 0-75]. 40%. 5 had severe neutropenia and/or plateletopenia in the 24 hours prior to ECMO, and alterations in acid-base balance (median pH 7. 1 [RIC 6.9-7.15]. 5 were on multiorgan failure. TPrimary ECMO transport was performed in 4 patients (44%). Cannulation was peripheral in 80% (57% cervical, 43% femoral) and central in 20%; 70% VA-ECMO. Median time of assistance was 15 days [RIC 3.5-31.5] in cardiac ECMO (4), and 29 days [RIC 13.5-42] and in pulmonary ECMO (n=5). The median total time of admission was 45 days [RIC 27-59]. 9 had an infection, 2 COVID after HSCT, and 8 bleeding complications, but only one required surgical revision. Renal replacement therapy was used in 5 (median 9 days [RIC 5-34.5]). Other therapies used were polymyxin hemadsorption(2), intratracheal surfactant(2), plasma exchange(1), infusion of mesenchymal cells(1) and specific memory T lymphocytes(2). 4 patients died, 5 survived decannulation, 2 died later, with an overall survival rate to hospital discharge of 33% (3/9).

Conclusions: Despite having a worse prognosis, ECMO can increase survival in immunosuppressed patients, in situations that are challenging and require a multidisciplinary approach.

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Clevidipine use for arterial hypertension (HT) in the pediatric ECMO patient

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Objectives: To present 3 cases of patients on ECMO with clevidipine use for difficult-to-control HT

Methods: A retrospective chart review was undertaken, and clinical, laboratory, and outcome data were collected.

Results: 3 patients, (2 infants aged 3 and 14 months, and a 12-year-old boy) had clevidipine infusions for refractory HT during ECMO support. The 14-month-old infant, a former 27-week preterm, was diagnosed with severe bronchopulmonary dysplasia on continuous oxygen therapy. ECMO assistance was used for severe acute respiratory distress with subsequent hemodynamic repercussion. The other two required ECMO for cardiogenic shock secondary to acute myocarditis, and the 12-year-old boy due to PIMS-TS. In all cases the assistance was peripheral veno-arterial, jugulo-carotid in the two infants and femoro-femoral in the boy. In the first 24 hours, they developed difficult-to-control hypertension with repercussions on their care. In all cases blood pressure control was attempted with Urapidil perfusion up to 2mg/kg/h and sodium nitroprusside up to 3mcg/kg/min. They also receive Levosimendan cycle at 0.2mcg/kg/min due to severe left ventricular dysfunction. After starting clevidipine, no patient presented severe hypotension events or required the initiation of vasoactive support. As the only side effect, triglyceride levels at the high limit of normality were detected in one of the patients receiving Propofol infusion, which resolved after its suspension. Blood pressure control was achieved in all cases with monotherapy. The mean infusion duration was 2 days. The two patients with a diagnosis of myocarditis required subsequent transition to oral anti-hypertensives and in one case even subsequent initiation of Urapidil infusion.

Conclusions: The use of continuous infusion clevidipine for blood pressure control in pediatric patients on ECMO appears to be effective and safe, although more experience is needed.

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First pediatric ECMELLA case in Spain

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Objectives: To present the first use of ECMO together with an Impella device in Spain in a myocarditis case.

Methods: Case report

Results: 13-year-old female with subacute clinical presentation and myocarditis with LVEF<10% despite intubation and inotropic support. She was cannulated on femoro-femoral V-A ECMO and and atrioseptosmy was performed. Myocardial biopsy was compatible with acute lymphocytic myocarditis. Immunoglobulins and corticosteroids were given. She had a progressive loss of pulsatility with absence of left ventricular (LV) unloading in echocardiographic controls in spite of ECMO assistance of 65 ml/kg/min. A second jugular venous cannula was placed without significant changes, so an Impella device was placed through a femoral access (Seldinger technique). Given the wide atrial septal defect (ASD), hypoxemia in the upper limbs was found with high Impella device flows and insufficient discharge of the LV with low flows. ECMO and Impella flows were adjusted to achieve optimal balance. The patient presents significant femoral bleeding that was refractory to local compression measures. After 5 days, an improvement in contractility was found, and the Impella was removed. ECMO withdrawal was achieved after 13 days of assistance, with adequate cardiac output. After ECMO withdrawal, she developed a supraventricular tachycardia at 160lpm with hemodynamic repercussions. She underwent several electrophysiological studies with attempts to ablate the ectopic focus, without achieving controlling the arrhythmia. Given the improvement of cardiac function, beta-blocker treatment was started with subsequent heart rate control.

Conclusions: The combined use of ECMO and Impella is feasible and can be useful in older children with inadequate left ventricular decompression.

Pediatric - Nurse

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Nursing care of an adolescent with pulmonary tuberculosis on prolonged veno-venous extracorporeal membrane oxygenation

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Objectives: Extracorporeal membrane oxygenation (ECMO) is a technique used to support the failing heart and lung when other conventional methods fail. Advances in materials and practices have led to an evolution of indications, patient groups and decrease in complications, allowing longer ECMO runs, defined as prolonged ECMO (pECMO). We report the case of our center's longest run patient to date (124 days), a 17-year-old female adolescent who presented to the emergency department with respiratory distress, hipoxemia and exhaustion, later diagnosed with pulmonary tuberculosis, and rescued on veno-venous ECMO due to respiratory failure. We describe and discuss nursing care of this adolescent in pECMO, addressing issues related to nursing care and prevention of complications, monitoring and management of the equipment and treatment, implications regarding nursing care and futility of treatment, and caring for patients extubated and awake while on ECMO.

Methods: Case Report

Results: The adolescent presented several complications throughout the admission: tuberculosis infection related (massive pulmonary necrosis, pneumothorax, bronchopleural fistulae, *cor pulmonale*), ECMO related (3 circuit changes, cannula haemorrhage, cannula change and repositioning) intensive care related (multiple agent infections and sepsis, delirium, depression, pressure lesions). She was extubated and managed awake for 90 days, then intubated and ventilated for a successful decannulation. She failed to recover from a subsequent tracheostomy procedure complication. Sequential monitoring by the nursing team using an ECMO checklist allowed prompt identification of signs of complications, whether patient or equipment related, thus minimizing complications, and maintaining safe care. Frequent nursing needs assessment allowed prevention of pressure lesions through mobilization and pressure relieve devices. While awake, adolescent involvement in decision making of care was felt as empowering and giving a sense of control over herself. The healthcare team adopted regular discussions addressing plan of care and futility of care queries to promote team engagement.

Conclusions: Prolonged ECMO care is demanding, involving consistent monitoring, teamwork and expertise, and engagement to provide high quality and safe care. Managing awake patients in ECMO is feasible and allows patients to express themselves more fully.

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A nursing care challenge: "Zero Pressure Ulcer" in children on extracorporeal membrane oxygenation (ECMO)

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Objectives: To identify increasing factors for Pressure Ulcer formation in children on ECMO during 2017-2022. To compare parietal and occipital Pressure Ulcer incidence in children on ECMO before and after the recurrent use of foam dressings during 2017-2022.

Methods: An observational analytic retrospective study performed at a Paediatric Intensive Care Unit, at a tertiary hospital – ECMO Centre, between 2017 and 2022. There were analysed data concerned to children who underwent ECMO over this time, getting as sample a total of 60 children. We defined a time period to create two cohorts: between 2017 and 2019 were used as pressure ulcer prevention hydrocolloids and gel devices; and between 2020 and2022 were introduced foam dressings as preventive care in all children on ECMO. Exclusion criteria included children who underwent ECMO for less than 24 hours, children who need a second ECMO run and other haemorrhage type. Final sample were 45 children, 21 belong to the first cohort and 24 to the second. Data collection was based on nursing documentation using PICIS (Critical Care Manager system) *software*. Data analyse concerned only nursing documentation while under ECMO treatment and all statistical analyses were performed with Exce® software.

Results: We can verify an incidence decrease from 38% to 21% of pressure ulcers in children on ECMO, after preventive dressing foam implementation.

Conclusions: As limitations for this study we can identify the small sample size and the accuracy of ulcer documentation since there were not a standard documentation implemented. Our main conclusions concern to: the importance of more studies and knowledge divulgation about this area among paediatric nurses; promoting the prevention of pressure ulcer as safety culture for the patient; identifyas benefit for nursing care a pressure ulcer preventive protocol; enhance the primordial role of nursing documentation as well as nursing diagnoses and directed interventions; to promote peer literacy as well as scientific knowledge and experience concerning pressure ulcer prevention; the complexity and level of technicity demand of ECMO whilst patient instability and device displacement during children manipulation.

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Implementation of an electronic nursing assessment checklist: A pathway for preventing and detecting ECMO-associated complications in a Portuguese pediatric referral centre

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Objectives: To present the Nursing ECMO Checklist, developed in the onset of a 13-year-old program, and continuously updated throughout 100 runs. To analyse the relationship between the items of the checklist and the identified ECMO-associated complications. To identify the contribution of the computerization of the tool in 2019, regarding high quality and safe healthcare delivery

Methods: Retrospective and descriptive analysis of ECMO-associated complications over a 3-year period.

Results: The nursing checklist was mainly developed as an effort of early identification of complications associated with ECMO in neonatal and paediatric patients, as well as a way of checking for emergency resources readiness. The checklist comprises three domains of assessment: Patient, Machine and Circuit, and Laboratorial findings. Regarding complications, 24 out of 34 patients had 49 events during single-run ECMO between November 2019 and December 2022. From previously conducted studies in our centre, the distribution of identified complications across the 13 years of the program is proportional to the number of runs in each year. Haemorrhagic complications, excluding central nervous system haemorrhage, were 49% of all events in neonatal and paediatric groups, but the incidence was higher in new-borns. Overall, 60% of the complications were detected during the assessment of one or more checklist parameters, allowing for timely interventions such as circuit change, heparin titration, or sedation management. The computerization of the checklist in the pre-existing electronic health record PICU system improved: data storage, access, and analysis; relationship with other monitored parameters over time; better checklist adherence; and enhanced, collaborative and multidisciplinary care.

Conclusions: Extracorporeal membrane oxygenation is a high-risk technique. This electronic checklist allows for a standardized assessment of the patient and the EC system as a whole, promoting safety and consistency in care delivery, guiding the decision-making process. The identified changes in the assessed parameters triggered nursing and medical interventions that prevented major and escalating complications. There is limited evidence on the use of such tools and further research is needed to identify which parameters best correlate with the prevention of complications.

Pediatric - Perfusion

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Carbon dioxide derived parameters during cardiopulmonary bypass predict acute kidney injury after pediatric cardiac surgery

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Objectives: This study aims to assess the prognostic performance of the ratio of venous-arterial CO_2 tension difference to arterial-venous O_2 content difference ($Pv\text{-}aCO_2/Ca\text{-}vO_2$) and venous-arterial CO_2 gradient ($Pv\text{-}aCO_2$) during cardiopulmonary bypass (CPB) for acute kidney injury (AKI) after pediatric cardiac surgery.

Methods: This is a retrospective, observational study. All paired arterial and venous blood gases during CPB were collected. Measured oxygen saturation, partial pressure of O_2 and CO_2, and hemoglobin concentration were extracted. The following pairs were included in the analysis: 30, 60, 90 minutes after aortic clamping. Pairs were assigned to a group if within ± 15 min of time category.

Results: A total of 84 of the 213 (39.4%) children developed AKI. 317 arterial and venous blood gas pairs from 30(n=207), 60(n=75) and 90 minutes(n=35) after aortic clamping were included in analysis. With the prolongation of aortic clamping time, the $Pv\text{-}aCO_2/Ca\text{-}vO_2$ and $Pv\text{-}aCO_2$ of children in AKI group increased gradually. Compared with the non-AKI group, $Pv\text{-}aCO_2/Ca\text{-}vO_2$(5.28(4.75-6.61) versus 3.88(3.16-4.40) mmHg·dL/mL, *P<0.001*) and $Pv\text{-}aCO_2$(14.6(12.2-15.4) versus 11.7(10.5-13.9) mmHg, *P=0.015*) in children with AKI were statistically higher at 90±15min. After controlling for covariates, the maximum $Pv\text{-}aCO_2/Ca\text{-}vO_2$ from all the three time points remained independent association with AKI (odds ratio, 1.337; 95% CI, 1.037-1.723).

Conclusions: The maximum $Pv\text{-}aCO_2/Ca\text{-}vO_2$ during CPB seems an independent predictor of AKI after pediatric cardiac surgery.

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Service mapping of the pediatric ECMO team

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Objectives: This project represents and analyzes the Pediatric ECMO Team process through Service Mapping (SM). The SM was used to analyze, represent and redesign the pathway of system delivery.

Methods: Since 2019 a regional project has regulated pediatric ECLS support in Tuscany. FTGM, located in Massa (north Tuscany), has the only pediatric ECMO center in the region. Following the hub and spoke model, our teamwork is programmed and organized according to operating instructions, checklist, responsibility matrix. We evaluated the interventions requested in the observed period following the Blueprinting model which synthetically reproduces the process. The structured drafting allows all professionals involved to understand and face the activities without role or personal influences.

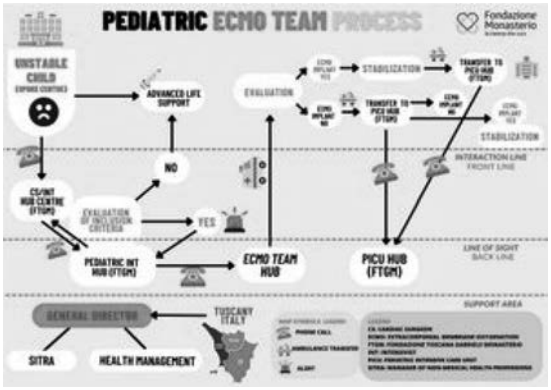
Results: From 2019 the pediatric ECMO team has been promptly activated 9 times with the following results:- 3 patients were cannulated and initiated on V-A ECMO at the spoke center (pediatric hospital Meyer, Florence) and subsequently transported to the hub

Table 1. Carbon dioxide derivative parameters at different time points during CPB and AKI

Time points during CPB	Carbon dioxide derivative parameters	All *n*=213	AKI group *n*=84	Non-AKI group *n*=129	*P value*
ACT 30±15min(n=207)	$Pv\text{-}aCO_2$(mmHg)[a]	13.1(11.2, 15.1)	13.8(11.4, 15.6)	12.7(11.2, 14.8)	0.108
	$Pv\text{-}aCO_2$/ $Ca\text{-}vO_2$(mmHg·dL/mL)[a]	4.35(3.59, 5.24)	4.66(3.96, 5.80)	4.04(3.41, 4.89)	<0.001
ACT 60±15min(n=75)	$Pv\text{-}aCO_2$(mmHg)[a]	13.3(11.8, 16.1)	14.0(12.4, 16.4)	12.6(11.2, 14.0)	0.023
	$Pv\text{-}aCO_2$/ $Ca\text{-}vO_2$(mmHg·dL/mL)[a]	4.50(3.53, 5.10)	4.68(3.84, 5.46)	4.09(3.09, 4.80)	0.005
ACT 90±15min(n=35)	$Pv\text{-}aCO_2$(mmHg)[a]	13.7(10.8, 15.3)	14.6(12.2, 15.4)	11.7(10.5, 13.9)	0.015
	$Pv\text{-}aCO_2$/ $Ca\text{-}vO_2$(mmHg·dL/mL)[a]	4.61(3.88, 5.45)	5.28(4.75, 6.61)	3.88(3.16, 4.40)	<0.001
	$Pv\text{-}aCO_2$max(mmHg)[a]	13.8(11.8, 16.1)	14.9(12.5, 16.6)	13.1(11.6, 15.2)	0.001
	$Pv\text{-}aCO_2/Ca\text{-}vO_2$max(mmHg·dL/mL)[a]	4.67(3.79, 5.53)	5.21(4.54, 6.08)	4.19(3.52, 4.98)	<0.001

a, M(Q1,Q3); max,maximum; ACT, aortic clamping time; AKI,acute kidney injury

(FTGM) by the mobile ECMO team - 3 patients were first transported to the hub center (FTGM) and then provided V-A or V-V ECMO - 2 patients died at the spoke center shortly after V-A ECMO establishment - 1 patient was transported to the hub center (FTGM) and successfully treated without ECLS support - The ECMO SM allows to: - Monitor the project implementation - Think critically about the service delivery system - Focus on specific aspects of the provided service



Conclusions: Service Mapping was a useful tool for the organization of the pediatric ECLS. It can be helpful in the healthcare quality improvement process and potentially extend to other settings. We hope our regional experience and service mapping can serve as a benchmarking model across realities.

Pediatric - Quality Improvement

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Safety and efficacy of a fixed versus variable weight-based concentration of heparin infusions in neonatal respiratory ECMO

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Objectives: The paediatric intensive care unit changed Heparin infusion dosing from a variable weight-based concentration (500 U/kg in 50mL) to a fixed concentration (5000 U/50mL) when pump-based drug library was introduced. This change meant significantly lower rates of infusion were needed for the same dose of heparin in the neonatal population. We performed a safety and efficacy assessment of this change.

Methods: We performed a retrospective single-centre service evaluation based on data from respiratory VA-ECMO patients weighing ≤ 5kg, pre and post 19th April 2019, when the change to fixed strength heparin infusion was introduced. Institutional approvals were obtained. Heparin infusions were usually titrated to achieve an ACT range of 180-200, subject to daily reviews. We defined in-range ACT values as those within the daily target range. Efficacy was analysed by distribution of ACT values and frequency of heparin dose changes between the groups. Safety was analysed using circuit related thrombotic and haemorrhagic complications. Analysis used MS Excel and R. Continuous variables were reported as median and interquartile ranges and non-parametric tests were used. Incidence rate ratios of circuit related thrombotic and haemorrhagic events between groups were analysed using poisson regression with offset for run hours.

Results: Data obtained from 33 infants were analysed (20 variable weight-based, 13 fixed concentration). Demographic, safety and efficacy data are summarised in Table 1. We observed a statistically significant, but clinically insignificant difference in ACT ranges/distribution between the 2 groups (Table 1). Incidence rate ratios (IRR [95% CI]) of thrombotic (fixed v weight-based) (1.9 [0.5 – 8], p= 0.37), and haemorrhagic events (0.9 [0.1 – 4.9], p=0.95) did not show statistically significant differences.

Table 1: Summary of the variables compared in both groups.

Variable	Fixed concentration	Weight-based dosing	p-value
Age in days [median (range)]	2 (1-11)	7 (0-90)	0.23
Sex-Male [n(%)]	8 (62)	12 (60)	0.78
Indication [n (%)]			0.64
Meconium aspiration syndrome	3 (23)	2 (10)	
Persistent pulmonary hypertension	7 (54)	11 (55)	
Congenital diaphragmatic hernia	2 (15)	6 (30)	
Others	1 (8)	1 (5)	
Total ECMO run hours (n)	1865	3536	
Proportion of in-range ACT n(%)	632 (35%)	1149 (34%)	0.30
Heparin dose (U/kg/h) [median (IQR)]	22 [13-32]	23 [12-33]	0.63
Median [IQR] ACT	194 [180-210]	191 [176-207]	<0.001
Median [IQR] flows mL/kg/min	120 [111-133]	123 [108-140]	<0.001
Clotting events (n)	4	4	
Clotting events/1000 circuit hours	2.1	1.1	
Bleeding events (n)	2	4	
Bleeding events/1000 circuit hours	1.1	1.1	

Conclusions: Fixed concentration dosing of heparin was at least equally effective and safe compared to a weight-based dosing

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A survey of current pediatric extracorporeal cardiopulmonary resuscitation (ECPR) practices in the USA

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Objectives: We hypothesized that pediatric ECPR practices in the USA are widely varied. Center-specific practice elements could include the staffing of ECMO extracorporeal membrane oxygenation (ECMO)

circuits, in-house call requirements, and hospital location(s) where pediatric patients are cannulated and provided care. Our goal was to survey USA centers that offer pediatric ECPR to describe the infrastructure and most common practices of pediatric ECPR programs to help inform best practice guidelines.

Methods: A 17-question RedCAP™ survey of center-specific demographics, practice structure, staffing requirements, transport capabilities, and ancillary service support was designed and distributed to USA pediatric ECMO programs after IRB exemption was obtained. Of the 154 centers (537 individuals) invited, 82 individuals from 63 centers responded.

Results: All applicable responses were tabulated so response totals may exceed 100%. Only 26% of centers perform/offer out-of-hospital ECPR whereas 97% perform in-hospital ECPR. ECMO cannulation is most frequently performed at the bedside (99%), in the OR (88%), in the cath lab (77%), and less frequently in the Emergency Department (35%). Pediatric ECMO patients are provided care in the PICU (93%), CVICU (71%), or NICU (58%). The individual cannulating the ECPR patient was most often a general (71%) or a cardiac (91%) surgeon, less frequently an interventional cardiologist (15%) or intensivist (10%). ECMO specialists prime the circuit 66% of the time and perfusionists 48%. Only 16% of responders report the individual who cannulates is in-house 24/7, while 90% report that individual is only in-house during work hours. It was reported by 61% that the individual who primes the circuit is in-house 24/7. The majority (68%) reported an expected 45-minute maximum call-response time with range 15-60 minutes. When ECPR is activated, centers vary in automatic notification of the following departments: blood bank (47%), radiology (13%), lab (17%), and OR (96%).

Conclusions: The variety of skilled providers responding to ECPR events may impact call schedules, hiring practices and potentially outcomes. More detailed practice inventory is necessary to inform impact on outcomes or identify similar clinical practices for trial design and recruitment.

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Anti-Xa-guided versus time-guided anticoagulation management in pediatric extracorporeal membrane oxygenation

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Objectives: Extracorporeal Membrane Oxygenation is associated with bleeding and thrombotic complications. Several strategies have been used to guide anticoagulation. Unfractionated heparin can be titrated with time-guided tests such as activated clotting time (ACT) or activated partial thromboplastin time (aPTT), or with measurement of heparin activity using anti-Xa. It remains unclear which strategy is associated with decreased complications and better outcomes. We compared the difference in complications between time-guided and anti-Xa-guided anticoagulation management.

Methods: In this single-center retrospective cohort study including pediatric patients between January 2010 to December 2021, we compared two anticoagulation strategies: time-guided, including both ACT and APTT, versus anti-Xa-guided. Patients with coagulation disorders, or mixed titration methods were excluded. Hemorrhagic and thrombotic complications were compared between both groups. Neurological complications, duration of hospitalization, survival, and exposition to blood products were also evaluated. Finally, mean and total dose of UFH was compared between both groups.

Results: Hundred seventeen runs in 99 patients were studied: 69 in the time-guided and 48 in the anti-Xa-guided group. There was no difference in hemorrhagic complications [anti-Xa: 60.4% vs. time-guided: 50.7% days; *p=0.300*] and in thrombotic complications [anti-Xa: 29.2% vs. time-guided: 40.6% ; *p=0.206*]. There was no difference in neurological complications [anti-Xa: 35.4% vs. time-guided: 23.2%; *p=0.148*]. Although, hospital stay was shorter in the anti-Xa-based group [anti-Xa: 31.5 (15.0-58.0) days vs. time-guided: 49.0 (23.5-86.0) days; *p=010*], there was no difference in survival to hospital discharge between both groups [anti-Xa: 45.8% vs. time-guided: 40.6%; *p=0.572*]. The time-guided group more often received red blood cell transfusions [anti-Xa: 91.7% vs. time-guided: 100%; *p=0.015*]. There was no difference in exposure to platelet transfusions [anti-Xa: 85.4% vs. time-guided: 95.7%; *p=0.051*], plasma transfusions [anti-Xa: 89.6% vs. time-guided: 94.2%; *p=0.356*], and fibrinogen transfusions [anti-Xa: 39.6% vs. time-guided: 55.1%; *p=0.099*]. The anti-Xa-based group received a significantly higher rate of UFH compared to the time-guided group [anti-Xa: 838.6 (651.0-981.1) IU/kg/day vs. time-guided: 437.1 (311.3-659.0) IU/kg/day; *p=0.000*].

Conclusions: In this comparison between a time-guided versus an anti-Xa-guided strategy, no difference in hemorrhagic or thrombotic complications was founded.

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Restoring quality of an ECMO education programmme from the aftermath of COVID-19 pandemic: Preliminary results from a continuous quality improvement process

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Objectives: Extracorporeal membrane oxygenation (ECMO) is a complex life support modality. To appropriately educate ECMO clinicians, a comprehensive program is required. However, there is no universal ECMO education (EE) program exclusively for intensive care unit Registered Nurses (RNs). Moreover, with the recent Coronavirus Disease 2019 (COVID-19) pandemic, the existing nursing shortage and the ability of ECMO programs to maintain an established EE program worsened. This continuous quality improvement (CQI) aims to reestablish the quality of an EE program at a large academic medical center at one of the past pandemic epicenters.

Methods: A CQI process with the Plan-Do-Study-Act (PDSA) cycle and Ishikawa diagram for root cause analysis (RCA), intervention implementation from July 2022 to June 2023

Results: The RCA revealed intrahospital pandemic-related restrictions for employee gathering, EE instructor unavailability, increased nursing turnover, increased nursing shortage, and incomplete recordkeeping of ECMO educational activity (EEA) RN attendance as dominant factors disrupting the established EE processes. Six interventions were implemented, with one added in later:

1. Schedule 1 Certification Lecture Day/Quarter (Q), 1 Re-Certification Lecture/Q, and 1 Circuit Skills Class/month, and 1 Simulation Lab/month
2. Reserve an education room for all EE activities, as COVID-19 policies allow
3. Increase the number of EE instructors
4. Increase Nursing Leadership-ECMO Manager collaboration for optimal RN signup
5. Optimize EEA schedule to help balance RN staffing needs
6. Develop a Master ECMO Folder in Google Drive and maintain updated attendance

Five interventions showed positive preliminary results, whereas it was too soon for any conclusion for one (Table 1).

Table 1. Excerpt from The PDSA cycle Restoring Quality of the ECMO Education Program.

Process Outcome	Preliminary Post intervention Data Results
CLD and RCL are held 1/Q; CSC and SL are held 1/month	2^ CDL and 1.5^ RCL/Q and 1 CSC and 1 SL/month held
EEAs are held in an edu room	76% ^^of all EEAs held in edu room
CLD and RCL lectures are held with dedicated EE instructors	86% of CLD, 100% of RCL held with dedicated EE instructor/lecture
≥1 NL-EM meeting /Q	2 NL-EM meetings/Q were held
EEAs scheduled 1-2/4-week staffing block^^^^	N/A^^^
No EEA on school recess, summer, or religious holidays	EEAs held on: school recess 0, summer 2, religious holidays 0
≥1 EEA held on each day Mon-Fri	EEAs held on: Mon 2, Tue 3, Wed 0, Thur 3, Fri 9
Master ECMO Folder is updated ≤24 hrs after each EEA	100% of held EEAs updated in Master ECMO ≤24 hrs after EEA

Table Legend: Certification Lecture Day- CLD, CSC-Circuit Skills Class, ECMO- Extracorporeal membrane oxygenation, Edu-Education, EM- ECMO Manager, EEA- ECMO Education Activity, GD- Google Drive, NL- Nursing Leadership, PDSA- Plan-Do-Study-Act, RCL- Re-Certification Lecture, RK- Recordkeeping, SL- Simulation Lab, Q- Quarter
^ There were 3 additional EEAs (1CDL and 2 RCL) added to the schedule (3+11) after plan implementation, intentionally for Zoom to better jump start attendance
^^ Of the 28% (4/14) held via Zoom, for one EEA there was no edu room available for the timeframe required, and 3* were added
^^^ This intervention was added in 10/2022, recognized delayed yet significant enough to add in after implementation (CQI)

Conclusions: While preliminary, the achieved results justify that restoring the quality of an ECMO education program after the negative impact of the recent pandemic is possible. However, final results are necessary to infer the effectiveness of each intervention.

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Review of threshold-based blood product usage in paediatric ECMO patients in a tertiary paediatric intensive care unit in the United Kingdom

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Objectives: There is a lack of evidence to guide blood product usage during ECMO, resulting in considerable variation in transfusion practice between institutions. Recent studies have demonstrated both Packed Red Blood Cells(PRBC) and platelet transfusions to be independent predictors of ECMO mortality. Analysing existing institutional practice could guide safe transition to more conservative blood product usage. The aim of this study is to review institutional practice around blood product usage in paediatric ECMO patients.

Methods: Retrospective data were reviewed from all ECMO patients admitted between September to December 2022. Blood product usage was evaluated against transfusion thresholds as per institutional guidelines which recommends Hb target of 100g/L and platelet target of $100x10^9$/L and $80x10^9$/L for bleeding and non-bleeding patients respectively.

Results: During the review period 16 patients received VA-ECMO with a total of 20 runs. Ages ranged from 1 day to 6 years, the majority were neonates (9/16). 9 patients received post-cardiotomy ECMO; other indications included PPHN, sepsis, and respiratory failure. 4615 hours of ECMO run were reviewed with individual runs ranging from 46-475 hours. 285/4615 ECMO hours(6%) were spent on bleeding transfusion thresholds, affecting 14/20 runs.

PRBC and platelet transfusion volumes are summarised below. Patients received a mean of 20ml/kg

PRBCs and 23.7ml/kg platelets per ECMO day. 30% of PRBCs and 13% of platelet transfusions were administered outside current recommended thresholds.

Severe bleeding(>5ml/kg/hr or intracranial haemorrhage) occurred in 7/20 ECMO runs(35%), 2 patients had significant intracranial haemorrhage. Significant circuit clots were noticed in 8/20 ECMO runs, 6 of these required circuit changes. 11 patients(69%) were successfully weaned off ECMO and 8 patients(50%) survived to PICU discharge.

Conclusions: This review demonstrates that simply lowering transfusion thresholds in institutional guidelines may be insufficient for restricting transfusions during ECMO. Indication-based transfusion and correlation with viscoelastic tests should be evaluated in future studies.

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Vascular integrity in survivors of pediatric ECMO

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Objectives: The objective of this retrospective case series study is to provide data for the design of a cross-sectional study to compare long-term outcomes in children who underwent vessel reconstruction or ligation.

Methods: The primary objective of this study is to determine the number of the participants who were exposed to vessel ligation or reconstruction and who survived to hospital discharge. The secondary objective is to estimate in each group the co-exposures in order to inform a sound statistical analysis plan: age at ECMO and in 2023, gestational age, sex, mode of ECMO, days on ECMO before separation, surgical operator, diagnoses categories, cardiopulmonary arrest, vascular patency of each vessel after ECMO, the type and size of cannula, and type of neuroimaging. The inclusion criteria for this study is ECMO between 2012 to 2019 and survived to hospital discharge.

Results: We retrieved 149 participants presumed alive who would be aged in 2023: 29 < 5 y, 53 between 5-7 y, 37 between 8-12 y, 18 between 13-18 y, 12 > 18 y. Among these 80 underwent peripheral cannulation

Conclusions: A majority of peripherally cannulated arteries and veins have been reconstructed in our institution. **Future steps:** Vascular imaging will be necessary to retrieve from the records to characterize vascular integrity on hospital discharge. Finally, in order to conduct a comparative multi-center study, it will be necessary to invite sites using ligation in order to understand the long-term impact of the vascular integrity. The design of the study will need to involve child, adolescent and adult assessment tools.

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Anticoagulation monitoring during pediatric ECMO - which is the best method?

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Objectives: During ExtraCorporeal Membrane Oxygenation (ECMO), a procoagulant state is dominant, determining the use of anticoagulation, with unfractionated heparin (UFH) being the anticoagulant of choice in most ECMO centers. The fine balance between bleeding and thrombosis is still a challenge establishing the need for a reliable and widely available method for anticoagulation monitoring. In most pediatric ECMO centers the activated clotting time (ACT) is still the preferred method, but its use has been questioned over the years. This study's primary goal is to assess the relationship between heparin dosage and ACT, Activated Partial Thromboplastin Clotting Time(aPTT) and anti-Xa, a direct measurement of heparin activity.

Methods: A prospective observational study was conducted in a pediatric intensive care unit (PICU)

	Total Transfusion (ml/kg) for all patients in 20 ECMO runs	Mean volume (ml/kg) per ECMO run	Total number of transfusions in all 20 ECMO runs	Number of transfusions outside recommended threshold, n(%)	Mean volume per transfusion (ml/kg)	Average transfusions (ml/kg) per ECMO day per patient
PRBC	3902	195	318	97 (30%)	12	20
Platelets	4561	228	283	37 (13%)	18	23.7

at a university-affiliated hospital. Daily measurements of anti-Xa, ACT, and aPTT were performed simultaneously and recorded against the level of UFH (which was adjusted to maintain the ACT between 180 and 220 seconds) in all pediatric patients under ECMO during a six-month period (July to December 2022). The different methods were compared using the Spearman's rank correlation coefficient.

Results: During the study period, 61 blood samples were obtained from six patients. Comparison of aPTT and ACT with anti-Xa revealed a good correlation between aPTT and anti-Xa (r=0,752; p<0,001) but no correlation was found between ACT and anti-Xa (r=-0,172; p=NS). Heparin dose had a good correlation with aPTT (r = 0,700; p<0,001) and anti-Xa (r= 0,729; p<0,001), however no correlation was found with ACT (r=-0,111; p=NS).

Conclusions: These results suggest that aPTT measurements significantly correlate with anti-Xa and heparin levels. As demonstrated in our and other studies, ACT poorly correlates with anti-Xa activity and heparin dose despite being the most used method for anticoagulation monitoring in this population. We suggest that aPTT, rather than ACT, should be used to titrate UFH dose in pediatric ECMO.

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Primary ECMO transport in Spain. Is a national program necessary? Experience of three centers

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Objectives: ECMO is a complex technique not available in all centres. The literature supports that transport on ECMO is safer than conventional transport for patients with an indication for ECMO. Spain lacks an organized system for transport on ECMO. We describe the experience of the 3 centers that perform primary paediatric ECMO transport in Spain.

Methods: Medical records of paediatric patients transported on ECMO (primary transport) were prospectively collected since 2012 in hospital 1 (n=43), 2019 in hospital 2 (n=12) and hospital 3 (n=6)) with a total of 61 transfers.

Results: Median distance was 205 km (range 8- 642 km), 5 were made by plane, the rest by ground ambulance. Median age: 6 months (IQI: 0.1-96); median weight: 5,5 kg (IQI: 3.2-25). Previously healthy: 59%. The main cause of cannulation was cardiorespiratory failure in 56% of the cases. Cannulation: peripheral veno-arterial (52) / veno-venous (7), central veno-arterial (2). Complications occurred in 58.2% of cases, the majority of low/intermediate risk (36.4%/27.3%) and related to transport (40%), the most frequent were hypothermia and hypotension, the most relevant was an unsuccesful arterial cannulation. 36% of cases required some intervention on ECMO on arrival at the receiving hospital (7 repositioning cannula, 4 atrioseptostomies, 4 conversion to veno-venous ECMO, 1 addition of an atrial cannula). Median time on ECMO was 11,5 days 8(IQI: 5-16]. Survival to discharge from the PICU was 70,4%, three cases with moderate and four cases with mild neurological sequels.

Conclusions: Paediatric ECMO transport is a procedure that, although not without risk, can be performed safely by an experienced and trained team. Communication and collaboration with the referring centre is essential. The survival achieved in our series (>70%) demonstrates theimportance of implementing a coordinated national system to ensure equity of care.

Pediatric - Respiratory failure

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Extracorporeal membrane oxygenation in pediatric burn care

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Objectives: We conducted a systematic review of the role of extracorporeal membrane oxygenation (ECMO) in pediatric patients with burn and smoke inhalation injury.

Methods: The systematic search of the literature was performed according to specific keywords (burn, burn injury, major burn, inhalation injury, smoke inhalation), and to determine the effectiveness of ECMO in this setting. The PICOS approach and PRISMA flow chart were used for this review.

Results: Fourteen articles out of 266 were suitable for analysis including pediatric patients. Four case reports presented single cases, two reports reported two cases each, four case series reported data on five, five, six, and 12 cases, and four investigations of the Extracorporeal

Life Support Organization (ELSO) registry were included. Prospective randomized trials were not found. In 14 articles, 327 patients were found. Of these, 291 patients were part of the four ELSO registry investigations.

Conclusions: Despite the limited number of studies on the subject, ECMO in burn and smoke inhalation injury provides an additional level of support in pediatric patients leading to positive outcomes. Venovenous ECMO demonstrated the best overall survival of all configurations, with similar outcomes to non-burned patients. Prolonged mechanical ventilation prior to ECMO decreases survival and increases mortality by 12% with each additional day off ECMO. Good outcomes have been described for scald burns, dressing changes and pre ECMO cardiac arrest.

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ECMO in congenital diaphragmatic hernia – 13-year experience of the Lisbon ECMO referral centre

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Objectives: To describe the 13-year experience of Lisbon's ECMO referral centre in the treatment of Congenital Diaphragmatic Hernia (CDH).

Methods: A descriptive/inferential retrospective study of the neonates with CDH requiring ECMO support treated in Lisbon's ECMO referral centre since May/2010-December/2022.

Results: There were 23 newborns with CDH treated with VA-ECMO (24 ECMO-runs), representing 23% of all patients treated at our centre. The majority were male (n=15; 65%); median gestational age was 39-weeks (35-41); median birth weight was 3200g (2220-4680). Eighteen (82%) newborns had prenatal diagnosis. Median age at cannulation was 2-days (1-22). Surgical repair was undertaken pre (n=9;39%), during (n=8;35%) or after (n=6;26%) ECMO support. Repair while on ECMO was significantly associated with higher volume of blood products peri-surgery needed, more frequent haemorrhagic complications and longer length-of-stay. The likelihood of survival was not significantly different across groups but of the 6 CDH repaired after ECMO only one died. The median ECMO-run duration was 17-days (2-45); 13 newborns (59%) had mechanical complications, mainly the presence of clots in the circuit; 21 (96%) had physiological complications, mostly haemorrhagic events (n=16;70%) and infection (n=13;59%). Surgical complications happened in 8 (36%) cases. The circuit was changed in 4 (17,4%) cases. When compared to all ECMO patients from our centre (n=99), CDH patients had significantly more haemorrhagic complications and were more likely to have a circuit change. Eighteen newborns survived ECMO (78%), but only 16 were discharged alive (70%). The 4 deaths in ECMO were mainly associated to massive haemorrhagic events and disseminated intravascular coagulation. The median length of PICU and hospital stay were 41 (19-111) and 69,5 days (29-167). Eleven (69%) infants were discharged on long-term oxygen therapy, suspended it mostly (n=7;64%) before age-2. The majority has normal growth (n=10;63%) and neurodevelopment (n=12;75%). The median follow-up time is 3,8 years (0,35-10,4 years).

Conclusions: Neonates with CDH are complex to manage, but survival and absence of long-term complications are considerably high. Postponing surgical repair until the patient is off ECMO might offer an advantage to operating on ECMO.

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Outcomes and ECMO criteria for neonates with severe respiratory failure referred to a regional neonatal transfer service for uplift transport between 2018 and 2020

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Objectives: There are multiple studies looking at predictors and outcomes of neonates referred for ECMO but limited evidence on whether the need for ECMO can be predicted earlier in their clinical course when patients are initially referred to tertiary neonatal intensive care due to respiratory failure. We aimed to describe this cohort of patients and identify if there were predictors requiring transfer to an ECMO center or death.

Methods: Retrospective cohort study of severe respiratory failure referrals to the Neonatal Transfer Service, London, UK January 1st 2018- December 31st2020. Inclusion criteria were: intubated and ventilated with a FiO2 above 60% at referral, more than 34 weeks corrected gestational age and birth weight greater than 2 kg. Clinical variables documented at multiple time points include ventilator parameters, inotrope score, patient physiology and response to nitric oxide.

Results: For the 3 year period 170 children meeting the above criteria were transferred. None died prior to being

transferred. Of these children, 110 patients were transferred on an FiO2 of 100%, 68 were transferred on inhaled nitric oxide and 24 had a vasoactive inotropic score of 50 or higher. There were 16 secondary transfers to ECMO centers and 12 deaths in the cohort. Of the children who died, only one had been transferred to an ECMO center, but demised prior to cannulation. Overall 5 children went on ECMO with 2 receiving VV and 3 receiving VA-ECMO. Of these 5 children, 3 were secondary transfers to the ECMO centers. Granular clinical variables and their association with outcome will be analysed.

Conclusions: 27 out of 170 (16%) patients referred for tertiary neonatal care required transfer to an ECMO center or died before discharge home. Associations between clinical variables and outcome are awaited but will be available for presentation in April.

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Ventricular function, ECMO mode, and outcome in neonates with respiratory failure

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Objectives: Neonates with severe respiratory failure requiring extracorporeal membrane oxygenation (ECMO) often have concomitant cardiac failure, in the form of decreased systolic function of one or both ventricles. Cardiac dysfunction impacts ECMO mode selection, with frequent preclusion of veno-venous ECMO since it offers no direct cardiac support. We describe our experience with cardiac dysfunction and ECMO modality in this population.

Methods: This retrospective chart review included all neonates (< 30 days of life) who underwent ECMO for primary respiratory failure between January 2010 and October 2022 and had an echocardiogram prior to ECMO cannulation. Demographic data, short term outcomes and mode of ECMO was documented. Echocardiogram reports were reviewed for description of moderate-severe systolic dysfunction. The echo prior to cannulation was compared with the final echo before decannulation for changes over time. Data was analyzed with descriptive statistics and univariate analysis.

Results: Of the 176 neonates treated with ECMO for respiratory failure, 157 had an echo prior to ECMO initiation. Sixty infants (39%) had systolic dysfunction: 39 (25%) right ventricular, 5 (3%) left only, and 16 (10%) had biventricular dysfunction. Primary diagnosis was CDH 26 (43%), MAS 8 (13%), and other 26 (43%). Thirty-nine (65%) were treated with VV ECMO with one conversion, and 21 (35%) were initially placed on VA (NS). VA ECMO was indicated due to inability to place VV cannula or lack of availability of VV cannula from 2019-2021. Survival to discharge did not differ between patients with dysfunction and those without (44/60 [73%] vs. 73/97 [75%]; p=0.788). Of those patients with dysfunction, 85% of patients on VV ECMO survived compared with 52% for VA ECMO, p=0.017. Most patients on either mode showed improvement in function over time.

Conclusions: The majority of cardiac dysfunction in patients with primary respiratory failure will improve over time, regardless of ECMO mode. Surprisingly, cardiac dysfunction was not a predictor of mortality.

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The role of ECMO in pediatric COVID-19: An updated systematic review and meta-analysis

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Objectives: The aim of this systematic review and meta-analysis was to evaluate the effectiveness of ECMO in pediatric COVID-19 patients in terms of mortality rate, rate of successful weaning, and frequency of complications.

Methods: A comprehensive search of electronic databases including PubMed, Cochrane Library, and EMBASE was conducted to identify relevant studies published up to December 2022. Inclusion criteria for the studies included observational studies and case series with a minimum of five patients that reported on the use of ECMO in children with COVID-19. Statistical analysis was performed using R version 4.0.3 and the metafor and meta packages.

Results: Seven studies involving a total of 73 pediatric COVID-19 patients who received ECMO were identified. The pooled estimate of mortality in children receiving ECMO was 21.5% (15 out of 73 patients; 95% CI: 9.9% to 40.5%; I2 = 14%). The success rate for weaning off/decannulation of ECMO was estimated to be 85.1% (52 out of 61 patients; 95% CI, 67.8–93.9; I2 = 1%). The overall complication rate was 32.6% (14 out of 43; 95% CI, 20.3–47.7; I2 = 0%).

Conclusions: The results of this systematic review and meta-analysis indicate that ECMO may be an effective treatment option for children with severe COVID-19, particularly those requiring mechanical ventilation. The success rate for weaning off/decannulation of ECMO was estimated to be 85.1%, while the overall complication rate was 32.6%. However, the small sample size

and high risk of bias in the included studies should be taken into consideration when interpreting these results. Further research is necessary to confirm the efficacy of ECMO in pediatric COVID-19 patients and determine the optimal use of this treatment.

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How we perform percutaneous multisite cannulation for VV ECMO in neonates and small children

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Objectives: VA ECMO with surgical access of the neck vessels have been historically considered the configuration of choice even for respiratory ECMO in neonates and small children due to the belief that femoral veins are too small for cannulation in that age. This dogma is questioned by the results of several centers where multisite cannulation is beeing used without significant complications. Since 2018 (the start of our pediatric respiratory ECMO program) at the Heim Pál National Pediatric Institue (Budapest, Hungary) we have used multisite cannulation in all of our patients, included 4 neonates and 13 childen below 15 kg body weight. The vast majority of cannulations were performed percutaneously by pediatric intensivists, only two femoral cannulas had to be placed surgically.

Methods: Since the launch of our program we use the same method with minor modifications: we cannulate the right jugular vein and mostly the right femoral vein with a 4 Fr introducer under ultrasound guidance. The guidewires are placed through this introducer, after confirming the proper position of both the guidewires in the IVC we dilate to the proper size with dilators and place the cannulas.

Results: Once the vessels were cannulated with the 4 Fr introducer all cannulations were uneventful. During this period only two patients needed surgical cannulation of the femoral vein (one in peri-arrest condition and one after a failed introducer insertion).

Conclusions: This method represents a feasible way of cannulation for VV ECMO even in neonates and infants.

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Use of novel oxygenated right ventricular assist device hybrid ECLS for adolescents with refractory hypoxemic respiratory dailure due to Covid-19 pneumonia

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Objectives: To describe institutional experience using Oxygenated Right Ventricular Assist Device (Oxy-RVAD) Hybrid ECLS for adolescents with respiratory failure due to SARS-CoV-2 pneumonia.

Methods: Between September and December 2021, 44 Covid-19+ patients were admitted to our regional Pediatric Intensive Care Unit (PICU), including 4 adolescents who required Extracorporeal life support (ECLS) due to refractory hypoxemia. Two patients were initially cannulated onto Veno-Venous (VV) ECLS and converted to Oxy-RVAD ECLS due to refractory hypoxemia; the others were cannulated directly onto Oxy-RVAD ECLS. Two patients had observed right ventricular (RV) dysfunction or failure on echocardiography. Cannulations were performed in the cardiac catheterization suite by an interventional cardiologist using percutaneous technique under fluoroscopy. Circuit construction was varied and included the use of a dedicated RVAD cannula or standard cannula used for VA/VV ECLS. All patients were connected to Cardiohelp systems with built in centrifugal pumps and oxygenators.

Results: Two patients were initially placed on VV-ECLS and converted to Oxy-RVAD ECLS days into their course due to severe, refractory hypoxemia with one having improvement in hypoxemia after the conversion. Two patients received renal replacement therapy (RRT) without complications, the others did not have indications for renal support. Two patients underwent tracheostomy on ECMO though none were able to separate from mechanical ventilation. Three patients survived to discharge. No incidents of circuit air or clotting were noted. The patient with the longest ECLS run required one circuit change and was the only patient to develop a superinfection: a successfully-treated fungal infection. All patients were mobilized on ECLS to sitting in a chair; one was able to ambulate.

Patient	Age/Sex	Admit BMI	RV dysfunction seen on echocardiography	Initial Cannulation	Oxy RVAD setup	Length of ECMO Run (hrs)	Survived to Discharge	Received CRRT
1	13/Male	60.1	Unable to obtain adequate windows	VV ECMO→ converted to Oxy- RVAD on day 8	-25F MPA Medtronic Biomedicus in L IJ -31 F Avalon Cannula in R IJ	249.8	No	Yes
2	19/Male	34.9	Moderately decreased RV function with mild RA dilation	Oxy-RVAD	31F Protek Duo™ Cannula in R IJ	123.2	Yes	No
3	17/Male	30.6	Unable to obtain adequate windows (severity of disease and body habitus)	VV ECMO→ converted to Oxy-RVAD on day 5	-23F MPA Biomedicus in L IJ -25F Edwards Quickdraw Femoral Venous Cannula	1323.4	Yes	Yes
4	14/Female	56.5	Moderate decreased RV function with mild RA dilation	Oxy RVAD	-23F R IJ metronic MPA Cannula -25 F Edwards Quickdraw Femoral Venous Cannula	91.9	Yes	No

Conclusions: Oxy-RVAD hybrid ECLS can be used to effectively support adolescents with severe respiratory disease from conditions associated with RV dysfunction. Pediatric providers can collaborate with adult critical care colleagues to use novel methods to support these patients. RRT can also be used with this circuit. While more experience and data on this modality is needed, Oxy-RVAD ECLS should be considered in patients with severe RV dysfunction and associated refractory hypoxemia.

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Modern indications for neonatal respiratory ECMO: The others

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Objectives: In 2021, 51% of neonatal respiratory extracorporeal membrane oxygenation (ECMO) runs were classified as *Other* versus only 5% in 1990. These patients do not fit traditional diagnoses such as congenital diaphragmatic hernia or meconium aspiration. Our objective was to evaluate neonatal respiratory runs in the Extracorporeal Life Support Organization (ELSO) Registry with a primary diagnosis of *Other* or persistent pulmonary hypertension/persistent fetal circulation (*PPHN/PFC)*to improve characterization and understanding of outcomes, including length of run (LOR) and survival.

Methods: Data from the ELSO Registry was obtained from January 2017 to July 2021 for cases of neonatal respiratory failure. Patients categorized as *Other* or *PPHN/PFC*were further classified, if possible, into modern categories based on primary and secondary diagnoses codes. Demographics, ECMO complications, and short-term outcomes including ECMO duration and survival were examined across groups.

Results: Of neonatal respiratory ECMO cases, 1332 of 3383 (39.4%) had a primary diagnosis code categorized as *Other* and 251 (7.4%) were classified as *PPHN/PFC*. Of these, 320 were reclassified into a classic ELSO category and 788 (23%) had a diagnosis of either respiratory failure or *PPHN/PFC* without additional specifics. Forty-four (1.3%) had no diagnosis consistent with an indication for ECMO. Modern categories identified included hypoxic ischemic encephalopathy (91pt, 79% survival, median LOR 121h), pulmonary hypoplasia due to structural lung anomaly (51, 53%, 158h), congenital pleural effusion (19, 37%, 261h), or renal anomaly (7, 43%, 161h), airway anomalies (12, 75%, 222h), aspiration of blood or fluid (13, 92%, 136h), alveolar capillary dysplasia (25, 0%, 337h), interstitial lung disease (6, 50%, 450h) and metabolic disease (8, 75%, 85h). As expected, survival, LOR and complication rates for this group were heterogenous and depended heavily on initial diagnosis.

Conclusions: We were able to identify several newer diagnosis groups and common themes among a modern cohort of patients. These clinical distinctions are currently being lost in the catch-all category of *Other*. However, categorization is limited by available information in the registry for many patients.

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The evaluation of the regional ventilation distribution in newborns with a congenital diaphragmatic hernia – a clinical PEEP-trial using electrical impedance tomography

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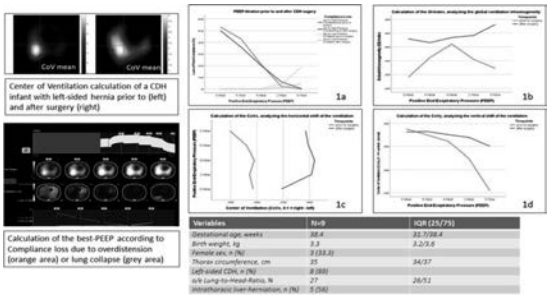
Objectives: As a bedside and radiation-free method, the electrical impedance tomography (EIT) offers the

possibility to evaluate regional ventilation changes and regional lung mechanics in infants with a congenital diaphragmatic hernia (CDH)

Methods: 9 newborns with CDH were prospectively evaluated with the EIT technique prior to and after surgical repair during a PEEP-titration maneuver (deescalating PEEP-levels from 8 mbar to zero PEEP in 2 mbar steps; 5 minutes for each PEEP-level; pressure-controlled ventilation with constant driving pressure). All measurements were performed with the PulmoVista 500 system (Dräger Medical, Lübeck, Germany).

Results:



The calculation of the optimal PEEP with the lowest compliance loss (CL) due to overdistension and the lowest CL due to lung collapse was calculated with a median PEEP of 2 mbar (1/3) preoperative and 1.5 mbar (1/ 2.3) postoperative (Figure 1a). The median value of the Global Inhomogeneity (GI) Index preoperative was at lowest at 8-6 or 2-0 mbar (Figure 1b). Postoperative, the median GI index value was equally distributed at all PEEP-levels. The median value for the horizontal center of ventilation (CoVx, Figure 1c) show a clear shift of the ventilation distribution towards the hypoplastic left lung after surgery (only left-sided CDH infants were included in this analysis). The median value of the vertical center of ventilation (CoVy, see Figure 1d) indicate a stronger ventilation shift towards ventral lung regions prior to surgery at lower PEEP-levels, while postoperative the CoVy was equally distributed at all PEEP-levels.

Conclusions: With the EIT it is possible to visualize regional ventilation distributions and lung mechanics perioperatively in CDH infants. The use of a subphysiological PEEP-level (<4mbar) and continuous EIT measurements can potentially minimize lung overdistension and VILI in these infants.

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Major surgery in children on V-V ECMO: A single center experience

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Objectives: The aim of this presentation is to show our experience in major surgeries performed in children and infants undergoing V-V ECMO treatment due to severe respiratory failure. In 2018 as the first in Hungary, our Institute (Heim Pal National Pediatric Institute, Budapest) started a dedicated V-V ECMO program. Since then 7 thoracotomies and 1 esophagus surgery have occurred in 5 V-V ECMO patients (median age: 28 months, median weight: 12,5 kg). The diagnoses were pleuropneumonia with significant bronchopleural fistula in 3 patients, an oesophago-bronchial fistula due to alkali ingestion and an acquired lobar emphysema.

Methods: The investigated period was 2018-2022, the investigated patient population included every V-V ECMO patient who underwent major abdominal or thoracic surgery (thoracotomy or laparotomy). The main goals of the investigation were: the safety of procedures on V-V ECMO, the feasibility of the V-V configuration in small children or infants, the assessment of the anticoagulation protocol in this patient population.

Results: The mortality was high (60%, 3/5) among patients who required surgery on ECMO, but only one fatal case was related to the procedure. The mean time of the ECMO run without heparin was 17,7 hours, it was stopped 2-4 hours prior to the operation. In 2 cases severe, but manageable bleeding occurred after the procedure, in only one case was significant clotting in the circuit due to the lack of anticoagulation. In one infant an elective V-V ECMO implementation was performed prior to lung surgery without any complication.

Conclusions: In our opinion it is safe operating on small children undergoing V-V ECMO. V-V configuration can be a suitable and effective alternative to V-A even in infants for elective surgeries on the respiratory tract. Bleeding is a severe and life threatening complication in

these patients, the timing of stopping and restarting the anticoagulation is crucial. Viscoelastic tests can be efficient to differentiate the cause of the bleeding. On the other hand it is important to avoid clots in the circuit. Further investigations are needed in this patient population.

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Efficacy and safety of multisite cannulation in venovenous ECMO to support neonates and infants with respiratory disease

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Objectives: A far smaller proportion of infants and neonatal patients with respiratory failure are supported with venovenous (VV) ECMO than the adult population. Due to concerns with VV dual lumen cannulae (VVDL), the percentage of neonates supported with VV ECMO has decreased to a nadir of 8% in 2021 internationally. Literature regarding the efficacy and safety of VV multisite (VVMS) cannulation in neonates is limited to small single centre studies and case reports. Our aim is to evaluate the efficacy and safety of VVMS internationally.

Methods: Ten year ELSO database study approved by steering committee: January 1st 2012- December 31st 2021, all patients aged 0-364 days receiving VV ECMO patients. Demographics, parameters pre-ECMO and on ECMO were collected. The primary efficacy outcome is oxygen saturations at 24 hours of ECMO, analysed as continuous and binary variable (saturation >85%). Comparison between the two groups (VVMS and VVDL) will be adjusted for confounders:

- Pre-ECMO variables related to outcome
- On-ECMO variables that may affect saturations (ventilatatory parameters)

Modelling will use a hierarchical generalized linear model, with appropriate link function. Similar analyses will be undertaken for the secondary outcome of complications.

Results: During the study period, there were only 144 neonates and infants supported with VVMS compared to 2,224 with VVDL. The use of VVDL declined over the time period. VVMS was shown to provide adequate ECMO with median flows of 106mL/kg (IQR 92-114) providing saturations of 95 % (IQR 92-99), median pH 7.33(IQR 7.23-pH 7.42) and CO2 of 6.1kPa (IQR 5.3-6.7kPa) in the neonatal group. For infants outside the neonatal period: flows were a median of 74mL/kg (IQR 46-119), saturations 96% (IQR 92-99%), median pH 7.40 (IQR pH7.35- pH 7.45) and CO2 5.9kPa (IQR-5.3-6.9kPa). Further analysis will be undertaken to look at complications, ventilator settings and cardiovascular parameters on ECMO of this VVMS group with comparison to VVDL patients.

Conclusions: To be presented after further analysis.

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Streptococcal toxic shock syndrome (STSS) and ECMO

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Objectives: Case report of a patient with streptococcal toxic shock, submitted to VV ECMO in an extremely severe systemic condition.

Methods: GM, 15 years old, previously healthy, was admitted to the intensive care unit due to initial sepsis associated with pharyngotonsillitis. At the time, she had fever, hypotension (80x50 mmHg), mental confusion and oliguria. She initiated vasomotor support and broad-spectrum antibiotic therapy. The patient evolved with progressive worsening of the condition, associated with medullary, hepatic and respiratory failure. She was intubated, demanding increasing MV parameters. Gasometry showing persistent hypoxemia, with P/F 78, despite optimized MV, NO, continuous neuromuscular blockade. Chest X-ray showed bilateral diffuse hypotransparency, with minimal air space. Severely compromised peripheral perfusion. Echocardiogram without alterations. It was decided to start support with VV ECMO, jugulofemoral cannulation. Femoral artery puncture was performed for subsequent support transition if necessary. After installation of VV ECMO, the patient was transferred to the ELSO center by air medical transport for continuity of care. Evolved with ventilatory and hemodynamic improvement. ECMO suspended on D6. Hospital discharge 21 days after onset of symptoms. As sequelae of the event, ischemia of the distal phalanges of the fingers and toes.

Results:

Conclusions: Streptococcal toxic shock is a serious condition with a fulminant evolution. The early diagnosis and installation of the ECMO within the correct timing was essential for the recovery of this child.

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Efficacy and safety of flexible bronchoscopy in pediatric ECMO patients

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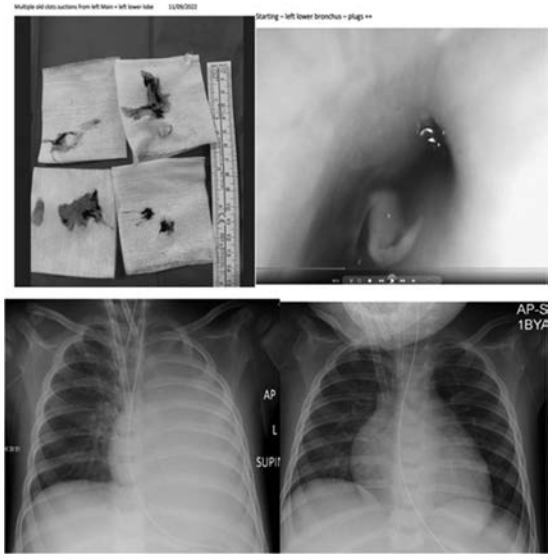
Objectives: Persistent chest x-ray(CXR) changes despite regular chest physiotherapy are a common finding in ECMO patients where flexible bronchoscopy(FB) can be a valuable tool for diagnosis and treatment. However, its use may be limited by concerns regarding the potential risk of bleeding and adverse events/complications. The aim of this study is to evaluate the diagnostic/therapeutic yield of flexible bronchoscopy on ECMO patients and its associated complications.

Methods: A retrospective review of patients who had FB on ECMO during the study period-6 years(2017-2022)

Results:



Among the 192 ECMO runs reviewed, 30 had FB with standard anticoagulation protocol. The median age was 2.5 months(8 neonates,14 infants). Median weight was 3.8kg(range 2.2kg-70kg)The majority of ECMO runs(18/30) were cardiac patients, 3 CDH, 2 PPHN, 4 ARDS, and 2 sepsis. 50% had direct central ECMO cannulation. The commonest indication for FB(24/30) was persistent changes on the CXR. Of these 24 patients,16(66%) had thick secretions or blood clots which were removed with the use of bronchoscopy. 13 of these patients(80%) had significant improvement in CXR within 24 hours,1 patient had a brief deterioration in lung compliance which resolved to baseline. 3/24 patients had no detectable secretion burden and 2/24 patients had airway clots unamenable to flexible bronchoscopic clearance and required rigid bronchoscopic evacuation. The indication for FB in the other 6/30 patients was purely diagnostic. 1 patient developed a pneumothorax during bronchoscopic lavage, necessitating chest drain insertion. 2 patients had mild mucosal bleeding which was managed conservatively and settled within 24 hours. There were no adverse events with ECMO flow, cannula displacement, or major bleeding.

Conclusions: This review suggests that flexible bronchoscopy is a useful and safe procedure in ECMO patients. Persistent CXR changes should be evaluated with flexible bronchoscopy.

Pediatric - Other

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Change in pSOFA Score as a Novel Outcome for Pediatric ECMO Research

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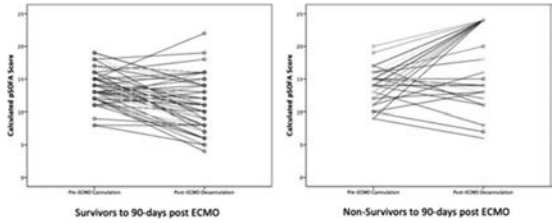
Objectives: We used the pediatric sequential organ function assessment score (pSOFA) to describe change in organ function during ECMO. We hypothesized that recovering existing or acquiring new organ dysfunction during ECMO can be associated with ECMO mortality.

Methods: Patients 0-<19 years who underwent first run ECMO at a single center from January 2015 - December 2016 were included. We used change in pSOFA scores from ECMO onset to decannulation, to compare organ function amongst those who survived to 90-days post-ECMO cannulation ('survivors') with 'non-survivors'. Area under a receiver operating curve (AUROC) was used to assess change in pSOFA score as a discriminator of 90-day post-ECMO mortality.

Results: The population of 124 children were median age 2.4 [IQR 0, 46] months, 56% male (69/124), 52% cardiac indication (65/124), and 31% (38/124) cannulated during cardiopulmonary resuscitation. Median duration of ECMO was 6 [IQR 3, 11] days and 13% (16/124) received subsequent ECMO support. Survival to 90-days post-ECMO cannulation was 59%. Change in pSOFA scores during ECMO support in survivors was median -3 [IQR -5, 0] and for non-survivors median +8 [IQR 0-11], p<0.001 (Figure). Change in pSOFA score

discriminated mortality at 90-days (AUROC: 0.88, 95% CI 0.81-0.94).

Conclusions: Change in organ dysfunction, assessed by pSOFA, from ECMO cannulation through decannulation was an excellent discriminator of early mortality in this complex population. Further validation of the change in pSOFA score using multi-center data may characterize this as a clinically meaningful outcome for clinical trials of infrequent therapies such as ECMO.



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The characterisation of protein binding in paediatric extracorporeal membrane oxygenation (ECMO) circuits using scanning electron microscopy (SEM) and proteomics

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Objectives: This study aims to characterise proteins bound to circuits collected from children on ECMO.

Methods: ECMO circuits were collected after patient decannulation, and 2cm circuit tubing were excised from post venous cannula location. Topography of circuit samples was imaged using SEM. For each sample, images from 5 random areas were captured, and thickness of 25 random fibrin fibres was measured within each image using Fiji ImageJ software. Protein quantification and characterisation from the corresponding circuit samples was performed using bicinchoninic-acid (BCA) protein assay and data-independent acquisition mass spectrometry (DIA-MS), respectively. Reactome over-representation pathway analysis tool was used to determine functional pathways corresponding to the proteins bound to each circuit.

Results: Six ECMO circuit samples were collected from six paediatric patients (4 males) undergoing VA-ECMO (Median age: 0.12 years; Range: 0.01-12.32 years). Representative SEM images showed heterogeneous binding to ECMO circuits between patients (Figure 1). Fibrin fibre thickness also varied between patients (median: 0.28μm; Range: 0μm-0.38μm). Protein concentration (Median: 34.6ug/mL; Range: 21.8ug/mL-57.3ug/mL), and number of proteins (Median: 2011; Range: 1435–2777) bound to the corresponding circuit samples differed between patients. A total of 933 proteins were identified as common proteins across all patients, with haemoglobin, albumin, fibrinogen, and apolipoprotein being the four most abundant proteins. Pathway analysis showed enrichment in 212 pathways, with apoptosis, cellular responses to hypoxia, and inflammation being the three most significant pathways.

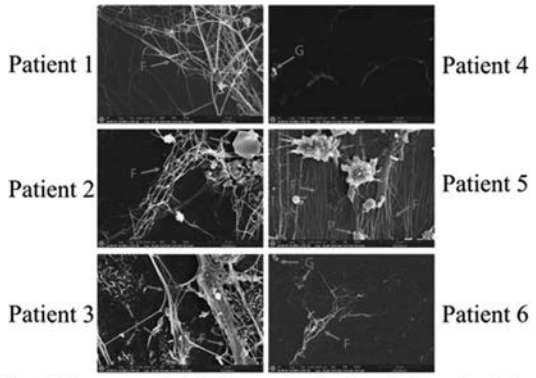

Figure 1. The representative SEM images of each patient circuit samples. Scale rule:10μm. Arrows: E-Erythrocytes; L-Leukocytes; P-Platelets; F-Fibrin network; G-Irregular granules.

Conclusions: This is the first study to characterise ECMO circuit binding in circuits collected from paediatric patients. Fibrin fibre thickness, protein concentration and composition differ between patients, and are factors that affect outcomes for these patients. Subsequent studies should focus on increasing sample size and further characterisation of ECMO circuit binding, particularly in the context of clinical outcomes.

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Discrepancy between bivalirudin level and HPTT to monitor bivalirudin therapy in pediatric extracorporeal life support: Age matters

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Objectives: Bivalirudin could be more effective and safer alternative to heparin in pediatric patients on extracorporeal life support (ECLS). The anticoagulant effect is usually monitored by activated partial thromboplastin time (aPTT), or aPTT with heparinase (HPTT) at our institution with target at 60-80 sec. Our study aimed to compare bivalirudin infusion rate (BIR), with HPTT, and bivalirudin levels measured by plasma diluted thrombin time (dTT) for therapeutic monitoring in pediatric ECLS.

Methods: Total 201 specimens from 21 children 0.03-19 years old receiving bivalirudin therapy during ECLS were collected and tested using HPTT and dTT on STA-R-Max analyzer (Diagnostica Stago, USA). BIR was extracted from hospital database. Bivalirudin level at 0.8-2.5 μg/mL was considered as target range equivalent to HPTT 60-80 sec based on *invitro*spiking experiments. Statistical analysis was performed with Pearson correlation, Mann-Whitney U-test using MS-Excel 2016; data is presented as mean±SD, with significance at $p<0.05$.

Results: BIR in neonates/infants were significantly higher when compared to older children. HPTT was significantly prolonged in the former group, while bivalirudin concentration was similar. BIR correlated better with bivalirudin level than with HPTT; stronger correlation was shown in infants, than in older children. The BIR increase of 0.1 mg/kg/hour was associated with bivalirudin concentration increments of 0.15±0.09 μg/mL in infants and 0.25±0.19 μg/mL in older children, $p<0.00001$. As HPTT values increased from below to above target range, the number (% in the table) of discordant to bivalirudin level were gradually increased in both groups. Notably, BIR in specimens with low bivalirudin level and target HPTT was significantly lower when compared to target bivalirudin level and HPTT subgroup both in infants (0.39±0.19 vs 0.69±0.25 mg/kg/h, $p=0.0002$) and in older children (0.38±0.24 vs 0.56±0.26 mg/kg/h, $p=0.0155$).

Group (number of specimens)	9 neonates & infants (n=98)	12 children & adolescents (n=103)	P value
Age	9±12 months	9.3±5.2 years	n/a
BIR, mg/kg/hour	0.59±0.55	0.4±0.27	**0.0085**
HPTT, sec	70.5±15.3	65.7±13.0	**0.023**
Bivalirudin level, μg/mL	0.75±0.58	0.75±0.65	0.58
BIR vs bivalirudin level	r=0.67	r=0.56	**<0.0001**
BIR vs HPTT	r=0.64	r=0.46	**<0.0001**
HPTT low, bivalirudin level on target	2/27 (7%)	7/37 (19%)	0.19
HPTT on target, bivalirudin level low	30/50 (60%)	29/54 (54%)	0.52
HPTT above target, bivalirudin level low or on target	18/21 (86%)	11/12 (92%)	0.62

Conclusions: Compared to older children, infants have diminished therapeutic response to bivalirudin and required higher BIR to maintain anticoagulant effect. All pediatric groups had high percentage of misleading "on-target" HPTT values on bivalirudin therapy while bivalirudin level in plasma was low, associating with decreased BIR.

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Respiratory physiotherapy for neonatal and paediatric ECMO patients: Current European practice

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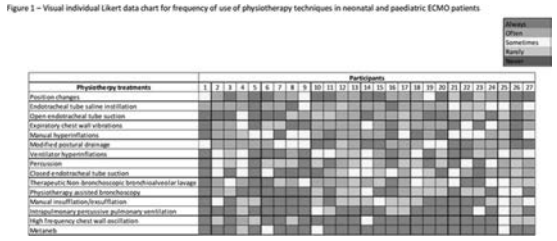
Objectives: The aim of this study was to describe current respiratory physiotherapy practice for neonatal and paediatric ECMO patients.

Methods: A bespoke, electronic survey was sent to the lead clinicians in all European neonatal and paediatric ECMO centres. They were asked to forward the survey onto the relevant physiotherapist or complete it themselves where appropriate. Main outcomes included provision of physiotherapy, indications for treatment and physiotherapy techniques.

Results: Thirty-three ECMO centres responded, accounting for 12 European countries. The survey was completed by 18 physiotherapists, 14 doctors/intensivists and one occupational therapist. 82% (27/33) of centres reported providing respiratory physiotherapy assessment and treatment to neonatal and paediatric ECMO patients. The most common indications for respiratory physiotherapy were thick secretions (81%, 22/27) and chest x-ray pathology (78%, 21/27). The most frequently used treatment was positional changes, used 'always' or 'often' by 78% (21/27) (Figure 1). Other popular techniques included endotracheal (ETT) saline instillation, open ETT suction and chest wall vibrations. Variation in practice was apparent

(Figure 1). Eighteen centres (67%) reported that central cannulation impacted physiotherapy, including limiting manual techniques. 96% (26/27) of ECMO units who provide respiratory physiotherapy also reported using mucoactives as an adjunct to treatment. DNase and 3% hypertonic saline were the most popular agents, both being used by 77% (20/26) of centres. DNase and N-acetylcysteine were given in nebulised and instilled forms, whereas hypertonic saline was predominantly nebulised.



Conclusions: The provision of respiratory physiotherapy is variable across Europe. This may be due to limited evidence to guide practice or differences in roles between centres. Further research into the safety and effectiveness of respiratory physiotherapy in this population is required. The development of consensus-based guidelines may assist in standardising practice and subsequent multi-site trials.

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The osmolality of oral liquid formulations and intolerance on ECMO patients

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Objectives: Patients on ECMO support are at higher risk of developing digestive problems, since splanchnic circulation may be reduced, favoring intestinal ischemia. Though no specific recommendations exist for the osmolality of oral medications used in pediatrics, it is knowns that administration of hyperosmolar oral medications may increase the risk for feeding intolerance and NEC. The American Academy of Pediatrics recommends a maximum osmolality of 450 mOsm/kg for formulas and enteral nutrition for term infants. This study aimed to determine the osmolality of oral medicines commonly administered to pediatrics.

Methods: Twenty oral medications commonly used in pediatrics were tested for osmolality. Oral medicines that were not commercially available in a liquid form were compounded according to recipes supported in the literature. Osmolality was measured by the freezing point depression method using the Osmomat® model 3300 (Gonotec, Germany). The osmolality of all medications was measured in triplicate, and the mean ± standard deviation was reported in mOsm/kg. Dilutions were performed for medicines that measured outside the instrument's calibration range of 100 to 1500 mOsm/kg.

Results: Of all the samples evaluated, only the caffeine citrate solution had an osmolality below 450 mOsm/kg. The 10% chloral hydrate solution (commonly used on PICU patients) showed the highest value, 4108 mOsm/kg. Another commonly used oral suspension is ursodeoxycholic acid which had an osmolality so high that the direct measure was not possible. Even after the second dilution with water, most oral formulations, whether compounded medicines or pharmaceutical specialties, maintained an osmolality value higher than recommended.

Conclusions: Considering the unknown pathophysiology of NEC, it is difficult to attribute its development solely to osmolality of medicines or formulas. Nevertheless, it is important to try to reduce the osmolality of medications. In fact, this study emphasizes the osmolality of the solutions can be lowered by dilution in water. Still, often this dilution exceeds the maximum volume suitable for oral administration in neonates or some pediatric patients. This highlights the need to reformulate not only compounded formulations but also commercial oral liquid medicines.

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Low volume is not always associated with higher mortality: The Lisbon story

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Objectives: To describe the patient clinical characteristics, indications, complications, and survival associated with the use of extracorporeal membrane oxygenation (ECMO) in a ECMO referral center.

Methods: Retrospective observational cohort study of all the patients treated with ECMO in a ECMO referral

center from May 1st, 2010 (beginning of our ECMO program) to December 31st, 2022.

Results: We had a total of 101 ECMO runs in 99 patients, with male predominance (n=53, 52.5%) and a median age of 12 days; 60% neonatal and 40% pediatric. Venoarterial ECMO was used in 75,3% of cases (98,4% of neonates and 40% of pediatric patients). We performed 56 transports on ECMO, 51 of which from the referring hospital. In neonates, the most frequent diagnosis was congenital diaphragmatic hernia (39.3%), followed by meconium aspiration syndrome (26.3%). In pediatrics, the most frequent diagnoses were pneumonia (30.0%) and acute bronchiolitis (12.5%). The median duration of ECMO run was 12 days. There were 170 registered complications (40,6% in neonatal patients and 59,4% in pediatric patients): clinical more frequent than mechanical (62.9% vs. 37%). Among clinical complications, access site bleeding was the most frequent (32.7%), and the most common mechanical complication was the formation of a thrombus in the circuit (39.7%). Overall survival to hospital discharge was 70.3% (neonatal 73.8% and pediatric 65%).

Conclusions: Since the beginning of the ECMO program in this unit, more than a hundred cases have been treated with this technique. Our results show that it is possible for a low volume center, with approximately 10 cases per year, to achieve very good outcomes. However, despite technological developments, many complications related to thrombus formation and bleeding are still observed.

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Whole genome sequencing as a first-tier test for extracorporeal life support

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Objectives: Extracorporeal life support (ECLS) is a life-saving therapy offered in neonatal and pediatric intensive care units (ICUs). Despite its successes, ECLS still carries a mortality of 10-40%. Better delineation of the primary disease, thrombotic/hemorrhagic risks, and specific drug dosing and/or response through whole genome sequencing (WGS) may help improve short and long-term outcomes in pediatric ECLS.

Objective: Assess whether universal WGS for infant ECLS can identify:1. An underlying Mendelian disease by ascertaining single nucleotide variants (SNVs), INDELs, and/or structural variants (SVs) responsible for the phenotype. 2. Alleles associated with increased risk for life threatening complications related to thrombosis, hemorrhage, and hemolysis. 3. Alleles known to be associated with variation in response of commonly used ECLS drugs such as fentanyl, morphine, lorazepam, furosemide, and pantoprazole.

Methods: This prospective, multicenter feasibility pilot study will determine the clinical utility of pre-cannulation WGS for ECLS patients under one year of age. Subject recruitment will occur across 8 partnering Children's Hospitals Neonatal Consortium (CHNC) ECLS centers, representing an ongoing collaboration between the CHNC ECMO and Genomic Focus Groups. Thirty probands and their parents will be enrolled, and samples will be batched. Research WGS will performed at ARUP Labs and data will be analyzed by the Utah Center for Genetic Discovery (UCGD). In addition to WGS, pharmacogenomics analysis will include a targeted panel assessing 120 variants for 36 genes.

Results: Recruitment remains ongoing with 12 (40%) patients enrolled across 8 partnering centers so far. Preliminary sequencing and analysis are underway with goal for enrollment completion by spring of 2023.

Conclusions: We anticipate this prospective, non-interventional pilot study will uncover the benefits of WGS in neonatal and infant ECLS. This research may identify new ways to improve the outcome and survival of the sickest neonates in the NICU while supporting a future multicenter randomized study to prospectively test the clinical utility of universal WGS for ECLS in the NICU.

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Usefulness of left pulmonary artery to main pulmonary artery ratio measured by echocardiography for predicting risk of death or ECMO in congenital diaphragmatic hernia

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Objectives: The purpose of this study was to predict whether underdevelopment of the left pulmonary artery measured by echocardiography immediately after birth in left CDH was related to death or the need for ECMO.

Methods: This study is a retrospective study of neonates with left CDH born between 2018 and 2022 in a single tertiary medical institution. Preterm infants under 34 weeks of gestational age, major congenital anomalies, chromosomal abnormalities, and absence of echocardiography immediately after birth were excluded. Diameter of left pulmonary artery (LPA) was measured at bifurcation, and diameter of main pulmonary artery (MPA) was used as a measure of maximal dimension during systolic phase. The McGoon index, Nakata index, and ejection fraction (EF) were analyzed in comparison with the LPA/MPA ratio as predictive values. Statistical analyses included univariate analysis, logistic regression analysis and receiver operating characteristic curves.

Results: Seventy neonates with left CDH were included, 17 (24.3%) died or need of ECMO and 53 (75.7%) survived without ECMO. Survival group had higher observed/expected lung to head ratio (o/e LHR) by prenatal ultrasound ($P = 0.000$), lower presence of liver herniation ($P = 0.000$), lower incidence of patch repair ($P= 0.000$). Lower o/e LHR, lower EF, lower LPA/MPA ratio, lower Nakata index, and lower McGoon index measured by echocardiography immediately after birth were risk factors for death or need of ECMO. Among the measurements LPA/MPA ratio had the highest AUC (0.967) with a sensitivity of 88.2% and specificity of 84.9% at a cut-off value of 33.6%.

Conclusions: In left CDH patients, the LPA/MPA ratio measured by echocardiography immediately after birth can be used as a predictor of death or need for ECMO.

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Blood transfusion requirements of neonates receiving Bivalirudin on ECMO as an anticoagulant

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Objectives: Bivalirudin has recently emerged as alternative therapy to unfractionated heparin (heparin, hereafter) for pediatric ECMO and may be associated with decreased blood product transfusion. However, there are no data about its usage in neonatal ECMO. This study aimed to analyze transfusion requirements for all newborns on ECMO anticoagulated with bivalirudin.

Methods: Retrospective chart review study of neonatal patients (≤28 days old at ECMO initiation) receiving ECMO from February-2018 to November-2022 in a large tertiary pediatric hospital. Statistical analysis was performed with Mann-Whitney U-test using MS-Excel 2016; data is presented as mean±SD, with significance at $p<0.05$.

Results: There were 26 newborns in the ICU treated with bivalirudin while on VA-ECMO (Table) with 16 of them started initially on heparin for 4.2±4.6 days, then switched to bivalirudin for 7.9±4.1 days; total length was 12.2±5.9 days with survival rate of 44%. The total transfusion volume of red blood cells, platelets, plasma and cryoprecipitate was not significantly lower on bivalirudin when compared to heparin: 127±56 vs 161±72 mL/day, p=0.14 as well as after adjustment per weight at birth 41.1±14.4 vs 56.5±37.6 mL/kg/day, p=0.11. Ten newborns on VA-ECMO were started with bivalirudin directly for 5.4±5.1 days with survival rate of 50%; total daily transfusion was similar to the previous group 138±34 mL/day and 46.4±11.2 mL/kg/day. ECMO survivors (n=12) required fewer total transfusions during bivalirudin anticoagulation (117±38 vs 144±53 mL/day, p=0.13), that was statistically significant after weight adjusting (37.2±11.3 vs 48.2±13.1 mL/kg/day, p=0.033), due to decreased platelet transfusion requirements (11.5±6.3 vs 17.1±7.2 mL/kg/day, p=0.06), possibly due to high incidence of bleeding complications (5 of 14) among non-survivors.

Gestational age	37.6±2.2 weeks
Birth weight	3.0±0.6 kg
Most common diagnosis	Congenital diaphragmatic hernia, persistent pulmonary hypertension, total anomalous pulmonary venous return, hypoplastic left heart syndrome, extracorporeal cardiopulmonary resuscitation, pulmonary atresia
ECMO complications	Intracranial bleeding (15%)
ECMO circuit / components change	Oxygenator, cone or whole circuit in 54% of patients
On heparin	2 circuit changes and 5 component changes in 56% patients
After switch to bivalirudin	5 circuit changes and 4 component changes in 56% patients
On Bivalirudin only	8 circuit changes and 1 component change in 50% patients
Cause to bivalirudin switching	Inability to reach therapeutic level despite a higher dose of heparin, circuit clots despite target heparin range

Conclusions: The use of bivalirudin as a rescue to heparin in neonatal ECMO was associated with a decrease in total daily blood transfusion volume by one-fourth. Non-survivors of ECMO on bivalirudin were transfused with higher load of blood products (mostly platelets) to mitigate bleeding complications. Further studies are needed to evaluate if the use of bivalirudin anticoagulation instead of heparin in neonatal ECMO reduces the overall need for blood transfusions.

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ECMO on wheels: 13 years of experience

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Objectives: To present our 13 years' experience in paediatric extracorporeal membrane oxygenation (ECMO) transportation.

Methods: Retrospective chart review of all patients transported on ECMO between 2010 and 2022 to or from an ECMO referral centre in Lisbon, Portugal.

Results: Our team performed 56 transports of 34 neonatal and 22 paediatric patients (55% of total ECMO runs in our centre); 39 were venoarterial ECMO and 17 venovenous ECMO. There were 51 primary retrievals and 5 were secondary transports, one of which was international. All transports were performed by a dedicated ECMO team which included an ECMO specialist physician and nurse, as well as a surgeon for cannulation of newborns and infants. The median age was 16 days (min 1 day, max 17 years), 30 were male (53,6%), The most frequent diagnoses were meconium aspiration syndrome (11), pneumonia (11), congenital diaphragmatic hernia (7), acute bronchiolitis (4) and congenital heart disease (4). Median distance travelled was 9,1 kilometres (min 3,2; max 1023), 55 by ground ambulance and one by fixed-wing aircraft. Rotaflow® bloodpump was used in 50 transports, Cardiohelp® in 5 and Centrimag® in one. Complications occurred in 10 patients (17,9%): 5 were patient-related (4 cases of access site bleeding and 1 hypertensive pneumothorax) and another 5 were equipment-related (1 oxygen supply failure, 1 battery failure, 2 decreased flow due to pump position and 1 case of equipment/aircraft incompatibility). No patient died during transport. Survival to discharge was 75% and we found no association between complication occurrence during transportation and mortality (p=0,68).

Conclusions: In our series transport of patients on ECMO support was safe and complications were successfully managed. To reduce equipment-related complications our dedicated ECMO team has developed and implemented several safety checklists.

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Impact of liver herniation on systemic anticoagulation in ECMO-treated neonates with congenital diaphragmatic hernia

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Objectives: Liver herniation into the thoracic cavity in neonates with congenital diaphragmatic hernia (CDH) may result in hepatic dysfunction due to anatomic distortion. Our objective was to determine whether liver herniation is associated with liver function in the first 24 hours of ECMO therapy, which may impact the time to therapeutic anticoagulation.

Methods: We conducted a retrospective cohort study using data from a quaternary single-center clinical registry. Inborn neonates with CDH who received treatment with ECMO between 2014 – 2022 were separated into 3 groups: left CDH with liver herniation (L+liver) and without (L-liver), and right CDH, all of whom have liver herniation (R+liver). Exclusion criteria included neonates with evidence of coagulopathy prior to initiation of ECMO therapy. To reduce survival bias, we excluded patients who died before ECMO day 7. Impact of liver herniation on distribution of time to therapeutic anticoagulation and liver laboratory values in the first 24 hours of ECMO therapy was compared using the Kruskal-Wallis test.

Results: Seventy-nine neonates met inclusion criteria (10 L-liver, 51 L+liver, 18 R+liver). Neonates without liver herniation had a significantly longer time (hours) to therapeutic anti-Xa (L-liver: 117 [27,545], L+liver: 30 [8,185], R+liver: 31 [10,103], p-value 0.006). There was no difference in liver injury based on hepatic enzyme levels in the first 24 hours of ECMO therapy, but there was a significant difference in liver function, specifically unconjugated bilirubin (mg/dL) (L-liver: 5.2 [2.9,6.5], L+liver: 3.9 [3.0,4.9], R+liver: 6.1 [4.9,6.4], p-value 0.001) and INR (L-liver: 1.3 [1.2,1.4], L+liver 1.5 [1.4,1.6], R+liver 1.5 [1.4,1.6], p-value 0.014).

Conclusions: Liver herniation in ECMO-treated neonates with CDH is associated with a shorter time to therapeutic anticoagulation. Despite no difference in hepatic enzymes, we hypothesize that some degree of liver dysfunction may affect time to therapeutic anticoagulation. Further studies need to be conducted to investigate the clinical impact of liver position on heparin needs, and bleeding and clotting complications in neonates with CDH.

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Review: Point of care ultrasound for children receiving ECMO

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Objectives: Point of care ultrasound (POCUS) is well-established in adult emergency and critical care medicine, including patients requiring ECMO. The advantages of POCUS in children are increasingly described by emerging literature, particularly for critically ill patients. We aim to describe the role of POCUS for children supported by ECMO.

Methods: A focused literature search was performed reviewing the use of POCUS in paediatric patients supported by ECMO. Major databases were searched including terms: "ECMO"/"ECLS" AND "ultrasound"/ "POCUS" AND "paediatric"/ "neonatal" for publications prior to December 31st2022.

Results: The PRISMA and total number of studies evaluated are awaited but will be complete for presentation. Roles of POCUS include: Respiratory pathology Lung pathologies (eg. subpleural consolidation, pleural effusion, pneumothorax, and pulmonary oedema) can be rapidly identified and can be monitored frequently at the bedside. Assessment of recruitment manoeuvres and response to interventions such as proning can be determined. Haemodynamic assessment Cardiac ultrasound can help rule out effusion during immediate resuscitation event and cannulation. It also allows the assessment of myocardial function and intravascular fluid status in order to guide interventions while on ECMO and assess recovery. It is not however substitute of formal echocardiography for detailed anatomical assessment. Percutaneous cannulation and ECMO cannula position Ultrasound appears superior to chest x-ray for evaluating ECMO cannula position. It allows dynamic visualisation of the cannula position when mobilising the patient or manipulating the cannula. Percutaneous cannulation using POCUS is standard in adult patients and paediatric intensivists are also adopting the technique. Transcranial Doppler (TCD) TCD ultrasound shows that cerebral blood flow is altered during ECMO. TCD may detect early changes in cerebral perfusion.

Conclusions: POCUS provides a detailed, multi-organ assessment of paediatric ECMO patients supporting clinicians in their decision-making. Benefits include instant feedback, minimal handling and intra-hospital transfer, and lack of radiation which are all particularly relevant for ECMO patients. The current evidence base is limited but the multiple benefits proposed in the literature encourage targeted use of POCUS for children on ECMO.

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Tuberculosis, ECMO and clinical pharmacists: A tale from Lisbon

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Objectives: To describe Pharmacy intervention in a particular clinical case.

Methods: Tuberculosis is associated with high mortality in the ICU, especially in patients with ARDS and candidacy for ECMO support remains controversial. These patients need long periods of anti tubercular drugs. It remains uncertain whether dose adjustments are required to dodge sub therapeutic drug levels in patients on ECMO support. A 17-year-old female adolescent was diagnosed with severe ARDS and was started on VV ECMO. As *Mycobacterium tuberculosis*was identified on the bronchoalveolar lavage fluid, she was started on IV empirical doses of rifampicin and isoniazid and enteric ethambutol, and pyrazinamide.

Results: The clinical pharmacist did several interventions, with 75% of approval rate. The most frequent interventions were drug interactions identification (linezolid, caspofungin, levothyroxine, ethynilestradiol, norelgestromin all with rifampicin and sertraline with linezolid) that required dose changing, cardiac monitoring or other. Hyperuricemia, a probable drug adverse reaction was also identified and successfully treated after

pyrazinamide suspension and treatment with allopurinol and rasburicase. Ethambutol and isoniazid levels were within the therapeutic range, but rifampicin, vancomycin and amikacin had subtherapeutic levels, therefore the doses needed to be adjusted. The patient was on ECMO for 124 days and the circuit was changed twice. Unfortunately, the patient passed away a week after decannulation.

Conclusions: This clinical case highlights the importance of drug screening and therapeutic monitoring on ECMO patients. As there are only limited data as to whether ECMO treatment affects PK/ PD parameters of ICU patients significantly and therapeutic drug monitoring is important but often difficult to access, this subject should be eligible for urgent clinical research.

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Congenital diaphragmatic hernia: Does ECMO play a role in surgical complications?

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Objectives: Extra-corporeal membrane oxygenation has shifted the prognosis of congenital diaphragmatic hernia (CHD) patients. However systemic complications are a concern. The objective was to determine whether ECMO influenced the surgical complication rate, and to evaluate the outcome of newborns which had CDH correction on a terciary center with ECMO support.

Methods: A restrospective study, including all CHD patients operated in a single terciaty center in the past 13 years (2009-2022). Prenatal determinants (LHR, gestational week at diagnosis), the location, size and content of the hernia, the medical support, the need for ECMO, the surgical timing, the surgical technical aspects and follow-up, were collected. A demographic characterization of the population was conducted, followed by subgroup analysis differentiating ECMO versus non-ECMO support, approaching surgical outcome and complication rates. Statistical analysis was performed (SPSS27®) and p-value<0,05 was considered significant.

Results: 38 newborns were admitted, with male predominance (68%). The median gestacional age at birth was 37week [30-41]. 78.9% had prenatal diagnosis of the malformation, with a median LHR of 59%. Overall mortality was 23.6%. Considering surgical aspects, 91.2% of CHD were left-sided. Most were classified as B type defect (29.4%). 11 patients had prosthetic repair (collagen mesh). 16 patients had ECMO support, of which, 7 were operated on ECMO. The subgroup of patients on ECMO had a similar demographic-surgical related characteristics, with nonstatistical difference. On surgical aspects, surgery on ECMO was not associated with more post-operative complications, despite all hemorrhagic complication occur on these patients (considering hemothorax requiring reintervention). Most long-term pulmonary complications occurred in patients which did need ECMO. In terms of post-operative care, ECMO patients remained ventilated for a longer period (20d vs. 30d, p=0.03) and had chest tubes for a longer period (9d vs. 17d, p<0.01). The mortality rate observed in this population was of 25%.

Conclusions: One of the major concerns are hemorrhagic complications of the surgical procedure, this fact being an argument for the concern on the timing of surgical correction according to ECMO support.

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Congenital diaphragmatic hernia and ECMO: What about medium and long-term respiratory outcomes?

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Objectives: To evaluate long-term respiratory outcomes of children with congenital diaphragmatic hernia (CDH) who required extracorporeal membrane oxygenation (ECMO) treatment.

Methods: We performed a retrospective chart review of all CDH patients followed up in our Respiratory Clinic who required ECMO treatment during neonatal period between 2010 and 2022. Demographics, clinical data regarding initial hospitalization, respiratory support in the outpatient setting, respiratory infections, wheezing symptoms, asthma diagnosis, pulmonary functions tests (PFT), musculoskeletal deformities and neurodevelopment impairment data were collected.

Results: A total of 14 patient were included, 57,1% were male, all were full term. Most (13/14) were diagnosed prenatally, all had left-sided hernia, 64,3% underwent primary surgical repair and 35,7% required a patch. The surgical repair was performed before ECMO in 28,6%,

during in 35,7% and after in 35,7%. The median time on ECMO was 16 days (min 1, max 45). The median time of follow up was 4,0 years (min 0,17, max 10,0). Two patients (14,3%) required continuous positive airway pressure (CPAP) support after the discharge (mean duration of 16,5 months), 10 (71,4%) required supplemental home oxygen (mean duration of 23,4 months). 50% (7) presented persisted polypnea (mean duration of 18,9 months), 42,9% (6) presented wheezing symptoms, 50% (7) presented history of respiratory infections, 28,6% (4) developed thoracic wall abnormalities. Half of the patients (7) had history of early pulmonary hypertension, but none persisted. Five patients (35,7%) completed PFT (mean age 7,36 years) – 1 was normal, 2 presented obstructive pattern and 2 were poorly collaborated.

Conclusions: In this small case experience, a significant proportion of patients presented with significant medium-and long-term respiratory comorbities but in our case series no mortality was registered. Our findings show that these patients require a demanding respiratory expert team approach on long term follow-up.

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Should activated clotting time give way to anti-factor Xa monitoring for anti-coagulation during paediatric extracoporeal membrane oxygenation? - A literature search for the evidence

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Objectives: A delicate balance to titrate anti-coagulation during ECMO is required to limit bleeding or thrombotic complications which negatively impact on survival outcome.[1]. The complexity of the clotting cascade makes whole blood tests like activated clotting time (ACT) less reliable than anti-factor Xa (anti-Xa) assay on heparin effect. Our aim is to search the evidence to find whether it supports moving from ACT to anti-Xa monitoring during paediatric ECMO.

Methods: A literature search was carried out using OpenAthens to access Clinical Key and Medline. Worldwide articles published in English since 2012 were filtered for paediatric population. 34 abstracts were screened for studies on heparin related complications during ECMO. 5 articles were selected for full review based on relevance of direct comparison of ACT with anti-Xa, then two studies were analysed to assess how time-based testing compared with anti-Xa effect outcomes including clotting, bleeding and mortality.

Results: A retrospective review of 168 patients found no significant difference in haemorrhagic or thrombotic complications (25% and 12.5% in ACT group, 39% and 14% in anti-Xa group).[2]. The apparent small non-significant increase in haemorrhagic events may be afforded to increased number of extracorporeal-cardiopulmonary-resuscitation and centrally cannulated patients in the anti-Xa group. Relative risk of bleeding was 1.56 with number needed to harm (NNH) of 7, and for thrombosis was 1.11 (NNH 100). From 7 observational studies with paediatric data (1048 neonates and children), meta-analysis found significantly more haemorrhagic events and higher mortality at 42% and 46% respectively in ACT group, compared with 34% and 37% in the anti-Xa group.[3]. Relative risk of bleeding and mortality was 0.82 and 0.81 respectively (number of patients needed to treat 13 and 110).

Conclusions: Beyond the time of heparin initiation during ECMO cannulation, analysis suggests moving from ACT to anti-Xa level to direct anti-coagulation strategies during ECMO is appropriate. High quality research on this topic is required.

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Risk factors and outcomes of technical induced-haemolysis in pediatric patients supported by extracorporeal membrane oxygenation (ECMO)

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Objectives: The main objective of our study was to demonstrate that clinical hemolysis is related to greater morbidity and mortality as well as to establish the risk factors for its development

Methods: Retrospective one center study of patients treated with ECMO >48 hours in the Pediatric Intensive Care Unit (PICU) of a tertiary hospital between November 2015 - December 2021. Epidemiological and analytical variables, circuit characteristics and clinical evolution were analyzed. To establish risk factors for development and prediction of clinical hemolysis, bivariate statistical analysis was performed.

Results: We collected 50 episodes of ECMO in 49 patients. Most were males (68%, n=34) with a median age

of 2.5 months (IQR: 0,3-20) and weight 4.7 kg (IQR: 3,5-10,3). Most frequent indication was cardiovascular surgery (48%) followed by respiratory failure (14%). All cases were VA ECMO, with central canulation in half of them (n=25) and median duration was 6 days (IQR: 4-10). 48% of patients developed clinical hemolysis with significant (p<0,05) higher mortality during ECMO (30,4 vs 7,7%), higher overall morbidity (55,9 vs 41,2%) need of CRRT after ECMO removal (70 vs 30%) In addition, thery requiered higher total number of red blood cells and platelets transfusions, more limb ischemic lesions. 84% recieved CRRT included in the circuit, demostrating higher incidence of hemolysis in this group (OR: 7,7; 0,87-68,2) with values close to statistical significance (p=0,055). Other factors analyzed such as CRRT flow, ECMO flow and rpm, mean/maximum flow ratio fo CRRT related to mean ECMO flow, as well as time until coagulation was started were not related to an increase in hemolysis.

Conclusions: Clinical hemolysis is a prevalent problem in ECMO support with repercussion on mortality and relevant morbidity (renal failure, limb ischemia,...). Therefore, we must be aware of its risk factors and minimize them. The addition of CRRT in the ECMO circuit, mandatory in many circumstances, should be carefully assessed

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Neurological complications of neonatal and pediatric ECMO – retrospective cohort study from an ECMO centre in Portugal

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Objectives: To characterize the neurological complications and outcome of neonates and children treated with ECMO.

Methods: We conducted a retrospective cohort study based on the review of the clinical records of all the patients treated with ECMO in a referral ECMO centre in Lisbon, Portugal, since the beginning of the ECMO programme in May 2010 until December 2022.

Results: We identified 16/99 (16%) patients with some kind of neurological complication, 8 were male, 11 were newborns. The median age at the beginning of ECMO support was 7 days (0 days – 14 years) and the mean time of ECMO support was 324 (± 225) hours. Venoarterial ECMO was used in 12 children and venovenous in 4. The time of appearance of complications had a median of 4 days (1 - 25). The main diagnosis were congenital diaphragmatic hernia (n=4), pneumonia (n=3), meconium aspiration syndrome (n=3) and acute bronchiolitis (n=2). The main neurological complications recorded were intracranial haemorrhage (n=9), ischemic stroke (n=9), and seizures (n=3). Three patients underwent neurosurgical intervention. Ten patients died: 1 during ECMO, 7 in the PICU after suspension of ECMO (in 6 of these patients ECMO support was stopped due to severity of complications), 1 in the ward after transfer from the PICU and 1 during follow-up due to severe neurological sequelae. The median time of follow-up is 24 months (4 - 124) with clinical and MRI assessment; 5 patients have neurological sequelae such as structural epilepsy, hemiparesis, or global developmental delay. One patient had full recovery. A chi-square test showed that there was no significant association between the type of ECMO (VA or VV) and neurological complications (p = 0.94).

Conclusions: In our case series, the morbidity and mortality associated to neurological complications were high. VA ECMO was not associated with the increased risk of neurological complications. The long-term cognitive and behavioural functioning are variables that have been described as impaired in other reported series and that should be considered in the discussion of the long-term neurologic impact of this technique.

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Chasing the dream (of Equipoise): Design and execution challenges of the multicenter *TITRE* trial of indication-based red blood cell transfusion in pediatric ECMO

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Objectives: To describe the challenges in the design and execution of a multicenter randomized clinical trial (RCT) of indication-based red blood cell (RBC) transfusion for the pediatric ECMO population, in a

landscape characterized by heterogeneity in standard of care (SOC) and stakeholders from multiple disciplines and specialties.

Methods: RBC transfusion during ECMO is necessary to improve delivery of oxygen to tissues and manage bleeding; however, the hemoglobin (Hb) level for optimal tissue oxygen delivery is unknown, thus exposing ECMO patients to unnecessary RBC transfusions. Further, RBC transfusion during ECMO is independently associated with increased morbidity and mortality. The *TITRE*Trial is the first RCT in the field of pediatric ECMO in decades and aims to address this knowledge gap. It is designed to answer the question of whether indication-based RBC transfusion based on reduced tissue oxygen delivery, compared with RBC transfusion based on institutional-specific Hb thresholds, reduces organ dysfunction by the time of decannulation, and improves 1-year neurodevelopment and functioning in children receiving ECMO.

Results: TITRE was funded in July 2022 with a network of 18 sites and planned trial launch by April 2023. The trial is pragmatic, i.e., each site's SOC for RBC transfusion will be the comparator to the indication-based RBC transfusion arm. The collaboration has identified important challenges with respect to equipoise that will be highlighted. A reluctance to randomize jeopardizes timely accrual if fewer programs are willing to enroll. Conversely, rapid changes in SOC towards an indication-based transfusion strategy and adoption of lower Hb thresholds for RBC transfusion during ECMO jeopardize the separation of treatments necessary to test TITRE's hypothesis. The elusive nature of equipoise is further compounded by multiplicity with respect to ECMO delivery, i.e., cardiac, medical/surgical, and neonatal intensive care programs. Trial site consensus meetings with changes to the original protocol have helped address some of these challenges to allow trial launch.

Conclusions: Execution of a pragmatic multicenter RCT with SOC as the comparator in a multidisciplinary care setting (ECMO) presents unique challenges that we have successfully addressed to launch the TITRE Trial. While TITRE will initially roll out in North America, we would welcome extension of the study into European centers to determine whether indication-based RBC transfusion during ECMO can improve patient outcomes.

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