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Pediatric COVID-19 extracorporeal membrane oxygenation transport during the pandemic

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Abstract

Introduction: ExtraCorporeal Membrane Oxygenation (ECMO) in pediatric patients with COVID-19 has a survival rate similar to adults. Occasionally, patients may need to be cannulated by an ECMO team in a referring hospital and transported to an ECMO center. The ECMO transport of a COVID-19 patient has additional risks than normal pediatric ECMO transport for the possible COVID-19 transmissibility to the ECMO team and the reduction of the ECMO team performance due to the need of wearing full personal protective equipment. Since pediatric data on ECMO transport of COVID-19 patients are lacking, we explored the outcomes of the pediatric COVID-19 ECMO transports collected in the EuroECMO COVID_Neo/Ped Survey.

Methods: We reported five European consecutive ECMO transports of COVID-19 pediatric patients collected in the EuroECMO COVID_Neo/Ped Survey including 52 European neonatal and/or pediatric ECMO centers and endorsed by the EuroELSO from March 2020 till September 2021.

Results: The ECMO transports were performed for two indications, pediatric ARDS and myocarditis associated to the multisystem inflammatory syndrome related to COVID-19. Cannulation strategies differed among patients according to the age of the patients, transport distance varied between 8 and 390 km with a total transport duration between 5 to 15 h. In all five cases, the ECMO transports were successfully performed without major adverse events. One patient reported a harlequin syndrome and another patient a cannula displacement both without major clinical consequences. Hospital survival was 60% with one patient reporting neurological sequelae. No ECMO team member developed COVID-19 symptoms after the transport.

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Conclusion: Five transports of pediatric patients with COVID-19 supported with ECMO were reported in the EuroECMO COVID_Neo/Ped Survey. All transports were performed by an experienced multidisciplinary ECMO team and were feasible and safe for both the patient and the ECMO team. Further experiences are needed to better characterize these transports and draw insightful conclusions.

Keywords
SARS-CoV-2, extracorporeal membrane oxygenation, COVID-19, pediatric intensive care unit, respiratory failure

Introduction

ExtraCorporeal Membrane Oxygenation (ECMO) is an advanced technique to support adults, children and neonates with a high risk of mortality secondary to respiratory and/or circulatory failure refractory to conventional treatment.[1,2] Unfortunately, this technology is often not available in many hospitals, therefore the hub and spoke model is generally used to support critically ill patients admitted in hospitals without ECMO facilities and presenting the indications for ECMO. In these circumstances, patients are usually cannulated at the referring hospital by an external ECMO team and subsequently transported to the nearest ECMO center. The inter-hospital ECMO transport requires an experienced team to overcome technical difficulties and reduce the risks of complications. Several studies have shown the feasibility and safety of ECMO transports when performed by highly specialized personnel.[3–5]

The transport of COVID-19 patients adds special risks, due to the possibility of the spread of virus through the patient's droplets and subsequent exposure of the transport team. Adult ECMO teams have been used to transport COVID-19 patients without complications, but proving to be particularly demanding both from the clinical and logistical standpoint.[6,7]

ECMO has been rarely used in pediatric patients with COVID-19. The main indications for ECMO in this group have been severe pediatric ARDS, myocarditis or multisystem inflammatory syndrome related to COVID-19 (MIS-C).[8,9]

So far, data on inter-hospital transport of pediatric COVID-19 patients supported with ECMO are lacking. Therefore, we aimed to report the outcomes of the first European ECMO transports of pediatric COVID-19 cases reported in the EuroECMO COVID_Neo/Ped Survey endorsed by the EuroELSO from March 2020 till September 2021 (12,13).

Methodology and general data of the five cases

The EuroECMO COVID_Neo/Ped Survey is the largest ECMO dataset of pediatric COVID-19 cases reported in Europe during the pandemic (12,13). After a careful analysis of this survey, we reported a total of five COVID-19 cases transported on ECMO from the beginning of the pandemic till September 2021 (Tables 1 and 2).

COVID-19 transported children had a wide range of age (42–144 months) and weight (13.5–52 kgs). Four patients had comorbidities. Three patients underwent ECMO for pediatric ARDS, while two for hemodynamic instability secondary to MIS-C and myocarditis. V-A ECMO was used to manage four patients despite the indication of ECMO support, while V-V ECMO was used only in one case of respiratory failure. Cannulation using the femoral vessels was used in three patients, while neck cannulation was used in the other patients. The duration of the ECMO run varied from a minimum of 69 h to a maximum of 1,104 h; one patient needed nitric oxide during ECMO for severe pulmonary hypertension despite ECMO. Most of the patients received adjunctive therapies during ECMO such as steroids, immunoglobulin, anakinra, tocilizumab and hyperimmune plasma.

Regarding the transport, the distance between ECMO centers and the referral centers ranged between 8 to 390 km, and time from the call to the ECMO deployment ranged between 2 to 8 h with a total duration of retrieval between 5 to 15 h. One transport was performed by air. Team composition was similar in all cases, with 6–7 members mixing pediatric intensivists, pediatric cardiac surgeons and at least a PICU nurse always present with a perfusionist available in four cases. The entire ECMO procedure was undertaken with PPE for all the teams. Cannulations and transports were reported as extremely challenging from all the ECMO teams due to the use of full PPE for the excessive sweating and the reduced visibility secondary to goggles fogging during the procedures. Nevertheless, the cost of a transport with PPE is higher than a normal ECMO transport for the need of PPE kits changing every few hours.

In all five cases, the transport on ECMO was successfully performed without major adverse events. We observed only the occurrence of a harlequin syndrome in one case and of a cannula displacement in another.

Table 1. ECMO and patients details of children transported.

		Demographics/Diagnosis				ECMO information				PRE-ECMO status/support				COVID-19 information		Outcome
Case	City (country)	Age (months) sex	Reason for ECMO support	Comorbidities	Weight (kg)	ECMO type[a]	Cannulation strategy	ECMO length (hours)	Oxygenator (O), pump (p), cannulas (C) and heater (H) brands/names	Ventilation mode and duration (days)	Worst OI/iNO	Highest VIS	Other treatments	Onset of symptoms to ECMO (days)	Therapy	Hospital survival/ sequelae
1	Madrid (Spain)	103 Male	pARDS and recurrent air-leak	STAT3 Immunodeficiency, Allogenic stem cell transplant	40	V-A	LFV: 19 Fr LFA: 17 Fr changed to V-V with RIJV: 15 Fr	720	O: Quadrox iR P: Cardiohelp C: Bio-medicus Medtronic H: HICO-variotherm 550	CV 25	OI: 49 iNO: No	20	Proning Chest tube for air leak (pneumothorax, pneumomediastinum and subcutaneous emphysema)	31 (+37 days after stem cell transplant)	Steroids; Azithromycin; Hydroxychloroquine; Lopinavir/Ritonavir; Immunoglobulin; Tocilizumab; Anakinra; Mesenquimal cells; Hyperimmune plasma; T-CD8 cells	No (cardiac arrest for massive pulmonary thromboe-mbolism)
2	Barcelona (Spain)	144 Female	Myocarditis MIS-C with cardiogenic shock	Graves-Basedow disease	47	V-A	RIJV: 25 Fr RCCA: 19 Fr	159	O: Maquet HLS MODULE ADVANCED 7.0 P: Cardiohelp C: Medtronic-Biomedicus H: Maquet HU-35	CV	iNO: No	270	Pre-ECMO cardiac arrest (CPR 2 min)	7	Steroids Immunoglobulin Anakinra	Yes (no neurologic sequelae)
3	Madrid (Spain)	132 Male	Myocarditis MIS-C MOF 2 episodes cardiac arrest	/	52	V-A	LFV: 19 Fr LFA: 19 Fr	96	O: Quadrox iR P: Cardiohelp C: Avalon elite, Getinge H: HICO-variotherm 550	CV 1	OI: 20 iNO: No	122	No	5	Steroids Immunoglobulin	Yes (hypoxic ischemic encephalopathy)
4	Madrid (Spain)	104 Male	pARDS	Severe combined immunodeficiency, Allogenic stem cell transplant	26	V-V	RIJV: 19 Fr double lumen	1104	O: EurosetsEU5045 P: Levitronix Centromag C: : Bio-medicus Medtronic H: HICO-variotherm 550	CV 1	OI: 26 iNO: No	13	/	36 (+143 days after stem cell transplant)	Steroids Remdesivir Tocilizumab Ruxoltinib Hyperimmune plasma T cells (mother) Beta-Interferon T-cells anti SARS CoV2	No (ECMO withdrawal for hyperinflammation state, pulmonary hypertension and MOF)
5	Padova (Italy)	42 Male	pARDS	VACTERL syndrome	13.5	V-V-A	RIJV: 14 Fr LFV: 12 Fr RCCA: 14 Fr	69	O: Eurosets 4000 EU5045 P: Livanova SCPC (lifebox during transport) C: Medtronic-Biomedicus H: Maquet HU35	CV 5	OI: 23 iNO:20 ppm	0	Proning	5	Hyperimmune plasma, Steroids Anakinra	Yes (no neurologic sequelae)

[a]V = venous, A = arterial.

ECMO: extracorporeal membrane oxygenation; OI: oxygenation index; iNO: inhaled nitric oxide; VIS: vasoactive-inotropic score; RIJV: right internal jugular vein; LFV: left femoral vein, RCCA: right common carotid artery; LFA: left femoral artery; PICU: pediatric intensive care unit; MIS-C: multisystem inflammatory syndrome in children associated with COVID; pARDS: pediatric acute respiratory distress; CV: conventional controlled mechanical ventilation; MOF: multiorgan failure.

Table 2. Transport details of children transported.

Case	Country (city)	Date	Location of referring hospital (country)	Transport distance (Km)	Mode of transport	Time from call to ECMO (hours)	Transportation time hospital to hospital (hours)	Total duration of retrieval (hours)	Ventilation during transport	Complications during retrieval	Team composition and team members COVID status[a]	Type of anticoagulation
1	Madrid (Spain)	April 2020	Madrid (Spain)	8	Road	2	0.3	7	CV: PIP 20, PEEP 10, VR 15, FiO_2 0.6	Harlequin syndrome. In PICU switch to V-V ECMO	2 Pediatric intensivist (*N*, *N*) 2 Pediatric cardiac surgeons (*N*, *N*) 1 PICU nurse (*N*) 1 Perfusionist (R)	Unfractionated heparin Not during transport
2	Barcelona (Spain)	September 2020	Mallorca (Spain)	205	Air (fixed-wing)	6	4	15	CV: PIP 25, PEEP 10, VR 20, FiO_2 0.6	ECMO heater failure	2 Pediatric intensivist (*N*, *N*) 1 Pediatric cardiac Surgeon (*N*) 2 PICU nurses (*N*, *N*) Military personnel	Unfractionated heparin Not during transport
3	Madrid (Spain)	November 2020	Toledo (Spain)	70	Road	3	1	8	CV: PIP 20, PEEP 10, RV 15, FiO_2 0.6	None. In PICU atrio-septostomy for left ventricular decompression	2 Pediatric intensivist (*N*, *N*) 2 Pediatric cardiac Surgeons (*N*, *N*) 2 PICU nurses (*N*, *N*) 1 Perfusionists (*N*)	Unfractionated heparin Not during transport

(continued)

Table 2. (continued)

Case	Country (city)	Date	Location of referring hospital (country)	Transport distance (Km)	Mode of transport	Time from call to ECMO (hours)	Transportation time hospital to hospital (hours)	Total duration of retrieval (hours)	Ventilation during transport	Complications during retrieval	Team composition and team members COVID status[a]	Type of anticoagulation
4	Madrid (Spain)	November 2020	Madrid (Spain)	8	Road	6	0.3	5	CV: PIP 20, PEEP 10, VR 18, FiO_2 0.6	Cannula displacement, reposition under echography in PICU	2 Pediatric intensivist (*N*, *N*) 2 Pediatric cardiac surgeons (*N*, *N*) 2 PICU nurses (R, *N*) 1 Perfusionist (*N*)	Unfractionated heparin Not during transport
5	Padova (Italy)	September 2021	Trieste (Italy)	390	Road	8	2.5	10	CV: PIP 24, PEEP 10, VR 20, FiO_2 0.7	Difficult cannulation, low ECMO flows	1 Pediatric intensivist (V) 2 Pediatric cardiac surgeons (V and V) 1 PICU nurse (V) 2 Perfusionists (V and V)	Unfractionated heparin not during transport

CV: conventional ventilation; PIP: peak inspiratory pressure; PEEP: positive end-expiratory pressure; VR: ventilator rate, FiO_2: fraction inspired of oxygen, V-V: veno-venous, PICU: pediatric intensive care unit, ECMO: extracorporeal membrane oxygenation.

[a]COVID-19 status of the team members: V = vaccinated, R = recovered from COVID-19 infection [date of positivity] *N* = No COVID-19 infection no COVID-19 vaccination (not available at that time).

Harlequin syndrome was first treated with esmolol infusion, and the next day the ECMO strategy was changed from a femoro-femoral V-A ECMO to a peripheral femoro-jugular V-V ECMO. Regarding the patient with cannula displacement towards the tricuspid annulus, the cannula was then correctly repositioned by echocardiography guidance. Hospital survival was 60% and one patient reported neurological sequelae with hypoxic-ischemic lesions at the brain magnetic resonance imaging and several seizures episodes which were controlled by antiepileptic drugs.

None of the health-care personnel developed any sign of COVID-19 in the following weeks even though vaccination was not available at the time of the transport for four out of five patients.

Discussion

This study reported five European inter-hospital ECMO transports of pediatric patients with COVID-19 and MIS-C collected by the EuroECMO COVID_Neo/Ped Survey from March 2020 till September 2021. In all cases, the ECMO transport was successful without transport-related major adverse events. Furthermore, no ECMO team member contracted COVID-19 following the transport.

Currently, several data support the use of ECMO to manage pediatric COVID-19 patients and patients with MIS-C refractory to maximal medical treatments.[8,10–12] ECMO survival in these children was 60%, close to the one reported in adults.[13] However, since ECMO runs are relatively infrequent for pediatric COVID-19, outcomes may be affected by center experience and the relatively small sample size included in our report. Recent guidelines suggest to manage these patients only in experienced centers or transport them to the closest ECMO facility.[14,15] The ECMO team members may vary across countries and centers, usually based on local expertise. These teams may include one or more cardiac or cardio-thoracic surgeons, intensivists, nurses and ECMO specialists or perfusionists. Several data showed that ECMO transport is generally safe in both adults and children, however data on ECMO transport of COVID-19 patients are lacking and do not include pediatric patients.

The transport of COVID-19 patients in ECMO is challenging and may increase the risk of patients' complications and team members' COVID-19 infection. The ECMO team needs to strictly adhere to airborne contact precautions and wear full PPE to protect themselves from SARS-CoV-2 infection during the whole ECMO procedure. Nevertheless, all these precautions may undermine the team performance (e g. fog on the visor, uncomfortable masks, non-breathable fabrics, increased fatigue due to the reduced possibility of taking pauses/rest, etc.) and increase the risk of patient adverse events. In addition, several factors may increase the risk of ECMO team exposure to SARS-CoV-2 during inter-hospital transport: a) the contact with the COVID-19 patient during the ECMO deployment, b) the time spent in the ambulance with an infectious patient and c) the absence of an effective air exchange or negative pressure airflow in the transport vehicle.

Our data shows that pediatric ECMO transport with ambulance was feasible and safe and that these positive results were not limited to transport related to metropolitan areas, but also to inter-regional transports. Hospital survival was 60% in our cohort and was consistent with the hospital survival of other pediatric ECMO COVID-19 patients not requiring transport.[8,10,11]

Our case series has several limitations and must be interpreted with caution. First, despite the inclusion of 52 neonatal/pediatric European ECMO centers, there is a possibility that we may have missed other pediatric cases of COVID-19 ECMO transports. Second, the retrospective nature of the study and the small sample size do not allow to reach any robust and generalizable conclusions. Third, all the centers included in the study have an extensive experience with ECMO and ECMO transports, thus, caution should be used when translating these results into the clinical practice of newer ECMO centers. However, complex patients on ECMO should always be managed in tertiary level hospitals in order to reduce their risk of morbidity and increase the likelihood of survival. Third, this study does not include a control group of non-COVID-related transports, thus definitive conclusions regarding safety of ECMO transport for both the patient and the team members cannot be achieved.

Conclusions

This study reports five pediatric COVID-19 patients in Europe in whom ECMO support was instituted at a referring hospital with subsequent transport to an ECMO center. All ECMO transports were challenging secondary to the use of full PPE equipment but no ECMO team member reported COVID-19 following the transports. Despite the limited number of patients treated, this study suggests that the ECMO transport of COVID-19 patients may be feasible and safe when performed by an experienced multidisciplinary team and following established protocols which include a strict adherence to airborne contact precautions.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Marco Daverio and Angela Amigoni. The first draft of the manuscript was written by Marco Daverio, Angela Amigoni, Belda Hofheinz Sylvia, Joan Balcells and Matteo Di Nardo. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Informed consent

All listed authors have approved the manuscript before submission, including the names and order of authors.

Statement

Reprints will not be ordered.

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